RHEUMATOLOGY

Rheumatology 2017;56:818–828
doi:10.1093/rheumatology/kew492
Advance Access publication 14 February 2017

Original article

Cross-cultural validation of Lupus Impact Tracker in five European clinical practice settings

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Abstract

Objectives. The aim was to evaluate the cross-cultural validity of the Lupus Impact Tracker (LIT) in five European countries and to assess its acceptability and feasibility from the patient and physician perspectives.

Methods. A prospective, observational, cross-sectional and multicentre validation study was conducted in clinical settings. Before the visit, patients completed LIT, Short Form 36 (SF-36) and care satisfaction questionnaires. During the visit, physicians assessed disease activity [Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA)-SLEDAI], organ damage [SLICC/ACR damage index (SDI)] and flare occurrence. Cross-cultural validity was assessed using the Differential Item Functioning method.

Results. Five hundred and sixty-nine SLE patients were included by 25 specialists; 91.7% were outpatients and 89.9% female, with mean age 43.5 (13.0) years. Disease profile was as follows: 18.3% experienced flares; mean SELENA-SLEDAI score 3.4 (4.5); mean SDI score 0.8 (1.4); and SF-36 mean physical and mental component summary scores: physical component summary 42.8 (10.8) and mental component summary 43.0 (12.3). Mean LIT score was 34.2 (22.3) (median: 32.5), indicating that lupus moderately impacted patients' daily life. A cultural Differential Item Functioning of negligible magnitude was detected across countries (pseudo-R^2 difference of 0.01–0.04). Differences were observed between LIT scores and Physician Global Assessment, SELENA-SLEDAI, SDI scores = 0 ($P < 0.035$) and absence of flares ($P = 0.004$). The LIT showed a strong association with SF-36 physical and social role functioning, vitality, bodily pain and mental health ($P < 0.001$). The LIT was well accepted by patients and physicians. It was reliable, with Cronbach α coefficients ranging from 0.89 to 0.92 among countries.

Conclusion. The LIT is validated in the five participating European countries. The results show its reliability and cultural invariability across countries. They suggest that LIT can be used in routine clinical practice to evaluate and follow patient-reported outcomes in order to improve patient–physician interaction.

Key words: systemic lupus erythematosus, Lupus Impact Tracker, patient-reported outcome tool, cross-cultural validation, differential item functioning/Rasch method

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Submitted 16 September 2016; revised version accepted 13 December 2016

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Rheumatology key messages

- The Lupus Impact Tracker is a new patient-reported outcomes questionnaire to monitor the impact of SLE.
- The Lupus Impact Tracker was accepted by patients and physicians during routine visits.
- The Lupus Impact Tracker showed reliability and cultural invariability across five European countries.

Introduction

SLE is a chronic, multisystem, autoimmune disease characterized by periods of activity (flares) alternating with periods of remission. It presents with various symptoms and clinical manifestations that may greatly impact patients' life [1, 2].

During routine visits, physicians may evaluate patient-reported outcomes (e.g. quality of life), co-morbidities, disease activity, organ damage, status of kidneys and eyes and drug toxicity, in accordance with the recommendations [3, 4]. A wide variety of tools are available to help physicians in SLE management. Certain instruments focus on symptoms and assessments to monitor disease activity and organ damage [5, 6]. Others have been developed and validated to address patient concerns regarding the impact of the disease on quality of life and outcomes [7]. As an example, the Lupus Patient-Reported Outcome tool (LupusPRO), a valuable 44-item quality-of-life tool, was recently developed and validated [7].

Qualitative work with lupus patients showed that there is often a gap in communication between SLE patients and their physicians. Patients tend to focus more on the disease burden and the impact on their lives, whereas physicians tend to focus primarily on patients' SLE-specific clinical manifestations and laboratory assessments [8].

The Lupus Impact Tracker (LIT), a patient-reported health outcomes questionnaire, has been developed to address this gap. This questionnaire has been designed to evaluate and monitor the impact of SLE over time and to assess patients' concerns regarding their daily lives. The LIT is a short, patient-friendly 10-question disease-impact tool derived from the LupusPRO. It was recently developed in the USA by Jolly *et al.* [9] and validated with patients in clinical settings. The tool was found to be reliable, valid and to have good acceptability by patients and physicians because of its brevity. It can be used routinely and longitudinally in clinical practice.

In order to be used in European clinical settings, the LIT also required testing in a real-world context by SLE patients and their physicians, in the interest of demonstrating its validity for use in routine practice in European countries.

The primary objectives of this prospective health outcomes study were to evaluate the cross-cultural validity of the LIT in five European clinical practice settings and to assess its acceptability and feasibility from the patient and physician perspectives. The secondary objective was to evaluate the effect of the LIT on communication between patients and physicians.

Methods

Study design

The LIT health outcome study (GSK study etrack number BEL117212) was a prospective, multicentre, cross-sectional, observational and validation study.

It was conducted in five countries (France, Germany, Italy, Spain and Sweden) among reference centres specializing in SLE management, over 10.5 months from the end of September 2013 to mid-August 2014.

A sample of 500 analysable patients was expected (100 patients per country on average). Each principal investigator included between 10 and 30 patients. Overall, 569 eligible patients were enrolled by 25 rheumatologists (6 in both France and Germany, 5 in both Italy and Spain and 3 in Sweden).

