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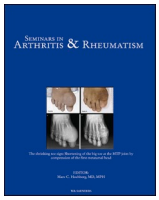

OMERACT systemic lupus erythematosus domain survey

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ABSTRACT

Background: Since the development of the OMERACT Systemic Lupus Erythematosus (SLE) Core Outcome Set (COS) in 1998, many new SLE domains have been identified and measures developed, creating a need to update the SLE COS. To revisit the 1998 SLE COS and research agenda domains, and generate new candidate domains, we conducted this study of patients with SLE and collaborators.
Objective: (1) To evaluate existing candidate SLE domains for inclusion in the SLE COS. (2) To generate additional candidate SLE domains for COS consideration. (3) To engage SLE collaborators, including patients, in developing the updated SLE COS.
Methods: The OMERACT SLE Working Group's steering committee developed a survey to assess the importance of candidate SLE domains and generate additional domains for consideration towards the SLE COS. Patients with SLE followed at the University of Toronto Lupus Clinic (patient group) and members of the OMERACT SLE Working Group (collaborator group) were invited to complete the survey between August 2022 and February 2023.
Results: A total of 175 patients were invited and 100 completed the survey. Of 178 collaborators invited, 145 completed the survey. Patients tended to prioritize life-impact domains while collaborators prioritized clinical domains. Both patients and collaborators recommended additional domains to those included in the 1998 SLE COS and research agenda.
Conclusion: The domain inclusion and importance results demonstrate that patients and collaborators prioritize different domains, so capturing the perspectives of both groups is essential to ensure a holistic assessment of SLE. The results of the study identify domains that already have a high level of agreement for potential inclusion in the SLE COS, domains that require further explanation, and novel domains that warrant consideration.

Background

Systemic Lupus Erythematosus (SLE) is a chronic multisystemic autoimmune disease with heterogeneous clinical manifestations characterized by recurrent flares in disease activity and damage in several organs [1,2]. The multisystemic nature of SLE has necessitated multiple outcome measures to be utilized in SLE randomized controlled trials (RCTs) and longitudinal observational studies (LOS) [1–4]. To standardize measurement in these clinical trials, the Outcome Measures in Rheumatology (OMERACT) SLE Working Group developed a Core Outcome Set (COS) for SLE in 1998 [5]. A COS is a set of outcome measures capturing the most important domains of a disease according to patients and investigators standardizing outcome measurement and reporting [4,5]. Many novel pertinent SLE domains and measures have been identified and developed since 1998 [1] necessitating an update of the SLE COS.

In 2018, a new OMERACT SLE Working Group was established to update the SLE COS [6]. The OMERACT SLE Working Group is undertaking multiple projects for this purpose. In the current study, we conducted a domain survey of collaborators, including patients, clinicians, researchers, members of the pharmaceutical industry, and more. The 1998 SLE COS did not have patient participation in its development creating a lack of patient representation which the updated SLE COS will address.

The primary purpose of this domain survey was to evaluate the continued importance of existing candidate SLE domains for potential inclusion in the updated SLE COS. The second purpose of the study was to further identify candidate SLE domains for SLE COS consideration. In addition, this study engaged different collaborators, including patients, to gain their unique perspectives in the development process of the new SLE COS.

Methods

Development of the survey

In 2022, the OMERACT SLE Working Group Steering Committee met every two weeks for a total of 10 meetings to discuss the list of candidate SLE domains to include in the domain survey. Domains from the 1998 OMERACT SLE COS and research agenda [4] (domains considered but did not meet inclusion requirements for the 1998 SLE COS) were retrieved and adapted to current-day terminology which resulted in 10 domains: Disease Activity, Damage, Health-Related Quality of Life, Tolerability / Adverse Events / Death, Economic Cost, Fatigue, Functional Ability, Psychosocial Factors, Work Status, and Comorbidities. An additional 8 domains commonly found in SLE research were proposed by the Steering Committee: Pain, Depressive Symptoms, Anxiety, Cognitive Function, Frailty, Sleep, Pregnancy, and Use of Steroids Including Demonstrated Tapering. The survey was written in lay English with simple straightforward questions (**Appendix A**).

Survey components

The survey began with an introduction to COS and the purpose of updating the OMERACT SLE COS. Following the introduction, the respondent was presented with a list of all 18 domains in the survey. Each domain had 2 questions relating to potential inclusion and its importance for the SLE COS. The inclusion question asked respondents whether the domain should be considered for inclusion in the SLE COS with response options (Yes, No, I don't know). The second question asked respondents to rank the importance of the domain for inclusion in the SLE COS graded on a 1–9 Rating Scale with 1 being least important and 9 being critically important. Respondents were given the opportunity to explain the reasoning for their responses. In the domain of Disease Activity, additional questions were deemed necessary by the Steering Committee. These additional items focused on whether we should measure Patient Global Assessment of Disease Activity (PaGA), Physician Global Assessment of Disease Activity (PhGA), and Patient Global Impression of Change (PGIC). In addition, respondents were asked if we should use validated measurement tools to capture disease activity and recommend other ways to measure disease activity. Two additional questions asked if bone density and fibromyalgia should be included in the comorbidities domain (comorbidity questions). At the end of the survey, respondents were again presented with the list of the 18 domains and asked if any additional domains should be considered with response options (Yes, No, I don't know). If "yes", space was provided to name them.

