

Original article

The substantial burden of systemic lupus erythematosus on the productivity and careers of patients: a European patient-driven online survey

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Abstract

Objective. The objective of this study was to explore the burden of SLE and its effect on patients' lives.

Methods. The Lupus European Online (LEO) survey included patient-designed questions on demographics, SLE diagnosis, and the impact of SLE on careers. Three SLE-specific patient-reported outcome (PRO) questionnaires were also completed: the Lupus Quality of Life (LupusQoL), the Fatigue Severity Scale (FSS), and the Work Productivity and Activity Impairment (WPAI)-Lupus v2.0. The survey was available online in five languages from May through August 2010. All self-identified SLE participants were eligible to respond. Survey results were analysed using descriptive statistics. Multivariate linear regression explored factors contributing to impaired productivity.

Results. Of the 2070 European SLE patients completing the survey, 93.1% were women, 86.7% were aged <50 years and 71.8% had a college or university education. More than two-thirds of respondents (69.5%) reported that SLE affected their careers; 27.7% changed careers within a year of diagnosis. All LupusQoL domains (score range 0–100) were impaired, with fatigue (median domain score 43.8) being the most affected and intimate relationships (median domain score 75.0) the least. Most patients (82.5%) reported fatigue (FSS score ≥ 4). Productivity was impaired across all WPAI domains, both at work and in general activities. Fatigue, an inability to plan and reduced physical health were significantly associated with impaired productivity. Patients whose careers were affected by SLE had worse health-related quality of life, more fatigue and worse productivity than patients whose careers were not affected.

Conclusion. LEO survey respondents reported that SLE negatively affects their daily lives, productivity and career choices.

Key words: SLE, HRQoL, fatigue, productivity, PRO.

Introduction

Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune rheumatic disease that predominantly affects

young women and usually develops between the ages of 20 and 40 years [1]. Effective treatments are difficult to develop for SLE [2] and thus disease burden remains high [2, 3]. Health-related quality of life (HRQoL) reductions in SLE patients are comparable to those in patients with other severe conditions such as RA, congestive heart failure and SS [4–6]. Common SLE symptoms known to contribute to poor HRQoL include fatigue [7], depression [8], pain [9], sleep disturbances and cognitive dysfunction [10, 11].

HRQoL measurements from patient-reported outcome (PRO) questionnaires can complement traditional physician-reported disease activity and damage outcomes [12, 13]. For this reason, HRQoL is listed as a core domain to be addressed in SLE clinical trials, in

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Submitted 18 October 2012; revised version accepted 25 July 2013.

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recommendations published by the Outcome Measures in Rheumatology initiative [14]. The most common generic instrument for measuring HRQoL is the 36-item Short Form Health Survey (SF-36) [15, 16]. In addition, several SLE-specific instruments have been recently developed, such as the Lupus Quality of Life (LupusQoL) questionnaire [6, 17]. While generic instruments allow comparisons to other chronic diseases, SLE-specific measures have greater sensitivity to change and contain items more relevant to patients with SLE [6, 18].

One aspect of HRQoL that is particularly pronounced in SLE is fatigue, which is experienced by up to 90% of SLE patients and is considered their most disabling disease symptom by ~50% of patients [19, 20]. Fatigue is often multifactorial in origin and can be mediated through disease-related factors, comorbid conditions or environmental factors [21].

SLE can also reduce a patient's ability to work and results in high rates of work disability, reductions in working hours and/or changes in the nature of a patient's work [22, 23]. As SLE occurs predominately in women of childbearing age, productivity losses in non-labour market activities such as childcare and housework are also high, and are important to measure and understand [12, 24].

In 2009, two patient-led online surveys were conducted in Europe [25] and the USA [26]. These surveys, which to our knowledge were the first of their kind for SLE patients, contained questions developed by SLE patients working with the medical advisory boards of two SLE patient organizations: LUPUS EUROPE and the Lupus Foundation of America. Their aim was to explore the effect of SLE on overall well-being and activities of daily living and employment, as well as patients' experiences with treatment. In Europe, 81% of respondents reported that SLE symptoms affected their careers. The most common symptoms reported included fatigue, arthritis, muscle pain/weakness or tendonitis and skin rashes, oral/nasal ulcerations or hair loss (86%, 84% and 70% of respondents, respectively). Fatigue was also reported as one of their three most severe symptoms by 67% of European respondents; the next most commonly listed was arthritis, muscle pain/weakness or tendonitis (63.1% of respondents). The strong response from the SLE patient community (>900 patients completed the surveys) demonstrated that such surveys are highly valued.