The study complied with local legal and regulatory requirements. It was approved by the Ethics Committees corresponding to the participating hospitals (as required in Germany, Italy and Sweden), and all patients signed the written informed consent before inclusion.

Inclusion and exclusion criteria

The physicians screened and included SLE patients meeting the following eligibility criteria: patients diagnosed with SLE according to the 1997 ACR classification criteria (meeting at least 4 out of the 11 ACR criteria) [10], aged at least 18 years, willing to participate in the study, willing and able to provide informed consent or agreement (according to local requirements) and able to read and understand the local language and complete the questionnaires.

Patients presenting with other autoimmune diseases (e.g. other CTDs, APS, RA, SS), with symptoms that may overlap with or resemble lupus symptoms, and women who were pregnant at the visit were not included in the study.

LIT questionnaire

The LIT comprises 10 questions. Patients could select responses from 0 (none of the time) to 4 (all of the time). Each individual total score (minimum: 0; maximum: 40) was converted to the lupus impact total score (minimum: 0; maximum: 100), where 100 denotes that lupus impacts 100% of the patient's daily life. Thus, LIT scores have a negative correlation with the patient's perceived quality of life; the higher the score, the greater the impact of lupus on daily life and the worse the patient feels.

The LIT was translated from English into the local languages using a validated methodology [11, 12] and standard PRO translation guidelines [13]. The forward translations were tested, reconciled to identify possible discrepancies, back translated to ensure that the items

were understood correctly, harmonized between countries and validated. The linguistic and cultural validity of the translations was also assessed to prevent misunderstandings and divergent interpretations across countries (translated LITs: supplementary data).

Collected variables

Data were collected through several questionnaires. Before the visit, patients completed the LIT questionnaire, a questionnaire concerning their satisfaction with their lupus specialist and care, and the Medical Outcome Study Short Form 36 (SF-36) Version 2.0 [14] in their local language.

During the visit, physicians collected information on patient demographics (age, gender and educational attainment), disease duration, co-morbidities (including FM) and current SLE treatments. They assessed disease activity using the Physician Global Assessment (PGA) tool, the Safety of Estrogens in Lupus Erythematosus National Assessment SLEDAI [SELENA-SLEDAI (SS)] [15, 16] and they evaluated flare occurrence according to the results of laboratory tests, examinations and their clinical assessment. Organ damage was assessed using the SLICC/ACR damage index (SDI) [17].

After the visit, patients and physicians completed the corresponding LIT feedback questionnaire, which was designed for this study to assess their feelings and interest with regard to the usefulness of LIT during the visit.

Statistical analysis

Analyses were performed using the SAS system version 9.1 (SAS Institute Inc., Cary, NC, USA) in Windows operating system support. Data were analysed on the overall data set and at the individual country level (per country).

The two-sample *t* test, analysis of variance or Mann–Whitney tests were used for quantitative variables and the χ^2 or Fisher's exact tests for qualitative variables. The Kruskal–Wallis test was used for multiple comparisons (>2). Statistical significance was set at 0.05.

Responses provided by patients on the LIT were analysed and converted into lupus impact scores. Psychometric properties of the LIT were assessed as recommended by international consensus [18, 19].

The validity of the LIT was evaluated by assessing the following four aspects: construct/divergent validity; convergent validity; face validity; and cross-cultural validity. Construct validity of the LIT was examined using the framework of divergent validity as assessed by the comparison of known groups [20], an approach that involves comparing mean LIT scores of patient subgroups known to differ on conceptually related criterion measures. It was hypothesized that LIT scores were likely to be higher in patients with higher disease activity and organ damage [21] than those in patients with lower disease activity and damage levels. The analysis, performed overall and per country (country by country), evaluated the relationship between LIT scores and disease profile characteristics [21]. Instrument/index scores [18, 19] were split into categories [PGA (0, 1, 2, 3), SS (0, 1–5, 6–10, >10) and SDI (0, 1, $\geqslant 2$)], as were flare occurrence (yes/no), gender (male/female) and age. Analysis of variance was used to assess differences in LIT scores among subgroups.

Convergent validity

As part of the construct validity, we evaluated the relationship between LIT and SF-36 scores. The concordance between LIT and SF-36 scores was evaluated using the Pearson correlation test (testing the null hypothesis: $\rho = 0$).

Face validity

The responses provided by patients and physicians on the LIT feedback questionnaires (patient and physician versions) were examined to evaluate the acceptability, usefulness and feasibility of using the LIT in routine clinical practice. The responses could be rated on five levels (from strongly agree to strongly disagree). The cross-cultural validity of the LIT, that is, whether there was variability or differences in item performance between countries, was analysed using the Differential Item Functioning (DIF) method [22] derived from the Rasch measurement model, an established standard for evaluating outcomes scales in rheumatology [23, 24]. The DIF detection was conducted using the Lordif package in R [25] version 0.2–2, which uses a set of hierarchical proportional odds logistic regression models for each item with the null model (intercept-only). The following three nested DIF models were used: trait-only (Uniform), trait + country (non-uniform), and trait + country + trait*country (Total DIF). They were compared using a χ^2 test, in order to identify significant uniform and non-uniform DIF. Trait estimates were derived from a graded response model. Total DIF magnitudes (uniform plus non-uniform) were characterized using McFadden's pseudo-R^2, that is, the DIF magnitude may be understood as the proportion of variance in sample trait scores attributable to uniform and non-uniform DIF. This magnitude was characterized as negligible, moderate or large based on cut-offs of $R^2 < 3.5$, 7 and 10%, respectively.