Survey administration

The study was reviewed and approved by the University Health Network Research Ethics Board (UHN CAPCR ID: 22–5256). The survey was developed and administered using REDCap [7] between August 2022 and February 2023. Patients with SLE were recruited from the University of Toronto Lupus Clinic at the Toronto Western Hospital. Inclusion criteria required all patients to: (1) meet the American College of Rheumatology (ACR) revised criteria for the classification of SLE [8], or 3 ACR criteria along with having a typical biopsy lesion of SLE [9; (2) be aged 18 or older; (3) be able to read and understand English; and (4) (only required for the online survey) have access to e-mail and the internet. Patients who consented to participate were either e-mailed a web link and completed the survey anonymously or could complete a paper copy in the clinic which was anonymously entered. The survey was sent to 175 patients who received bi-weekly reminders for four weeks to complete the survey.

Collaborators from the OMERACT SLE Working Group were e-mailed a web link and completed the survey anonymously between August 2022 and February 2023. The survey was administered to 178 collaborators of the OMERACT SLE Working Group by email, with bi-weekly reminders for eight weeks.

For the purpose of this manuscript, patients with SLE followed at the University of Toronto Lupus Clinic will be referred to as the patient group, and other collaborators from the OMERACT SLE Working Group will be referred to as the collaborator group.

Sample size

A sample size calculation with a 10 % margin of error and 95 % confidence level was performed. The maximum heterogeneity (50/50) was assumed for the binary inclusion question (whether a domain should be considered for inclusion in the SLE COS). The calculation reveals any population size >20,000 requires a sample size of 96. In the example calculation, a population of 1,000,000 was used.

$$N_s = \frac{(N_p)(p)(1-p)}{(N_p-1)\left(\frac{B}{C}\right)^2 + (p)(1-p)}$$

$$= \frac{(1,000,000)(0.5)(1-0.5)}{(1,000,000-1)\left(\frac{0.1}{1.96}\right)^2 + (0.5)(1-0.5)} = 96$$

N_s = sample size, N_p = population size, p = proportion of population choosing one response, B = margin of error (10 % = 0.1), C = Z score with confidence interval (95 % = 1.96)

Statistical analysis

Statistical analysis was performed using Rstudio version 1.3.1073 (Integrated Development Environment for R. Rstudio, PBC, Boston, MA, USA) [10]. Summary statistics were performed for the inclusion variables, the importance variables, the additional disease activity questions, additional comorbidities questions, and the additional domains to consider question. Distributions for all variables were examined for normality using the Kolmogorov-Smirnov test and probability plots. Statistical tests to examine potential differences between the patient and collaborator groups were performed including a Chi-Squared test for the inclusion responses, the additional disease activity responses, the comorbidities responses, and the additional domains to consider questions (Yes, No, I don't know). A Mann-Whitney U test was performed for the importance variables (1–9 Rating Scale). An additional Chi-square test was performed to compare solely the "Yes" and "No" responses of the patient and collaborator groups inclusion variables and additional questions to test for significant differences.

Results

There were 100 responses from the 175 patients with SLE approached (57.1 % response rate) and 145 responses from the 178 collaborators invited (81.5 % response rate). The collaborator group was comprised of clinician researchers (78 %), clinicians (8 %), researchers (6 %), members of the pharmaceutical industry (4 %), nurses (2 %), and others (2 %).

Responses of the inclusion questions

Table 1 contains the responses of patients and collaborators regarding the candidate domains inclusion in the SLE COS. Across all domains, the percentage of patients who supported inclusion consideration (responded "Yes") for a given domain ranged from 61 % to 96 %, while the percentage of collaborators ranged from 45 % to 98 %. Large and unique differences were observed between patients and collaborators. Domains preferred by patients included Fatigue, Pain, Depressive Symptoms, Anxiety, Cognitive Function, Frailty, Comorbidities, and Sleep. By contrast, collaborators favoured Disease Activity, Damage, and

Table 1
Consideration of domains for inclusion in the SLE COS.