To extend the findings of this initial research, a new patient-led initiative, the Lupus European Online (LEO) survey, was undertaken in 2010. The LEO survey aimed to describe HRQoL and fatigue levels in European patients and to explore the relationships between fatigue, HRQoL, career choices, employment and productivity using both patient-developed questions and validated PRO measures.

Patients and methods

Survey

The LEO survey was instigated by LUPUS EUROPE, the European umbrella organization of lupus patient groups

and a UK registered charity. It was developed together with the LUPUS EUROPE Clinical Advisory Committee and UCB Pharmaceutical SA. UCB facilitated the organization, planning and development of the survey by providing coordination and communication, technical support and scientific expertise. Since this was a non-experimental, voluntary survey, no ethical approval was required; however, LUPUS EUROPE represented patient interests and contributed to the design of the survey.

The first part of the survey included demographic questions covering age, civil status, diagnosis, employment status, treatment, body systems affected at diagnosis and at the time of survey completion and effects of SLE on patients' work productivity, daily activities and career choices (supplementary Fig. S1, available at *Rheumatology* Online). These questions were developed by the steering committee consisting of members of the LUPUS EUROPE Clinical Advisory Committee, a LUPUS EUROPE board patient representative and five appointed language contacts from the national patient groups in England, France, Germany, Spain and Italy.

The survey also included three SLE-specific PRO questionnaires: the LupusQoL questionnaire, Fatigue Severity Scale (FSS) and the Work Productivity and Activity Impairment (WPAI)-Lupus v2.0 questionnaire.

The LupusQoL measures aspects of HRQoL during the prior 4 weeks and includes 34 items across eight domains (body image, burden to others, emotional health, fatigue, intimate relationships, pain, physical health and planning) [18]. Overall scores range from 1 to 100, with higher scores indicating better HRQoL.

The nine-item FSS, originally developed and validated on SLE and multiple sclerosis patients, measures the impact of fatigue on specific types of functioning in the prior 2 weeks; scores are rated between 1 and 7, with higher scores indicating greater levels of fatigue [27]. A normative range for the FSS has been established, with a score <4 considered normal [21].

The WPAI questionnaire measures levels of impairment in work and general activities and has been validated for several indications [28–31]. An SLE-specific version has been designed (WPAI-Lupus v2.0) and was used in this survey. The WPAI questionnaire records impairment due to SLE during the prior 7 days and has six items grouped into four domains [32]. Outcomes for each domain are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity. The four WPAI domains are described as follows: absenteeism (percentage of time missed from work; a higher percentage corresponds to more time missed from work); presenteeism (percentage impairment of productivity while at work; a higher percentage corresponds to worse productivity while at work, i.e. patients are more limited in the amount or nature of work they can do); overall work impairment (combination of absenteeism and presenteeism domains; a higher percentage corresponds to more time missed from work and worse productivity while at work) and activity impairment (percentage

impairment in activities outside of work; a higher percentage corresponds to worse productivity while doing regular daily activities such as housework, shopping, childcare, exercising, studying, etc.).

Survey implementation

The LEO survey was developed in English, French, German, Italian and Spanish by specialist translators and was verified by the five appointed language contacts from national patient groups. For the PRO questionnaires, linguistically validated/culturally adapted versions were included. The LEO survey was available online via SurveyMonkey (www.surveymonkey.com/), launched on World Lupus Day 2010 (10 May) and promoted through the LUPUS EUROPE network by mail, national organizational magazines, web communications and social media. Members of the national lupus groups within Europe were invited to respond. All self-identified SLE patients were eligible to respond, all responses were anonymous and individuals were not obliged to answer every question. The survey closed on 15 August 2010.