The reliability of the LIT, that is, internal consistency of the questionnaire, was assessed per country by calculating Cronbach's α coefficient [26]. A value >0.7 is usually considered satisfactory ($0.7 \leqslant \alpha < 0.8$: acceptable; $0.8 \leqslant \alpha < 0.9$: good; and $\alpha \geqslant 0.9$: excellent).

Results

Demographics, quality of life and satisfaction with care

The study population mostly comprised outpatients (91.7%) and females (89.9%) (Table 1). The mean (S.D.) age of the patients was 43.5 (13.0) years, and the majority (60.2%) were 18–45 years old. Patients were highly educated; 48.1% completed the secondary education level and 29.6% completed university studies.

Quality of life and well-being were moderate to good. The majority of patients (45%) declared that their health was good, 35% that it was fair, 10% excellent/very good and 10% poor. The mean (S.D.) physical component summary score was 42.8 (10.8). The mean (S.D.) mental component summary score was 43.0 (12.3). Both scores were

TABLE 1 Demographics, satisfaction and quality of life, overall and per country

Variable	France (n = 122)	Germany (n = 125)	Italy (n = 128)	Spain (n = 125)	Sweden (n = 69)	All (n = 569)	P-value[a]
Outpatients, %	86.9	98.4	87.4	90.4	98.6	91.7	<0.001
Women, %	90.8	85.6	92.1	91.2	89.9	89.9	0.471
Age, years							
Mean (S.D.)	40.2 (11.8)	43.4 (13.0)	41.5 (11.2)	46.0 (12.1)	48.7 (17.0)	43.5 (13.0)	<0.001
Median	39.0	43.0	41.0	45.0	51.0	42.0	
Minimum–maximum	21–76	18–83	18–76	18–81	21–88	18–88	
Age categories							
18–45 years old, %	75.4	53.6	66.9	52.8	46.4	60.2	<0.001
46–65 years old, %	19.7	40.8	30.7	40.0	37.7	33.5	
>65 years old, %	4.9	5.6	2.4	7.2	15.9	6.3	
Education level							
Primary education, %	5.8	13.2	26.2	40.3	27.5	22.3	<0.001
Secondary education, %	38.8	67.8	54.8	39.5	33.3	48.1	
University studies, %	55.4	19.0	19.0	20.2	39.1	29.6	
Quality of life and well-being							
SF-36[b] total score							
Physical component summary score, mean (S.D.)	44.8 (9.6)	45.2 (9.5)	43.2 (11.4)	39.6 (11.0)	40.1 (11.4)	42.8 (10.8)	<0.001
Median	46.8	45.8	45.0	38.6	42.7	43.9	
Minimum–maximum	16–61	16–60	10–62	15–63	15–60	10–63	
Mental component summary score, mean (S.D.)	40.8 (12.0)	45.7 (11.6)	42.5 (12.2)	42.4 (12.3)	44.4 (13.3)	43.0 (12.3)	0.028
Median	41.5	47.6	44.0	42.9	44.8	44.2	
Minimum–maximum	13–62	12–72	9–65	16–65	16–64	9–72	
Satisfaction with care							
Very satisfied, %	57.4	64.8	44.1	49.6	48.5	53.3	0.011
Satisfied, %	36.1	28.8	37.0	41.6	32.4	35.4	
Average, neither satisfied nor dissatisfied, %	5.7	5.6	15.0	6.4	11.8	8.6	
Poorly satisfied/not satisfied, %	0.8	0.8	3.9	2.4	7.4	2.7	

[a]Comparison between countries. No individual comparisons were reported for categorical variables at country levels. [b]SF-36 questionnaire: Medical Outcome Study Short Form 36 (SF-36) Version 2.0.

significantly varied between countries; physical component summary ($P < 0.001$) and mental component summary ($P = 0.028$).

Overall, 88.7% of patients were satisfied/very satisfied with their care, 8.6% rated their satisfaction as average and 2.7% were not satisfied. Patients were more often satisfied in France, Germany and Spain ($P = 0.011$).

Clinical profile characteristics

The mean (S.D.) disease duration was 12.3 (9.2) years. More than half of the study population had one or more co-morbidities (55.9%; data not shown); these were more frequent in Germany (81.6%) and Sweden (69.6%) compared with the other countries ($P < 0.001$; Table 2).

Patients presented mainly with mild to moderate disease activity. At inclusion visit, 104 patients (18.3%) were experiencing a flare, mainly of mild/moderate severity, with differences among countries ($P = 0.009$), and more often in Sweden and France.

The mean (S.D.) SS score was 3.4 (4.5), and more than one-third of patients (36.0%) had an SS score of 0. The same proportion (36.2%) had no system/organ involvement. Disease activity was mild for 42.3% of patients, moderate for 14.6% and severe for 7.1%. The mean (S.D.) PGA score was 0.6 (0.8), and more than half of patients (51.8%) had a PGA score of 0.

The mean (S.D.) SDI score was 0.8 (1.4). Almost two-thirds of patients (63.4%) had a SDI score of 0, and an equal proportion (65.9%) had no system/organ damage.

At inclusion visit, all patients were currently treated for SLE; 75.2% with antimalarials, 67.1% with CSs and 51.1% with immunosuppressants (including biologics).