Domain	Total (n = 245)				Patients (n = 100)				Collaborators (n = 145)			
	Yes n (%)	No n(%)	I don't know n(%)	missing	Yes n (%)	No n (%)	I don't know n(%)	missing	Yes n (%)	No n(%)	I don't know n(%)	missing
Disease Activity	226 (92.24)	2(0.82)	17(6.94)	0	84 (84.00)	1 (1.00)	15(15.00)	0	142 (97.93)	1(0.69)	2(1.38)	0
Damage	215 (88.84)	5(2.07)	22(9.09)	3	79 (79.00)	1 (1.00)	20(20.00)	0	136 (95.77)	4(2.82)	2(1.41)	3
Health Related Quality of Life	230 (94.65)	3(1.23)	10(4.12)	2	94 (94.95)	1 (1.01)	4(4.04)	1	136 (94.44)	2(1.39)	6(4.17)	1
Tolerability / Adverse Events / Death	205 (84.02)	9(3.69)	30(12.30)	1	77 (77.78)	5 (5.05)	17(17.17)	1	138 (88.28)	4(2.76)	13(8.97)	0
Economic Cost***	148 (60.91)	34 (13.99)	61(25.10)	2	61 (61.52)	5 (5.05)	33(33.33)	1	87 (60.42)	29 (20.14)	28(19.44)	1
Fatigue	211 (86.12)	14 (5.71)	20(8.16)	0	91 (91.00)	4 (4.00)	5(5.00)	0	120 (62.76)	10(6.9)	15(10.34)	0
Functional Ability	223 (91.39)	7(2.87)	14(5.74)	1	92 (92.93)	0(0)	7(7.07)	1	131 (90.34)	7(4.83)	7(4.83)	0
Psychosocial Factors	160 (65.84)	16 (6.58)	67(27.57)	2	68 (68.69)	3 (3.03)	28(28.28)	1	92 (63.89)	13 (9.03)	39(27.08)	1
Work Status*	177 (72.54)	32 (13.11)	35(14.34)	1	76 (76.00)	7 (7.00)	17(17.00)	0	101 (70.14)	25 (17.36)	18(12.50)	1
Comorbidities*	191 (78.60)	11 (4.53)	41(16.87)	2	69 (69.00)	3 (3.00)	28(28.00)	0	122 (85.31)	8(5.59)	13(9.09)	2
Pain***	204 (83.95)	20 (8.23)	19(7.82)	2	94 (95.92)	1 (1.02)	3(3.06)	2	110 (75.86)	19 (13.10)	16(11.03)	0
Depressive Symptoms**	193 (79.10)	27 (11.07)	24(9.84)	1	88 (88.89)	3 (3.03)	8(8.08)	1	105 (72.41)	24 (16.55)	16(11.03)	0
Anxiety***	167 (68.44)	44 (18.03)	33(13.52)	1	84 (84.85)	6 (6.06)	9(9.09)	1	83 (57.24)	38 (26.21)	24(16.55)	0
Cognitive Function** ^	192 (78.69)	20 (8.20)	32(13.11)	1	84 (84.00)	1 (1.00)	15(15.00)	0	108(75)	19 (13.19)	17(11.81)	1
Frailty***	145 (59.67)	51 (2.099)	47(19.34)	2	68 (68.00)	7 (7.00)	25(25.00)	0	77 (53.85)	44 (30.77)	22(15.38)	2
Sleep***	149 (61.07)	56 (22.95)	39(15.98)	1	84 (84.00)	7 (7.00)	9(9.00)	0	65 (45.14)	49 (34.02)	30(20.83)	1
Pregnancy*	173 (71.19)	29 (11.93)	41(16.87)	2	70 (70.71)	5 (5.05)	24(24.00)	1	103 (71.53)	24 (16.67)	17(11.81)	1
Use of Steroids Including Demonstrated Tapering	212 (87.24)	7(2.88)	24(9.88)	2	84 (84.00)	2 (2.00)	14(14.00)	0	128 (89.51)	5(3.50)	10(6.99)	2

Chi-squared test (Yes-No only) : * = significant $p < 0.05$, ** = significant $p < 0.005$, *** = significant $p < 0.0005$ | Chi-Square test: ^ = significant $p < 0.05$.

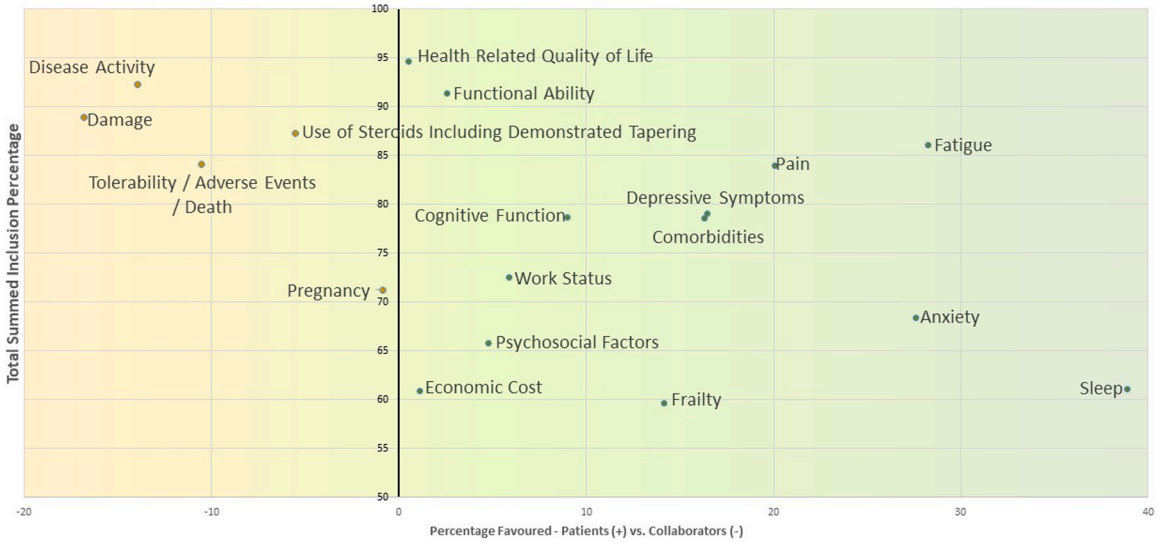

Fig. 1. Domain SLE COS inclusion consideration preferences
Scatter plot of total summed percentage of inclusion "Yes" responses versus the difference of percentage of inclusion "Yes" responses between the patient group and collaborator group. The green/right side of the graph and green points represent domains that patients preferred, while the yellow/left side of the graph and yellow points represent domains collaborators preferred. The numbers on the X-axis depict the difference in the percentage of "Yes" responses of total responses between the patient and collaborator groups. Domains close to 0 on the X-axis represent domains where patients and collaborators demonstrated similar levels of agreement levels regarding inclusion.