Statistical analyses

Survey data were reported using descriptive statistics. Mean LupusQoL domain scores of respondents who were fatigued vs not fatigued were compared using a *t*-test. Mean LupusQoL domain scores, mean FSS scores and mean WPAI domain impairments of respondents who experienced different effects of SLE on their careers were compared using analysis of variance (ANOVA). In order to identify variables associated with productivity impairment (WPAI domains), a univariate analysis was performed that included almost all questions/items covered in the survey. Variables that were significant at $P < 0.2$ in the univariate analysis were included in a multivariate linear regression model. Backward selection was then used to produce a final model containing only variables with $P < 0.01$. A chi-square test and a one-way ANOVA were used to test for differences between countries. The chi-square test assessed education level, gender, age, civil status, parental status, time since diagnosis, current medication use, effect on career and body systems currently affected by SLE. The one-way ANOVA assessed mean scores for each WPAI domain, FSS and all LupusQoL domains. These tests were not pairwise comparisons and did not identify which differences might be driving significance for a given variable.

Results

Demographics

Of 2188 individuals completing the survey, 118 were caregivers for SLE patients and were excluded from further analysis. Of the 2070 respondents with self-reported SLE, 93.1% were women, 86.7% were aged <50 years, 39% had been diagnosed within the previous 5 years, 62.6% were married and 71.7% had a college or university education (Table 1). Muscles and joints were the most commonly affected body parts, both at diagnosis (63.7%)

and at the time of survey completion (75.9%). The most commonly prescribed medications were corticosteroids (61.6%), followed by antimalarials (55.3%) and immunosuppressants (38.9%).

HRQoL

All domains of the LupusQoL were impaired, with the most affected being burden of others (mean score 45.2) and fatigue (mean score 46.5) and the least affected being intimate relationships (mean score 63.6) (Table 2 and supplementary Table S1, available at *Rheumatology Online*).

Fatigue

Fatigue was common and had a broad negative impact. Most (82.5%) reported experiencing fatigue (FSS score ≥ 4) and fatigue affected all nine FSS items, indicating high levels in respondents' daily lives. More than half (57.2%) completely agreed that their motivation was lower when fatigued, 45.8% completely agreed that fatigue was among their three most disabling symptoms and 45.5% completely agreed that fatigue interfered with their physical functioning. Those experiencing fatigue (FSS score ≥ 4) had significantly lower quality of life compared with those without fatigue (all LupusQoL domain scores were lower; $P < 0.001$; Table 2 and supplementary Table S1, available at *Rheumatology Online*).

The effect of SLE on employment, career choices and productivity

Most respondents reported that SLE burden had affected their employment, career choices and productivity. Approximately two-thirds (71.8%) were college or university educated, but only 65.1% were currently in paid employment, self-employed or continuing their studies (Table 1). In addition, 27.7% had changed careers within the first year after diagnosis, and 60.0% had reduced their working hours by $\geq 50\%$ because of SLE.

More than two-thirds (69.5%) of responders reported that SLE had affected their career. Of those who reported the nature of this effect, 29.4% chose 'I now have to work flexible hours', 28.4% chose 'I have had to apply for social or disability allowance', 26.7% chose 'I have had to apply for sick leave' and 15.5% chose 'I have had to change career'. All LupusQoL domain scores were significantly different depending on the effect of SLE on respondents' careers: quality of life was lowest in those receiving social or disability allowance and highest in those who worked flexible hours and/or had changed their career ($P < 0.001$; Table 3 and supplementary Table S2, available at *Rheumatology Online*). Those who reported an effect on their career also had significantly higher levels of fatigue than those reporting no career effects ($P < 0.001$; Fig. 1); respondents receiving social or disability allowance were the most fatigued.

SLE had a substantial negative effect on productivity, as assessed by the WPAI questionnaire, both at work and in general daily activities. Respondents who were working reported missing 13.4% of their paid work time because

TABLE 1 Demographics of all LEO survey respondents and for the five main countries, combined and individually