LIT responses and scores

Patients completed almost all LIT items, from 94.0% (item no. 4: was limited in fulfilling family responsibilities) to 98.1% (item no. 1: woke up feeling worn out). They were more likely to be impacted by lupus during three daily situations (items 1, 2 and 6; Table 3). The three dominant areas of impact shown by LIT were the following. Item 1, I woke up feeling worn out, was reported as most/all of the time by 32.5% of patients and some of the time by 35%. Item 2, I felt pain and aching in my body, was reported as most/all of the time by 28.2% and some of the time by

Table 2 Patient clinical disease profile, overall and per country

Variable	France (n = 122)	Germany (n = 125)	Italy (n = 128)	Spain (n = 125)	Sweden (n = 69)	All (n = 569)	P-value[a]
Disease duration, years							
Total score, mean (S.D.)	10.2 (8.1)	13.0 (8.7)	12.7 (9.0)	12.1 (9.2)	14.1 (11.7)	12.3 (9.2)	0.044
Median	8.0	12.0	12.0	11.0	10.0	11.0	
Minimum–maximum	0–46	0–36	0–36	0–35	0–50	0–50	
Disease activity							
SELENA-SLEDAI[b] disease activity index							
Total score, mean (S.D.)	2.8 (3.7)	3.8 (4.4)	4.0 (5.0)	2.9 (4.3)	3.7 (4.9)	3.4 (4.5)	0.108
Median	2.0	2.0	2.0	2.0	2.0	2.0	
Minimum–maximum	0–16	0–31	0–27	0–31	0–22	0–31	
No activity, score = 0, %	43.4	28.0	29.4	37.6	46.4	36.0	0.004
Mild activity, 1–4, %	39.3	43.2	46.8	49.6	24.6	42.3	
Moderate activity, 5–9, %	11.5	21.6	13.5	8.8	20.3	14.6	
High activity, $\geqslant$10, %	5.7	7.2	10.3	4.0	8.7	7.1	
PGA							
Total score, mean (S.D.)	0.6 (0.9)	0.6 (0.7)	0.8 (0.8)	0.6 (0.8)	0.8 (0.7)	0.6 (0.8)	0.141
Median	0.0	0.5	1.0	0.0	1.0	0.0	
Minimum–maximum	0–3	0–3	0–3	0–3	0–3	0–3	
No activity, score = 0, %	63.1	50.0	42.2	59.2	39.1	51.8	<0.001
Mild activity, 1, %	18.0	41.9	40.6	27.2	44.9	33.6	
Moderate activity, 2, %	14.8	7.3	16.4	10.4	14.5	12.5	
High activity, $\geqslant$3, %	4.1	0.8	0.8	3.2	1.4	2.1	
Flares at inclusion visit, %	25.4	11.2	14.8	16.8	27.5	18.3	0.009
Mild/moderate flares, %	71.0[c]	85.7[c]	63.2[c]	61.9[c]	94.7[c]	74.0[c]	0.086
Organ damage							
SLICC/ACR[d] damage index							
Total score, mean (S.D.)	0.2 (0.7)	0.8 (1.5)	1.0 (1.3)	1.0 (1.6)	1.1 (1.9)	0.8 (1.4)	<0.001
Median	0.0	0.0	0.0	0.0	0.0	0.0	
Minimum–maximum	0–4	0–8	0–6	0–8	0–9	0–9	
No damage, score = 0, %	86.9	64.8	50.8	54.4	59.4	63.4	<0.001
Mild/moderate damage, 1, %	7.4	12.8	21.1	21.6	15.9	15.8	
High damage, $\geqslant$2, %	5.7	22.4	28.1	24.0	24.6	20.7	
Patients treated for SLE, %	99.2	88.8	87.4	90.4	89.9	91.2	0.011
Treatments for SLE							
Antimalarials, %	84.4	68.8	68.0	82.4	71.0	75.2	0.003
CSs, oral/injection, %	59.8	65.6	86.7	56.8	65.2	67.1	<0.001
Immunosuppressants, oral/injection, %	35.2	66.4	64.8	41.6	43.5	51.1	<0.001

[a]Comparison between countries. No individual comparisons were reported for categorical variables at country levels. [b]SELENA-SLEDAI (SS): Safety of Oestrogens in Lupus Erythematosus National Assessment version of the SLEDAI. [c]Percentage calculated on the number of patients who were experiencing flares at inclusion visit. [d]SLICC/ACR Disease Index (SDI). PGA: Physician Global Assessment.

32.5%. Response to Item 6, I was anxious, was described most/all of the time by 20.3% and some of the time by 28.8%.

Consequently, items 1, 2 and 6 received the highest scores: 1.9, 1.8 and 1.5, respectively (Table 3). Overall, the mean (S.D.) total LIT score was 34.2 (22.3), median: 32.5 (ranging from 28.0 in Germany to 37.2 in Sweden and 37.8 in Spain). Given that LIT total scores could range from 0 to 100, these scores demonstrate a low to moderate impact of lupus on patients' daily lives.

Among the five participating countries, patient responses showed a significant difference for 6 items out of the 10, including the most highly scored items (nos 1, 2, 6) as well as item nos 3, 7 and 9 (Table 3).