Tolerability / Adverse Events / Death. Domains similarly ranked by both groups were Health-Related Quality of Life, Functional Ability, Psychosocial Factors, Work Status, Economic Cost, Pregnancy, and Use of Steroids Including Demonstrated Tapering. The results of Table 1 are illustrated in Fig. 1.

Responses of the importance questions

Table 2 presents the importance ratings of domains by patients and collaborators on a 1–9 rating scale. Domains rated more important by patients included Economic Cost, Fatigue, Functional Ability, Psychosocial Factors, Work Status, Pain, Depressive Symptoms, Anxiety, Cognitive Function, Frailty, Sleep, and Pregnancy. Domains favored by collaborators were Disease Activity, Damage, and Tolerability / Adverse Events / Death. Domains with similar importance ratings between both groups include Health-Related Quality of Life, Comorbidities, and Use of Steroids Including Demonstrated Tapering. The results of Table 2 are illustrated in Fig. 2.

Explanations of responses to the inclusion and importance questions

Many of the respondents provided statements to support their selection and importance responses. The majority of the respondents agreed that most domains were important, with only a few not considered clinically relevant. For example, "although [Sleep] is an important aspect of daily life[,] I don't know how […] relevant [it is] in the overall management of the disease" (Collaborator Response). Some respondents provided low ratings to domains that they discovered difficult to measure, "[Cognitive Function is] too difficult to standardize and collect uniformly. An important outcome in many [longitudinal studies] but difficult in RCTs" (Collaborator Response). Similarly, candidate domains were rated lower if their attribution to SLE was complex or unclear. For example, "[f]or anxiety[,] the difficulty in the attribution is even more difficult" (Collaborator Response). Patients rated most domains of high importance, but in particular emphasized the importance of domains that resonated with their experience of SLE, "in my case the permanent decline [in cognitive function] came gradually and escalate[d] during flares. For example, something as simple as playing poker or instructions on learning a new game [was difficult], never mind completing tasks at work" (Patient Response). Another reason patients scored certain domains low appeared to be due to a lack of understanding of what the domain comprises, "I do not know what "damage" includes" (Patient Response). A sample of patient and collaborator quotes explaining domain inclusion and importance responses are reported in **Appendix B**.

Responses of additional disease activity questions

Table 3 shows responses to the additional disease activity questions. There was a high level of agreement among collaborators for capturing PaGA and PhGA, whereas patients were more unclear on the topic voting more often "I don't know". Both the patient and collaborator groups had a similar level of agreement with approximately 60 % of votes indicating "Yes" to capturing PGIC. However, the remainder of the responses for

Table 2
Importance of domains for the SLE COS.