Demographic characteristic	All respondents with SLE (n = 2070)	All five main countries (n = 1566)	France (n = 139)	Germany (n = 537)	Italy (n = 357)	Spain (n = 267)	UK (n = 266)
Gender, % (n)							
No. of respondents	2058	1557	137	536	355	265	264
Female	93.1 (1915)	92.5 (1440)	92.7 (127)	91.2 (489)	91.0 (323)	96.2 (255)	93.2 (246)
Age, % (n), years							
No. of respondents	2048	1550	136	531	352	265	266
≤25	7.7 (158)	7.5 (117)	9.6 (13)	8.1 (43)	5.4 (19)	8.7 (23)	7.1 (19)
26–35	24.7 (505)	23.5 (364)	38.2 (52)	20.0 (106)	26.7 (94)	26.0 (69)	16.2 (43)
36–45	33.5 (687)	35.8 (555)	31.6 (43)	34.5 (183)	44.3 (156)	36.2 (96)	28.9 (77)
46–55	22.5 (460)	21.5 (334)	16.9 (23)	24.5 (130)	17.9 (63)	21.1 (56)	23.3 (62)
56–65	9.7 (198)	9.5 (148)	3.7 (5)	10.2 (54)	4.8 (17)	7.2 (19)	19.9 (53)
>65	2.0 (40)	2.1 (32)	0 (0)	2.8 (15)	0.9 (3)	0.8 (2)	4.5 (12)
Civil status, % (n)							
No. of respondents	2064	1562	138	537	356	266	265
Single	27.0 (557)	26.9 (420)	26.1 (36)	27.7 (149)	31.5 (112)	24.1 (64)	22.3 (59)
Married/living with partner	62.6 (1293)	62.9 (982)	62.3 (86)	61.8 (332)	58.4 (208)	68.0 (181)	66.0 (175)
Divorced	8.9 (183)	8.8 (137)	10.9 (15)	8.8 (47)	9.3 (33)	5.3 (14)	10.6 (28)
Widowed	1.5 (31)	1.5 (23)	0.7 (1)	1.7 (9)	0.8 (3)	2.6 (7)	1.1 (3)
Children, % (n)							
No. of respondents	2053	1554	136	537	354	264	263
Yes	53.9 (1106)	51.7 (804)	56.6 (77)	53.8 (289)	42.4 (150)	51.1 (135)	58.2 (153)
Diagnosis, % (n)							
No. of respondents	2064	1561	139	535	355	267	265
Before 1985	6.2 (127)	6.1 (95)	7.2 (10)	4.5 (24)	7.3 (26)	8.6 (23)	4.5 (12)
1985–89	6.7 (139)	7.2 (112)	1.4 (2)	7.1 (38)	9.3 (33)	9.4 (25)	5.3 (14)
1990–94	10.4 (214)	10.8 (168)	5.8 (8)	10.3 (55)	14.1 (50)	9.4 (25)	11.3 (30)
1995–99	16.0 (330)	15.5 (242)	16.5 (23)	18.5 (99)	13.5 (48)	15.7 (42)	11.3 (30)
2000–4	21.8 (449)	20.9 (326)	25.9 (36)	21.9 (117)	18.3 (65)	19.1 (51)	21.5 (57)
2005–10	39.0 (805)	39.6 (618)	43.2 (60)	37.8 (202)	37.5 (133)	37.8 (101)	46.0 (122)
Highest level of education, % (n)							
No. of respondents	2032	1535	135	516	356	266	262
Basic education	28.2 (574)	28.3 (434)	15.6 (21)	35.3 (182)	16.0 (57)	28.2 (75)	37.8 (99)
College education	36.6 (744)	37.7 (578)	25.2 (34)	37.2 (192)	55.9 (199)	33.1 (88)	24.8 (65)
University education	35.1 (714)	34.1 (523)	59.3 (80)	27.5 (142)	28.1 (100)	38.7 (103)	37.4 (98)
Employment status, % (n)							
No. of respondents	1931	1463	121	520	330	240	252
Employed	52.4 (1011)	53.6 (784)	67.8 (82)	47.7 (248)	61.5 (203)	49.6 (119)	52.4 (132)
Self-employed	7.0 (135)	7.0 (102)	2.5 (3)	5.2 (27)	11.2 (37)	7.5 (18)	6.7 (17)
Looking for employment	9.4 (182)	10.3 (150)	14.9 (18)	6.2 (32)	18.5 (61)	12.5 (30)	3.6 (9)
Not in paid employment	25.5 (493)	24.1 (352)	8.3 (10)	37.1 (193)	2.7 (9)	23.3 (56)	33.3 (84)
Studying	5.7 (110)	5.1 (75)	6.6 (8)	3.8 (20)	6.1 (20)	7.1 (17)	4.0 (10)
No. of years disease duration, median (range)	8.0 (0–47)	8.0 (0–47)	7.0 (0–36)	9.0 (0–41)	9.0 (0–47)	8.0 (0–32)	6.0 (0–36)
No. of respondents	2064	1561	139	535	355	267	265