Construct/convergent validity of LIT

Strong positive correlations were observed between LIT scores and the level of disease activity and organ damage, flare occurrence, young age, gender and the degree of dissatisfaction with care (Table 4). Overall and in each country, LIT scores increased proportionately with the level of PGA, SS, SDI scores and patient dissatisfaction with care. The LIT scores were also higher in patients aged 46–65 years old, with flare occurrence at inclusion visit and in women. In contrast, there was a negative correlation between LIT scores and quality-of-life situations (SF-36 scores) of moderate to strong magnitude (Pearson coefficient of correlation: $0.5 < \rho < 1$). Five items showed the strongest relationships: physical role functioning,

Table 3 Lupus impact scores, overall and per country

Variable	France (n = 122)	Germany (n = 125)	Italy (n = 128)	Spain (n = 125)	Sweden (n = 69)	All (n = 569)	P-value[a]
Range of response rates for the items below, %[a]	95.9–99.2	93.6–99.2	95.3–98.4	88.8–95.2	98.6–100	94.0–98.1	
1. I woke up feeling worn out	2.1 (1.2)	1.6 (1.2)	1.6 (1.2)	2.1 (1.2)	2.3 (1.2)	1.9 (1.2)	<0.001
2. I felt pain and aching in my body	1.9 (1.1)	1.6 (1.1)	1.3 (1.2)	2.0 (1.2)	2.2 (1.1)	1.8 (1.2)	<0.001
3. I was unable to perform my usual activities for long periods of time because of pain and fatigue	1.3 (1.2)	1.0 (1.1)	1.1 (1.2)	1.5 (1.3)	1.4 (1.1)	1.3 (1.2)	0.012
4. I was limited in fulfilling family responsibilities because of my physical health	1.2 (1.2)	1.1 (1.2)	1.1 (1.2)	1.3 (1.2)	1.4 (1.2)	1.2 (1.2)	0.295
5. My lupus interfered with my ability to plan activities and schedule events	1.3 (1.3)	1.1 (1.2)	1.5 (1.4)	1.5 (1.3)	1.5 (1.2)	1.4 (1.3)	0.090
6. I was anxious	1.7 (1.1)	0.8 (1.1)	1.6 (1.2)	1.8 (1.2)	1.3 (1.1)	1.5 (1.2)	<0.001
7. I was depressed	1.4 (1.2)	1.0 (1.1)	1.2 (1.2)	1.5 (1.2)	1.2 (1.1)	1.2 (1.2)	0.025
8. I experienced difficulty concentrating	1.4 (1.2)	1.2 (1.1)	1.4 (1.1)	1.3 (1.2)	1.4 (1.2)	1.4 (1.2)	0.648
9. I was self-conscious about my appearance	1.0 (1.2)	0.8 (1.2)	1.3 (1.4)	1.3 (1.3)	1.2 (1.2)	1.1 (1.3)	0.003
10. My lupus medication(s) caused bothersome side-effects	1.1 (1.3)	0.9 (1.2)	1.3 (1.2)	1.0 (1.1)	1.0 (1.2)	1.1 (1.2)	0.101
Converted LIT score							
Mean (S.D.)	36.1 (22.9)	28.0 (20.3)	33.5 (22.3)	37.8 (23.0)	37.2 (21.4)	34.2 (22.3)	0.004
Median	33.8	22.5	30.0	37.5	40.0	32.5	
Minimum–maximum	0–95	0–85	0–95	0–100	0–85	0–100	

The results for each LIT question are presented as the mean (S.D.). [a]Comparison between countries. No individual comparisons were reported for categorical variables at country levels. [b]Range of response rates for the 10 items: the lowest and highest proportions of patients that answered the items are presented in the table. For example, in France 95.9% of patients (117/122) answered questions 4, 5 and 9, and 99.2% (121/122) answered questions 1, 2, 3, 7 and 10. LIT: Lupus Impact Tracker.

social role functioning, vitality, bodily pain and mental health ($P < 0.001$ each).

Nevertheless, some significant differences across countries were observed between LIT and instrument scores: in patients with a PGA score = 0 ($P = 0.011$), SS score = 0 ($P = 0.020$), SDI scores = 0 ($P = 0.034$) or 1 ($P = 0.038$), no flare at visit ($P = 0.004$), young age (18–45 years old; $P = 0.002$), women ($P = 0.014$) and high satisfaction with care ($P = 0.037$; Table 4). Differences appeared most frequently in Germany compared with the other countries.

Acceptability of LIT and feasibility in routine clinical practice

As stated above, the rate of LIT completion was good (Table 3). Overall, each item received 94.0–98.1% of responses (Table 5). More than half of patients found that the LIT helped them to remember specific ways in which lupus impacts their life [65.9%; question (Q) 1 of the patient feedback questionnaire], to remember to discuss the impact of lupus on their daily life (68.4%; Q2), that it was useful (60.7%; Q4) and that it improved communication with the physician (54.3%; Q5).

More than three-quarters of patients found that completing the LIT was not a burden for them during the office visit (80.3%; Q3), did not disrupt their office visit (79.6%; Q6) and was easy to score (77.2%; Q9).

More than half of physicians found that the LIT helped them to remember to ask about specific ways in which lupus impacts the patient's life (61.7%; Q1 of the physician feedback questionnaire), to discuss with the patient the impact lupus has on his/her daily life (62.8%; Q2), improved communication with the patient (53.3%; Q5) and worked well for this particular patient (52.1%; Q6). As a result, 55.6% of physicians would like to use this tool again for this particular patient in the future (Q8). Nevertheless, they sometimes perceived its completion as a burden during their visit (16.8%; Q3) and found it to be not necessary for some patients (13.3%; Q4).