	Rating Scale Scoring Total (n = 245)				Rating Scale Scoring Patients (n = 100)				Rating Scale Scoring Collaborators (n = 145)			
Domain	9–7 n(%)	6–4 n (%)	3–1 n (%)	Missing	9–7 n (%)	6–4 n (%)	3–1 n (%)	Missing	9–7 n(%)	6–4 n (%)	3–1 n (%)	Missing
Disease Activity***	209 (93.30)	13 (5.80)	2(0.89)	21	70 (86.42)	9 (11.11)	2(2.47)	19	139 (97.20)	4(2.80)	0(0)	2
Damage***	178 (82.41)	37 (17.13)	1(0.46)	29	57 (76.00)	17 (22.67)	1(1.33)	25	121 (85.82)	20 (14.18)	0(0)	4
Health Related Quality of Life	208 (92.04)	17 (7.52)	1(0.44)	19	82 (96.47)	3(3.53)	0(0)	15	126 (89.36)	14 (9.93)	1(0.71)	4
Tolerability / Adverse Events / Death	182 (86.26)	24 (11.37)	5(2.37)	34	59 (84.29)	8 (11.42)	3(4.29)	30	123 (87.23)	16 (11.35)	2(1.42)	4
Economic Cost***	114 (59.69)	55 (28.80)	22 (11.52)	54	46 (82.14)	9 (16.07)	1(1.79)	44	68 (50.37)	46 (34.07)	21 (15.56)	10
Fatigue***	184 (82.14)	31 (13.84)	9(4.02)	21	82 (97.62)	1(1.19)	1(1.19)	16	102 (72.86)	30 (21.43)	8(5.71)	5
Functional Ability***	180 (80.72)	40 (17.94)	3(1.35)	22	76 (92.68)	6(7.32)	0(0)	18	104 (73.76)	34 (24.11)	3(2.13)	4
Psychosocial Factors***	125 (60.98)	69 (33.66)	11 (5.37)	40	57 (85.07)	9 (13.44)	1(1.49)	33	68 (49.28)	60 (43.48)	10 (7.24)	7
Work Status***	145 (72.50)	46 (23.00)	9(4.50)	45	61 (89.71)	7 (10.29)	0(0)	32	84 (63.64)	39 (29.55)	9(6.81)	13
Comorbidities*	175 (84.13)	28 (13.46)	5(2.40)	37	61 (89.71)	7 (10.29)	0(0)	32	114 (81.43)	21 (15.00)	5(3.57)	5
Pain***	169 (75.78)	46 (20.63)	8(3.59)	22	82 (92.13)	6(6.74)	1(1.12)	11	87 (64.93)	40 (29.85)	7(5.22)	11
Depressive Symptoms***	162 (75.70)	39 (18.22)	13 (6.07)	31	77 (96.25)	2(2.50)	1(1.25)	20	85 (63.43)	37 (27.61)	12 (8.96)	11
Anxiety***	125 (63.45)	53 (26.90)	19 (9.64)	48	69 (93.24)	5(6.76)	0(0)	26	56 (45.53)	48 (39.02)	19 (15.45)	22
Cognitive Function***	154 (75.12)	44 (21.46)	7(3.41)	40	68 (90.67)	7(9.33)	0(0)	25	86 (66.16)	37 (28.46)	7(5.38)	15
Frailty***	109 (57.67)	57 (30.16)	23 (12.17)	56	55 (83.33)	10 (15.15)	1(1.52)	34	54 (43.90)	47 (38.21)	22 (17.89)	22
Sleep***	116 (60.73)	53 (27.75)	22 (11.52)	54	72 (91.14)	6(7.59)	1(1.27)	21	44 (39.29)	47 (41.96)	21 (18.75)	33
Pregnancy	150 (77.32)	32 (16.49)	12 (6.19)	51	54 (84.38)	10 (15.62)	0(0)	36	96 (73.85)	22 (16.92)	12 (9.23)	15
Use of Steroids Including Demonstrated Tapering	188 (87.44)	24 (11.16)	3(1.40)	30	68 (91.89)	6(8.11)	0(0)	26	120 (85.10)	18 (12.77)	3(2.13)	4

Mann-Whitney U test : * = significant $p < 0.05$, ** = significant $p < 0.005$, *** = significant $p < 0.0005$.