TABLE 2 Mean LupusQoL domain score for all respondents and by presence or absence of fatigue

LupusQoL domain	Mean (s.d.) LupusQoL score ^a		
	All participants	Patients with no fatigue (FSS <4)	Patients with fatigue (FSS ≥4)
Physical health	58.7 (25.5)	82.2 (19.3)	53.8 (23.9)*
No. of respondents	1845	313	1532
Pain	57.6 (29.6)	81.0 (22.1)	52.8 (28.6)*
No. of respondents	1823	309	1514
Planning ^b	58.6 (31.7)	84.9 (22.1)	53.2 (30.7)*
No. of respondents	1822	308	1514
Intimate relationship ^c	63.6 (33.2)	84.3 (24.8)	59.4 (33.1)*
No. of respondents	1800	306	1494
Burden to others	45.2 (32.0)	68.8 (27.6)	40.3 (30.7)*
No. of respondents	1826	309	1517
Emotional health	61.0 (24.6)	76.9 (21.5)	57.7 (23.9)*
No. of respondents	1811	311	1500
Body image	61.1 (28.8)	74.2 (27.4)	58.9 (28.5)*
No. of respondents	1171	163	1008
Fatigue	46.5 (26.4)	74.7 (21.2)	40.7 (23.4)*
No. of respondents	1830	312	1518

^aRange for all scores: 0–100; higher scores indicate a better HRQoL. ^bInability to plan due to disease unpredictability. ^cThe effect of SLE on the level of interest in an intimate relationship. *Fatigue vs no fatigue (*t*-test); *P* < 0.001.

TABLE 3 Relationship between LupusQoL and self-reported effect of SLE on career (*P* < 0.001)

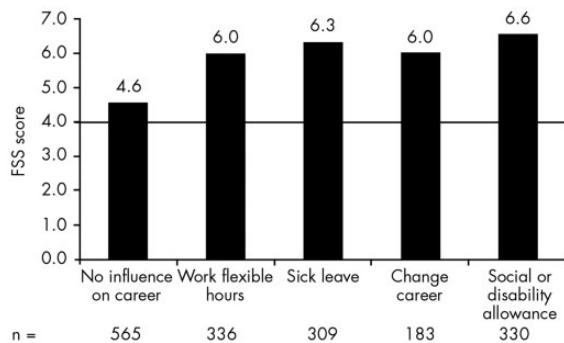
	No influence on career	Work flexible hours	Sick leave	Change career	Social or disability allowance
Mean (s.d.) LupusQoL score ^a					
Physical health	76.7 (20.8)	57.2 (20.4)	52.6 (24.0)	58.1 (20.3)	37.7 (22.7)
No. of respondents	544	328	298	179	327
Pain	75.1 (24.8)	57.2 (27.6)	49.8 (28.9)	54.4 (25.1)	38.3 (27.8)
No. of respondents	535	324	293	178	323
Planning ^b	80.4 (24.1)	56.3 (29.3)	47.4 (30.3)	55.7 (27.8)	37.5 (27.8)
No. of respondents	536	323	295	177	323
Intimate relationship ^c	78.6 (28.7)	64.5 (30.1)	53.9 (32.8)	65.4 (29.8)	47.4 (33.6)
No. of respondents	530	323	290	175	320
Burden to others	60.4 (30.4)	43.9 (31.0)	35.2 (30.4)	41.2 (29.5)	33.6 (30.4)
No. of respondents	536	324	294	179	322
Emotional health	70.4 (22.9)	59.8 (24.1)	54.6 (24.0)	59.2 (24.0)	53.7 (24.3)
No. of respondents	536	320	291	179	315
Body image	70.2 (25.6)	59.7 (30.1)	55.6 (30.2)	65.4 (28.0)	54.1 (28.2)
No. of respondents	342	218	133	125	266
Fatigue	62.1 (25.5)	43.6 (23.0)	39.2 (24.8)	41.7 (23.6)	33.3 (23.3)
No. of respondents	540	325	295	179	320

^aRange for all scores: 0–100; higher scores indicate a better HRQoL. ^bInability to plan due to disease unpredictability. ^cThe effect of SLE on the level of interest in an intimate relationship.

of SLE and 40.4% reported impairment in the amount or nature of tasks that they could do while at work. Overall, 43.2% reported impairment in work-related productivity and 55.8% reported impairment of activities outside of work (housework, shopping, studying, exercising, etc.).