Cross-cultural validation and reliability of LIT

The cross-cultural variability of LIT among countries was evaluated using the DIF method (Table 6). The DIF was significant for 6 out of 10 items (nos 2, 4, 5, 6, 9 and 10). The magnitude of total DIF (uniform + non-uniform) was classified as moderate but was at the very low end of this category (R^2 of 0.04) for only one item (no. 6: I was anxious) and was negligible (R^2 of 0.01–0.03) for the five others. Of the variation in item responses, $\leqslant 4\%$ were attributable to a country effect and $\geqslant 96\%$ were attributable to the effect of the disease. The Cronbach α coefficients were generally good and very close among countries: France: 0.92; Germany: 0.88; Italy: 0.90; Spain: 0.91; and Sweden: 0.89.

Discussion

The study confirmed LIT reliability and internal consistency across the five participating European countries. The data validated the LIT instrument, which can be used in routine clinical practice and support patient–physician interaction. The LIT may help to evaluate the patient's reported outcomes during the visit, as recommended in guidelines [3, 4].

The construct and convergent validity assessment showed a strong positive correlation between LIT scores and the level of disease activity and organ damage in each country. The associated rates of increase of LIT scores, as a function of these instrument/index scores, were similar to those reported in the cross-sectional US LIT study 2 [9]. Moreover, flare occurrence reported by lupus patients is an important variable in the selection of lupus health parameters, because they may greatly impact patients' life. However, this variable has not been included in the LIT questionnaire [8].

In contrast, a moderate to strong negative relationship was also observed between LIT and SF-36 scores in each country, as described in the US LIT study 2 [9]. The correlation between LIT scores and variables of interest showed some significant differences across countries in one category of some instrument/index and subgroups of interest. Differences were observed in patients with low/no disease activity (SS and PGA scores = 0, with no flare occurrence) and low organ damage (SDI scores = 0 or 1), and in women, young patients (18–45 years old) and patients who were very satisfied with their care.

The DIF analysis showed slight variations across countries; $\geqslant 96\%$ were attributable to the impact of the disease and $\leqslant 4\%$ to a country-specific effect. The magnitude of the DIF effect (negligible to moderate) was minimal, and the trait estimates derived from the unmodified questionnaire allow for comparison between countries, showing clearly the invariability of LIT between countries. The invariability in responses across countries suggests a correct understanding and comprehensiveness of the unmodified LIT questions.

The slight differences across countries may be attributable to different patients' disease profiles, levels of educational attainment, social behaviour, patient–physician interaction or may even have occurred by chance.

The study shows the acceptability of the LIT and its feasibility in routine clinical practice, both overall and in each country. The LIT was well accepted by patients and by the majority of physicians, overall and within each country. Both patients and physicians found that the LIT improved the communication between them, helped them to remember specific ways in which lupus impacts patients' daily life and to discuss the impact of lupus. In fact, the use of PRO measurement tools in clinical practice is increasingly encouraged and has been shown to improve patient satisfaction and quality of care [8]. The physicians found that the LIT could be useful in particular situations as well as for particular subsets of patients. These patients may not think to report relevant symptoms or difficulties that could better inform the physician about their disease and its consequences. The LIT could be used as a checklist to ensure that most important points

Table 4 Overall construct/convergent validity of lupus impact scores

LIT lupus impact scores	Valid n	Mean (S.D.)	Minimum–maximum	Median	P25%, P75%	P-value[a]
SELENA-SLEDAI disease activity index						
SS score: 0	204	33.2 (21.6)	0–100	32.5	15.0, 47.5	0.020
SS score: 1–5	240	32.1 (21.6)	0–95	30.0	15.0, 47.5	0.155
SS score: 6–10	83	37.2 (22.5)	0–88	37.5	17.5, 57.5	0.457
SS score: >10	40	46.8 (25.3)	0–95	52.5	25.0, 65.0	0.832
Physician Global Assessment						
PGA score: 0, no activity	294	30.6 (21.3)	0–100	27.5	12.5, 45.0	0.011
PGA score: 1, mild activity	191	35.1 (21.3)	0–95	35.0	17.5, 50.0	0.117
PGA score: 2, moderate activity	71	43.5 (24.6)	0–95	45.0	20.0, 65.0	0.432
PGA score: 3, high activity	12	54.0 (24.2)	5–88	55.0	46.3, 68.8	0.443
Flare occurrence						
None	465	31.7 (21.3)	0–100	30.0	15.0, 45.0	0.004
Flares, severity: mild/moderate	77	46.0 (22.6)	0–90	45.0	30.0, 65.0	0.511
Flares, severity: severe	27	44.1 (25.7)	0–95	50.0	20.0, 60.0	0.558
SDI (SLICC/ACR damage index)						
SDI score: 0	361	32.8 (22.8)	0–95	30.0	12.5, 50.0	0.034
SDI score: 1	90	35.0 (21.3)	0–85	33.8	17.5, 50.0	0.038
SDI score: ⩾2	118	38.0 (21.1)	0–100	40.0	20.0, 50.0	0.759
Age, years						
Age: 18–45 years old	342	33.0 (22.4)	0––95	30.0	15.0, 50.0	0.002
Age: 46–65 years old	190	37.0 (22.6)	0–100	37.5	20.0, 52.5	0.659
Age: >65 years old	36	31.9 (18.9)	0–68	30.0	17.5, 42.5	0.815
Gender						
Female	508	35.1 (22.4)	0–100	32.5	17.5, 50.0	0.014
Male	57	27.4 (20.8)	0–83	20.0	12.5, 40.0	0.518
Satisfaction with care						
Very satisfied	302	30.7 (20.6)	0–100	27.5	15.0, 45.0	0.037
Satisfied	201	34.5 (23.5)	0–95	32.5	15.0, 50.0	0.482
Average	49	47.8 (19.9)	15–90	50.0	35.0, 60.0	0.282
Poorly satisfied	13	57.7 (15.3)	28–85	57.5	50.0, 65.0	0.225
Not satisfied	0	0	0	0	0	0
LIT lupus impact scores	Valid n				Pearson coefficient	P-value[a]
Medical outcome SF-36						
Physical component summary	561				−0.640	<0.001
Social component summary	561				−0.675	<0.001
Physical role functioning	566				−0.745	<0.001
Social role functioning	569				−0.713	<0.001
Vitality	568				−0.707	<0.001
Bodily pain	566				−0.701	<0.001
Mental health	567				−0.641	<0.001