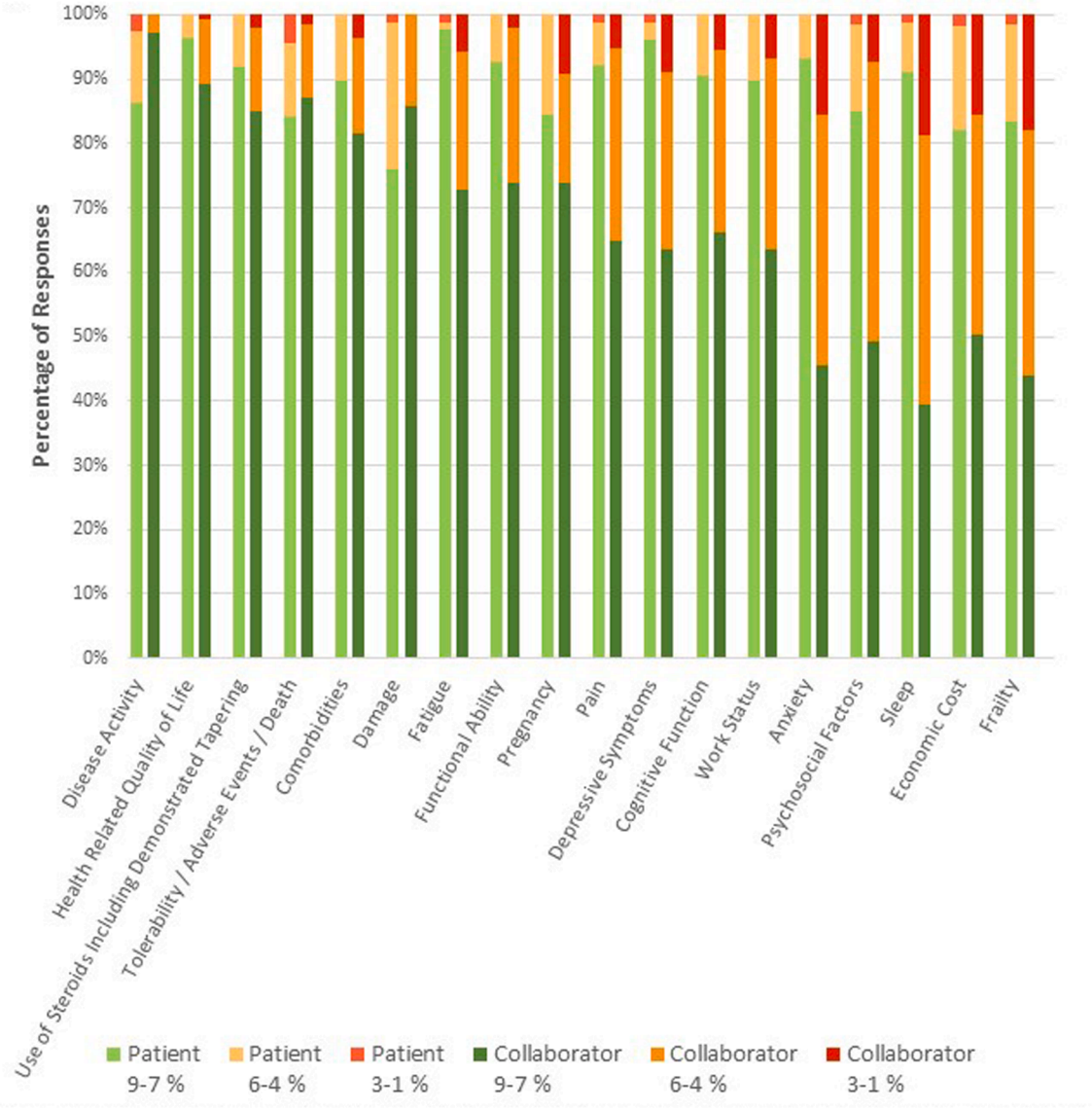

Fig. 2. Importance scores of domains for the SLE COS
Stacked column chart of the percentage of rating scale scores in the 9–7 (green), 6–4 (yellow), and 3–1 (red) ranges for the patient group (left columns/lighter colours) and collaborator group (right columns/darker colours). The green represents 9–7 (high importance) percentage of scores, yellow represents 6–4 (medium importance) percentage of scores, and red represents 3–1 (low importance) percentage of scores. Domains are organized left to right by the overall summed percentage of responses in the 9–7 category from both groups with higher scores on the left.

patients were mostly "I don't know", whereas there were more "No" responses for the collaborator group. When asked about measuring Disease Activity using validated tools, patient responses were split between "Yes" and "I don't know", while almost all collaborators responded "Yes". Lastly, when asked "are there other ways to measure Disease Activity", patients mostly selected "I don't know" and collaborators had "Yes" for half of their responses with the remaining split among "No" and "I don't know". The results in Table 3 are illustrated in Fig. 3.

There was a good level of agreement between patients and collaborators for measuring disease activity using validated tools, measuring PaGA, and measuring PhGA. Each method of measuring disease activity was supported by approximately 80 % of respondents in the "Yes" category and was favoured by the collaborators. PGIC had a slightly lower level of agreement overall with 62 % of responses in the "Yes" category and was favoured slightly by patients. Respondents were also requested to suggest additional ways to measure disease activity which are reported in Appendix C.

Responses of comorbidities questions

Table 4 shows the responses to the additional comorbidities questions. Patients responded "Yes" for including Bone Density in the Comorbidities domain to a greater extent (85 %) compared to collaborators (55 %). The two groups yielded a similar percentage of "Yes" votes to include Fibromyalgia in the Comorbidities domain (68 %), though again the collaborators yielded a much higher percentage of votes for "No" while patients had a higher percentage of "I don't know" votes. Respondents were requested to suggest additional comorbidities to include, which are reported in Table 5.

Of note, eight identical potential comorbidities were recommended by both patients and collaborators. Each group identified several unique potential comorbidities with many related between the groups.

Responses of additional domains to consider for the sle cos question

Total summed responses were similarly split between "Yes" (37 %),

Table 3
Additional Disease Activity questions.

Domain	Total (n = 245)				Patients (n = 100)				Collaborators (n = 145)			
	Yes n (%)	No n (%)	I don't know n(%)	missing	Yes n (%)	No n (%)	I don't know n(%)	missing	Yes n (%)	No n (%)	I don't know n (%)	missing
Should we measure Patient Global Assessment of Disease Activity?	193 (78.78)	12 (4.90)	40 (16.33)	0	65 (65.00)	3 (3.00)	32 (32.00)	0	123 (88.28)	9(6.21)	8(5.52)	0
Should we measure Physician Global Assessment of Disease Activity?	204 (83.95)	8(3.29)	31 (12.76)	2	73 (73.00)	1 (1.00)	26 (26.00)	0	131 (91.61)	7(4.90)	5(3.50)	2
Should we measure Patient Global Impression of Change? **	152 (62.30)	31 (12.70)	61 (25.00)	1	66 (66.00)	4 (4.00)	30 (30.00)	0	86 (59.72)	27 (18.75)	31(21.53)	1
Should we measure disease activity using validated tools (ex. SLEDAI, BILAG, and others)?	194 (79.51)	4(1.64)	46 (18.85)	1	58 (58.00)	2 (2.00)	40 (40.00)	0	136 (94.44)	2(1.39)	6(4.17)	1

Chi-squared test (Yes-No only) : * = significant $p < 0.05$, ** = significant $p < 0.005$, *** = significant $p < 0.0005$ | Chi-Square test: ^ = significant $p < 0.05$.