Those with fatigue (FSS score ≥ 4) reported higher rates of impairment (i.e. worse productivity) across all four WPAI domains than those without fatigue: absenteeism (16.4% vs 2.5%), presenteeism (44.7% vs 20.5%), work impairment (48.7% vs 21.4%) and activity impairment (61.6% vs 29.1%). In addition, respondents whose careers had been

Fig. 1 Respondent-reported mean FSS scores based on the effects of SLE on career.



FSS score ≥ 4 indicates fatigue; $P < 0.001$ for those self-reporting an effect on their career vs those who self-reported no effect.

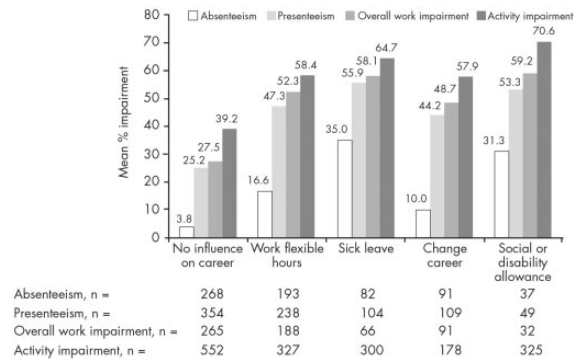
affected by SLE reported significantly worse productivity than those not affected ($P < 0.001$; Fig. 2); e.g. those receiving social or disability allowance because of SLE reported much higher impairment in regular daily activities (other than work) than those reporting no effect of SLE on their careers (70.6% vs 39.2%; Fig. 2). Interestingly, even respondents whose careers had not been affected by SLE still reported impairments across all four WPAI domains (Fig. 2).

The multivariate analyses identified variables associated with impairment for each WPAI domain (Table 4 and supplementary Tables S3–S6, available as supplementary data at *Rheumatology* Online) that explained 14–56% of their variability. Difficulties in performing physical activities (the LupusQoL physical health domain) was strongly associated with all four WPAI domains. Both measures of fatigue included in the survey (the LupusQoL fatigue domain score and FSS score) as well as the inability to plan activities (the LupusQoL planning domain score) were independently associated with all of the WPAI domains except absenteeism. Other variables that were significantly associated with one or more WPAI domains and were thus retained in the final model were the LupusQoL domains emotional health and pain (Table 4).

Differences in responses between five main countries

The number of responders exceeded 100 in five countries (France, Germany, Italy, Spain, UK; Table 1). Chi-square tests showed significant differences ($P < 0.001$) between individual country cohorts and all five countries combined in education level, age, parental status, current corticosteroid use, current antimalarial use, current immunosuppressant use, effect on career, current SLE disease activity in the skin and current SLE disease activity in the muscles and joints (supplementary Tables S7–S9, available at *Rheumatology* Online). A one-way ANOVA found that the mean WPAI activity impairment score, FSS score, and all LupusQoL domains also differed

Fig. 2 Relationship between mean WPAI impairment (%) and career.



$P < 0.01$ for those self-reporting an effect on their career vs those who self-reported no effect.

between country cohorts ($P < 0.001$; supplementary Table S10, available at *Rheumatology* Online).

Discussion

The burden of SLE disease, as reported by patients in this online survey, is substantial. Patients whose careers were affected by SLE had significantly lower HRQoL, higher levels of fatigue and worse productivity than patients whose careers were not affected. Fatigue, an inability to plan and reduced physical and emotional health were all significantly associated with impaired productivity. These results are consistent with those of the first European online survey [25].