[a]Comparisons across countries were assessed using the Kruskal–Wallis test in order to detect significant difference among the five countries for each construct/convergent validity analysis performed. Construct validity evaluated the relationship between LIT scores and the scores of SS, PGA, SDI and age, gender and satisfaction with care. Convergent validity evaluated the relationship between LIT and SF-36 scores. LIT: Lupus Impact Tracker; PGA: Physician Global Assessment.

are assessed during the routine visit and to gain a better understanding of patient needs.

The LIT scores reflected the patients' overall health status. In fact, the most highly rated items were in line with disease profile, that is, disease activity, organ damage, flare occurrence and quality-of-life scores. Three LIT items, one psychological and two physical and components, showed the highest scores: I was anxious; I woke up feeling worn out; and I felt pain and aching in my body. Three other items received medium scores: I was unable to perform my usual activities; I was depressed; and I was self-conscious about my appearance. The overall total LIT score, reflecting the physical and mental impact of lupus on patients' daily life, was low to moderate (overall mean total LIT score: 34.2). It also reflected patients' disease activity, which was generally mild.

The patient sample is large for this autoimmune disease and for this type of validation study. This contributed to obtaining robust and significant results.

Nevertheless, this LIT European study has certain limitations. The study mainly included outpatients, who were recruited in centres specializing in lupus care management and were generally presenting with controlled disease on prior treatment. The relatively small number of inpatients, community patients and patients with severe

Table 5 Acceptability of lupus impact scores by patients and physicians, overall and per country

Variable	France (n = 122)	Germany (n = 125)	Italy (n = 128)	Spain (n = 125)	Sweden (n = 69)	All (n = 569)	P-value[a]
Patients' perspective							
Responses (agree/strongly agree)							
1. Helped me to remember specific ways lupus impacts my life	55.4	65.3	73.0	68.6	68.1	65.9	0.034
2. Helped me to discuss the impact lupus has on my daily life	67.0	62.0	76.0	66.7	71.0	68.4	0.104
5. Improved communication between my physician and me	52.2	49.6	65.6	50.8	51.5	54.3	0.004
7. My doctor and I spoke more about the impact lupus has on my life today	33.0	25.6	41.3	27.4	37.6	32.7	0.006
8. I would like to use this tool again, when visiting my doctor	50.0	41.1	60.8	46.2	51.4	49.9	<0.001
9. Scoring the LIT was easy	82.9	75.8	83.4	75.0	62.3	77.2	0.009
10. I would like to use this tool at home between doctor visits	26.4	26.1	36.0	42.7	27.5	32.1	<0.001
Responses (disagree/strongly disagree)							
3. Was a burden to me during the office visit	71.1	74.2	92.1	76.1	92.8	80.3	<0.001
4. Is not necessary	63.2	43.5	73.8	62.1	60.3	60.7	<0.001
6. Disrupted my office visit	86.5	61.8	94.4	72.4	84.0	79.6	<0.001
Physicians' perspective							
Responses (agree/strongly agree)							
1. Helped me to remember to ask about specific ways in which lupus impacts his/her life	46.7	48.8	77.9	89.5	31.9	61.7	<0.001
2. Helped me to discuss, with my patient, the impact lupus has on his/her daily life	59.8	49.6	73.2	79.8	42.0	62.8	<0.001
5. Improved communication between my patient and me	32.2	44.0	66.1	76.8	42.0	53.3	<0.001
6. Worked well for this particular patient	43.5	50.4	56.0	50.8	65.2	52.1	<0.001
7. My patient and I spoke more about the impact lupus has on his/her life today compared with office visits when I did not use the LIT	38.5	37.9	55.9	64.5	42.0	48.4	<0.001
8. I would like to use this tool again, for this particular patient, in future	47.6	49.6	51.2	70.9	60.8	55.6	<0.001
Responses (disagree/strongly disagree)							
3. Was a burden to me during the office visit	55.7	40.8	53.5	55.6	41.8	49.6	<0.001
4. Is not necessary	59.9	47.2	52.7	57.2	46.4	53.2	<0.001
Concordance between patients' and physicians' responses							
κ coefficient: minimum	−0.060	0.074	0.101	−0.047	−0.038	0.048	
κ coefficient: maximum	0.083	0.214	0.223	0.147	0.256	0.191	

All values are given as percentages, unless otherwise stated. [a]Comparison between countries. No individual comparisons were reported for categorical variables at country levels. LIT: Lupus Impact Tracker.