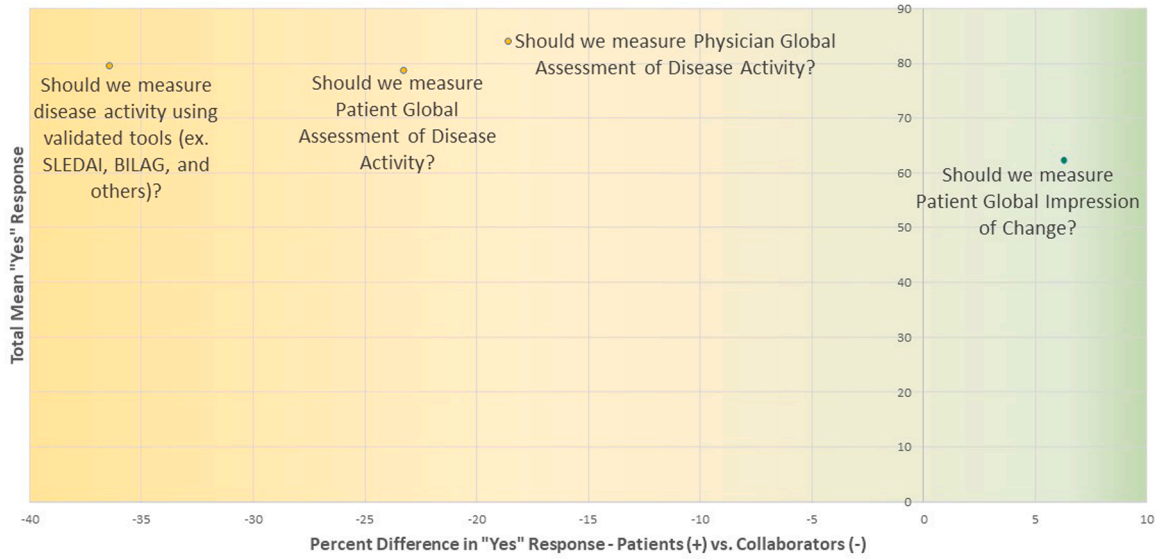

Fig. 3. Additional Disease Activity questions
Scatter plot of total summed percentage of "Yes" responses versus the percentage difference in "Yes" responses between the patient group and the collaborator group. The green/right side of the graph and green point represent items that patients preferred (had a higher percentage of "Yes" votes), while the yellow/left side of the graph and yellow points represent items collaborators preferred. Items close to 0 on the X-axis represent having similar levels of agreement between patients and collaborators.

Table 4
Additional Comorbidities questions.

Question	Total (n = 245)				Patients (n = 100)				Collaborators (n = 145)			
	Yes n (%)	No n (%)	I don't know n (%)	missing	Yes n (%)	No n (%)	I don't know n(%)	missing	Yes n (%)	No n (%)	I don't know n (%)	missing
Should we measure Bone Density in the Comorbidities domain?***	163 (67.36)	40 (16.53)	39(16.12)	3	85 (85.00)	1 (1.00)	14 (14.00)	0	78 (54.93)	39 (27.46)	25(17.61)	3
Should we evaluate for Fibromyalgia in the Comorbidities domain?**	164 (67.77)	31 (12.81)	47(19.42)	3	67 (67.00)	4 (4.00)	29 (29.00)	0	97 (68.31)	27 (19.01)	18(12.68)	3

Chi-squared test (Yes-No only) : * = significant $p < 0.05$, ** = significant $p < 0.005$, *** = significant $p < 0.0005$ | Chi-Square test: ^ = significant $p < 0.05$.

"No" (36 %), and "I don't know" (27 %). Patients were 25 % "Yes", 25 % "No", and 50 % "I don't know", while collaborators were 44 % "Yes", 44 % "No", and 12 % "I don't know". The Chi-squared tests identified no statistically significant difference between the patient and collaborator responses. The additional suggested domains by respondents are shown in Table 6.

The results reported in Table 6 are reported directly as written by respondents. Similar concepts are reported by patients and

Table 5
Additional Comorbidities to include in the Comorbidities domain.

Recommended by Patients	Recommended by Patients and Collaborators	Recommended by Collaborators
1. Body Pains	1. Antiphospholipid Syndrome	1. Arterial and Venous Thromboembolism aspects
2. Brain Fog	2. Anxiety	2. Coronary Artery Disease
3. Cancer	3. Cardiovascular Disease	3. Cardiovascular Morbidity
4. Cognitive Effects	4. Depression	4. Cognitive Function
5. Diabetes Mellitus	5. Diabetes	5. Chronic Obstructive Pulmonary Disease
6. Fibromyalgia	6. Infections	6. Dementia
7. Forgetfulness	7. Metabolic Impairments	7. Glomerular Filtration Rate
8. Irritable Bowel Syndrome	8. Osteoporosis	8. Hyperlipidemia
9. Idiopathic Thrombocytopenic Purpura		9. Obesity
10. Kidney Failure Dialysis		10. Osteoarthritis
11. Kidneys		11. Osteonecrosis
12. Lupus Nephritis		12. Papilloma Virus Infection
13. Malignancies		13. Poor Muscle Mass
14. Multiple Sclerosis		14. Renal Failure
15. Raynaud's Syndrome		15. Sleep Quality
16. Scleroderma		16. Stroke
17. Sjögren's Syndrome		
18. Thyroid		
19. Total Colectomy		

Table 6
Additional domains to consider for the SLE COS.