In this survey the most affected LupusQoL domains were burden to others and fatigue, consistent with the results of an earlier report on SLE patients where fatigue and burden to others were also the most affected domains [18]. Interestingly, all LupusQoL domain scores in the LEO survey were lower than those reported in this earlier study. As most studies of SLE patients have used generic instruments such as the SF-36 to measure HRQoL, comparison of the LEO survey with other studies is difficult [6]. However, previous studies have shown a strong correlation between comparable domains of the LupusQoL and SF-36 questionnaires in SLE patients [18, 33], and further work is under way to compare these two instruments in patients with moderate to severe SLE disease activity [34].

The FSS was developed and tested on patients with SLE and has been used in the majority of studies exploring fatigue in these patients. Most respondents (82.5%) in the LEO survey reported fatigue (FSS score ≥ 4), which is consistent with fatigue being one of the most affected LupusQoL domains, and consistent with results in previous studies [20, 35].

SLE symptoms can often begin between 15 and 25 years of age, at the career-building phase of life. This survey showed that SLE burden negatively affected a patient's productivity and career choices. More than

TABLE 4 Variables significantly ($P < 0.01$) associated with the different WPAI domains

	Point estimate	95% CI	P	R ^{2a}
Absenteeism				0.1418
LupusQoL, physical health	-0.408	-0.491, -0.324	<0.001	
Presenteeism				0.4352
LupusQoL, planning	-0.170	-0.244, -0.095	<0.001	
LupusQoL, fatigue ^b	-0.164	-0.256, -0.071	<0.001	
LupusQoL, physical health	-0.250	-0.354, -0.146	<0.001	
LupusQoL, emotional health	-0.129	-0.210, -0.048	0.002	
Fatigue (FSS score ≥ 4) ^a	5.746	1.425, 10.067	0.009	
Overall work impairment				0.4642
LupusQoL, fatigue ^b	-0.257	-0.356, -0.157	<0.001	
LupusQoL, physical health	-0.301	-0.425, -0.178	<0.001	
LupusQoL, planning	-0.170	-0.256, -0.084	<0.001	
Fatigue (FSS score ≥ 4) ^b	8.785	3.781, 13.790	<0.001	
Country				
UK	-	-		
Spain	-4.765	-10.759, 1.229		
Italy	5.325	-0.080, 10.570		
Germany	2.587	-2.523, 7.697		
France	-2.233	-9.139, 4.673	0.007	
Activity impairment				0.5635
LupusQoL, physical health	-0.322	-0.390, -0.255	<0.001	
Fatigue (FSS score ≥ 4) ^b	10.971	8.056, 13.886	<0.001	
LupusQoL, fatigue ^b	-0.171	-0.230, -0.112	<0.001	
LupusQoL, planning	-0.102	-0.149, -0.056	<0.001	
LupusQoL, emotional health	-0.079	-0.129, -0.030	0.002	
LupusQoL, pain	-0.080	-0.133, -0.027	0.003	

^aEstimates the extent to which the variables shown predict each domain score (e.g. the three variables shown for absenteeism predict 14% of the absenteeism score). ^bFatigue measured by both the LupusQoL questionnaire (as an HRQoL domain) and the FSS questionnaire (as a mean across nine items that each look at the effect of fatigue in different areas of a respondent's life). For FSS, the higher the score, the greater the level of fatigue. For LupusQoL, the higher the score, the lower the level of fatigue.

two-thirds of respondents reported that SLE had affected their career, with one-third having changed careers within the first year of their diagnosis. A similarly high rate of employment changes was found in a structured cohort survey of 982 US patients [23]. Moreover, approximately half of respondents to the LEO survey reported that they were either looking for employment or not in paid employment; this is likely to be a result of their SLE disease. Such numbers are consistent with the 46% unemployment found in the structured cohort survey [23], although they are higher than the 33% reported in a recent general literature review of 26 publications on SLE and employment [22].

In addition to employment status, consideration should also be given to the effect of SLE on presenteeism and productivity outside of work. While many European studies have shown that SLE can lead to loss of employment [36–40], few have shown that SLE can reduce overall productivity outside of paid employment [41, 42]. As SLE occurs predominantly in women of childbearing age, who often have the responsibility of childcare and housework, productivity losses outside of paid employment are particularly important to measure and understand [12, 24, 43]. In the

LEO survey, respondents reported that SLE impaired the amount or nature of work they could do (presenteeism) as well as their general activities outside of work (such as housework, shopping, studying, exercising, etc.).