TABLE 6 Variability assessment across countries, differential item functioning

LIT items	Total DIF[a] (P-values)	R^2-change	Magnitude of effect
1. I woke up feeling worn out	NS	–	–
2. I felt pain and aching in my body	<0.001	0.03	Negligible
3. I was unable to perform my usual activities for long periods of time because of pain and fatigue	NS	–	–
4. I was limited in fulfilling family responsibilities because of my physical health	0.03	0.01	Negligible
5. My lupus interfered with my ability to plan activities and schedule events	0.03	0.01	Negligible
6. I was anxious	<0.001	0.04	Moderate
7. I was depressed	NS	–	–
8. I experienced difficulty concentrating	NS	–	–
9. I was self-conscious about my appearance	0.001	0.02	Negligible
10. My lupus medication(s) caused bothersome side-effects	<0.001	0.02	Negligible

The total DIF (uniform + non-uniform) is presented in the table. [a]DIF detection using likelihood ratio test comparing model with country effect to model with only LIT effect (uniform DIF) or model with country*LIT effect interaction to model without it (non-uniform DIF) or model with country*LIT effect interaction to model with LIT effect (total DIF). The total DIF (uniform + non-uniform) is presented in the table. After detection, the magnitude of DIF was calculated using the R^2 change statistic. DIF: Differential Item Functioning; LIT: Lupus Impact Tracker; NS = not significant.

disease represents a limitation in terms of the exhaustiveness of the clinical profiles studied. Although the samples collected at the country level reflect the local SLE population, the overall sample may not be representative and generalizable to the SLE population of all European countries. Of note, the demographics and disease profile of the European sample were similar to those described in the US LIT study in terms of age, sex ratio, educational attainment, flare occurrence evaluated during the visit, and SS and PGA scores [9].

Some variables regarding demographics, education levels, participation in clinical trials or the presence of FM might have been potential confounders and effect modifiers; however, the proportions were very low, $\leqslant$5% each.

As a topic for further research, the LIT could be tested and retested by calculating the intraclass correlation coefficient in a longitudinal, prospective follow-up study, which could also serve to consolidate its responsiveness and sensitivity to change [19]. However, both retest and responsiveness assessment were already successfully performed in the US LIT study [9, 27].

In conclusion, the study enabled the validation of the LIT, and its main findings mirror those observed in the US LIT study [9, 27]. It showed the internal consistency and therefore the reliability of the LIT and its cultural invariability across the five participating European countries. The LIT was well accepted by patients and physicians. It could be used in routine clinical practice; indeed, physician responses indicate that they intend to use it in specific situations and for specific patient profiles, as a checklist to assess patient needs.

Acknowledgements

We greatly thank all the experts, principal investigators and their co-investigators and team members for their active participation in the study: France: Professors Amoura (Paris), Bonnotte (Dijon), Fauchais (Limoges), Hachulla (Lille) and Viallard (Bordeaux); Germany: Professors Anders (München), Rech (Erlangen), Schwarting (Bad Kreuznach), Specker (Essen) and Dr Max (Heidelberg);

Italy: Professors Doria (Padova), Mathieu (Cagliari), Meroni (Milano) and Tincani (Brescia); Spain: Drs Calvo Alén (Torrelavega), Freire González (A Coruña), Rúa Figueroa (Gran Canaria), Uriarte Isacelaya (San Sebastian); Sweden: Professor Sjöwall (Linköping) and Dr Dupre-Jungnell (Visby).

All co-authors participated actively in conducting the study, reviewed the manuscript content and approved it for publication. We thank Dr Jolly (Chicago, IL, USA), who designed the LIT PRO questionnaire, for her constructive review of the manuscript and recommendations. We also thank Dr Hankins (IMS Health, London, UK) and his team for the statistical analyses. The LIT questionnaire was designed and tested in the USA by Dr Meenakshi Jolly, MD (Rheumatologist at Rush University Medical Centre, 1611 W Harrison Street, Suite 510, Chicago, IL 60612, USA). The five European versions are available at *Rheumatology* online and can be used after permission from the owner, Dr Meenakshi Jolly. The use of LIT in one of the six available languages is free for physicians' clinical use, for non-lucrative purposes or for scholarly research. Please click on the lupusPro link for further information: http://www.lupuspro.com.

Funding: This work was supported by GlaxoSmithKline (GSK), Brentford, UK; study etrack number: BEL117212.

Disclosure statement: F.M. and A.G. are employees of IMS and conducted this study on behalf of GSK. H.D. was invited to the EULAR congress by GSK in 2015 and

received honoraria from GSK in 2014 and 2015 (<1000 euro per year). R.P. and A.P are employees and stockholders of GSK. M.S. has held consultancies, received research grants and been a member of the speakers' bureau for GSK, UCB, Astra-Zenenca and Lilly. All other authors have declared no conflicts of interest.

Supplementary data

Supplementary data are available at *Rheumatology* Online.

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