Multivariate analysis modelling identified variables that were significantly associated with productivity impairment as assessed by the four WPAI domains. Notably, the two measures of fatigue in the survey (FSS and LupusQoL fatigue) were both independently associated with three domains (presenteeism, overall work impairment and activity impairment), suggesting that these PROs measure complementary aspects of fatigue in SLE patients. Neither measure was associated with absenteeism, which may indicate that while fatigue levels in SLE patients are sufficient to impair performance at work, they do not entirely prevent patients from working. Chi-square and one-way ANOVA testing showed that some variables differed among responders from the five main countries (notably WPAI activity impairment score, FSS score, and all LupusQoL domain scores). Owing to the large number of potential confounding factors, our analyses could not be reasonably designed to determine what factors were driving these differences.

This analysis has the limitations commonly associated with open online patient surveys. As no inclusion or exclusion criteria were applied, the survey may not reflect SLE patients that fulfil four or more ACR classification criteria for SLE. In addition, the survey may not fully represent the general population; e.g. there is an over-representation of college- and university-educated respondents and some countries deviate from the rest with respect to demographic characteristics such as age distribution. There are also substantial differences in country-level responses, potentially complicating a generalized European interpretation of the data. Another limitation is that patients who do not have access to the Internet were not included in the survey, which may result in some groups being under-represented and a bias towards more highly qualified individuals or towards those from countries with more widespread Internet access. The survey can only include patients with the time and inclination to respond, and thus the true proportion of patients who work or who have childcare responsibilities may be different from that reported here. Another potential limitation is that because respondents were not obliged to respond to every item, each survey item had a varying number of respondents and some category sample sizes were relatively small. While the PRO questionnaires used in the LEO survey are validated instruments in their paper forms, they have not been validated when used in an electronic survey. In addition, respondents self-reported their SLE diagnosis and clinical features with no confirmation by physicians or other third parties. However, the profile was typical of SLE patients in SLE clinics. Lastly, in the WPAI questionnaire, respondents who are unemployed are asked to skip the work productivity questions; this may exclude some very ill patients who are unemployed and who will therefore complete only one question in this PRO on general impairment outside of work.

Despite these limitations, this survey clearly shows the substantial burden of SLE and the limitations of current treatment. There is a need for improved treatments for SLE to reduce the negative effects of this disease on patients' lives. Further work is needed to educate physicians and healthcare workers on the consequences of reduced HRQoL in SLE patients, to understand these associations better and to define the burden of SLE in individual countries.

Rheumatology key messages

- SLE is associated with low HRQoL and high levels of fatigue.
- SLE has negative effects on SLE patients' daily lives, productivity, and career choices.

Acknowledgements

The authors would like to thank the network of LUPUS EUROPE who participated in this survey, Christophe Gengler for data analysis, MAPI Consultancy for their

consulting support on the statistical analysis, Marinella Govoni for providing consultation during the setup of the survey and Nick Hicks of Commutateur for consultation and facilitation services. The authors would also like to thank Liz Haygreen, of Darwin Healthcare Communications, for provision of medical writing support. This article is dedicated to the memory of Mr Rudi Hocks, vice-chair of LUPUS EUROPE, who was instrumental in implementing the first survey in 2009. Rudi won great respect from all who met him for his untiring support for lupus patients throughout Europe and his determination to make lupus known worldwide. Rudi's work and vision live on.

Funding: This work was supported by UCB Pharma. UCB Pharma provided financial support for the organization, facilitation and communication of the survey to LUPUS EUROPE and funded the assistance of Liz Haygreen (Darwin Healthcare Communications) with medical writing support.

Disclosure statement: M.S. has received grants/research support from UCB Pharma. D.S.P. is an employee of UCB Pharma. C.G. has acted as a consultant for UCB Pharma, been a member of a speakers' bureau and has received honoraria from UCB Pharma. K.L. is a representative of LUPUS EUROPE. E.N. is an employee of UCB Pharma. D.I. received a consulting fee from UCB Pharma and donated it to charity. Y.N. is a representative of LUPUS EUROPE.

Supplementary data

Supplementary data are available at *Rheumatology* Online.

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