Domains and Concepts as Reported by Patients	Domains and Concepts as Reported by Collaborators
• Access to patient care	• Awareness of others
• Arthritis	• Body Image
• Availability of medical support and nutritional advice	• Comorbidities
• Cardiac risk	• Coping strategies
• Care management	• Covid-19
• Coordination of care	• Diagnostics
• Domains of people in remission	• Diet quality
• Drug interaction between SLE medication and other basic medication	• Discrimination
• Fertility	• Disease status
• Hair loss, beauty issues	• Ethnicity
• Heart Impacts	• Gender transition
• Hereditary markers and pregnancy/ inheriting	• Growth impact
• Impact of existing treatments	• Healthcare access
• Joint stiffness	• Impact on others
• Kidney impacts	• Memory effects
• Mobility	• Mortality
• Quality of care	• Patient beliefs
• Rashes	• Patient knowledge
• Raynaud's phenomenon	• Physical activity
• Self-esteem	• Role participation
• Supplements and diet	• Satisfaction
• Vision impairment/retina and eye problems/itching	• Self-efficacy
• Weight gain	• Severity
	• Sexuality
	• Side effects
	• Skin manifestations
	• Social functioning
	• Social support
	• Sociodemographic
	• Stress
	• Support
	• Therapeutic adherence
	• Treatment burden

collaborators, though no identical concepts were identified.

Discussion

The findings of this domain survey represent an important step in the identification of candidate domains for the SLE COS. The purpose of this survey was not to eliminate domains from consideration, but to evaluate the continued importance of 1998 SLE COS, re-evaluate the 1998 SLE COS research agenda domains, and evaluate known SLE domains proposed by the OMERACT SLE Steering Committee, in addition to identifying new candidate SLE domains. The survey also provided an opportunity to engage patients in COS development to gain their unique perspectives.

In general, the patient and collaborator groups agreed upon the consideration for inclusion of candidate domains for the SLE COS and rated their importance similarly. However, the domain survey revealed a trend with the patient group valuing life impact domains higher, while the collaborator group placed greater emphasis on clinical domains. These differences are understandable as the collaborator group is largely comprised of clinicians, particularly rheumatologists, and researchers who often focus on achieving remission through reduced disease activity and minimizing accrual of damage. On the other hand, patients experience the direct effects of SLE through life impact domains and prioritize the domains that they deem more impactful. Similar trends have been seen in other rheumatic conditions including rheumatoid arthritis where qualitative interviews revealed patients prioritised life impact domains [11] and psoriatic arthritis where a nominal group technique demonstrated patients favored life impact domains [12]. Furthermore, patients experience SLE differently because of the heterogenous manifestations of SLE where one patient can have predominantly skin rashes while another patient experiences lupus nephritis. This might have an implication on patient prioritizations for one domain over others. None of the domains were deemed unfit for the SLE COS by a majority of respondents, as no domain had more than 7 % of patients and 34 % of collaborators voting "No" for inclusion. The differing views of domain importance between the patients and collaborators demonstrate the importance of involving patients in SLE COS development. Including patients ensures that the new COS development captures patients' values and knowledge of how SLE impacts their lives with the differences in domain prioritizations reported further supporting the need to update the SLE COS.

The Importance ratings demonstrated significant differences between the two groups for most domains. However, there was a trend for patients to rate more domains higher for importance, which can explain the large number of significant differences. The Chi-squared tests only looking at (Yes, No) did reveal significant differences for many domains when few patients selected "No" while multiple collaborators did select "No". There was a lack of statistically significant differences in the inclusion questions when observing all responses with the Chi-squared test which can be in part attributed to many respondents selecting the "I don't know" response (ranging from 0 % to 33 % for patients and 0 % to 21 % for collaborators), which reduced the overall differences among the "Yes" and "No" responses between the two groups.

The 8 domains recommended for inclusion by the Steering Committee (Pain, Depressive Symptoms, Anxiety, Cognitive Function, Frailty, Sleep, Pregnancy, and Use of Steroids Including Demonstrated Tapering) had good agreement for SLE COS importance between the groups and scored relatively similarly to those domains retrieved from the 1998 SLE COS and research agenda. These domains have also been demonstrated to be important in other rheumatic conditions including psoriatic arthritis [13], myositis [14], and vasculitis [15].

With regards to the additional questions about measuring Disease Activity, collaborators had a similar percentage of votes for "Yes" for measuring PhGA, PaGA, and disease activity with validated tools at around 80 %, which was marginally higher than the percentage of patients voting "Yes". Slightly more patients voted "Yes" to measure PGIC than collaborators. Although collaborators had on average higher scores, the other responses of patients were mostly "I don't know" while the other votes from collaborators had many more "No" responses. In regards to the additional ways to measure disease activity, the majority of collaborators listed the name of currently existing tools in the SLE field while the patients' list was focused on explicit parameters of

disease activity such as blood work, biological factors, and imaging.

The Comorbidities domain demonstrated similar agreement between the groups for the inclusion of fibromyalgia, whereas patients favoured the inclusion of bone density over collaborators (85 % / 54.93 %). The additional comorbidities suggested will be reviewed and considered for the definition of the Comorbidities domain. Both groups proposed many important comorbidities. Of interest, the majority are already being measured in SLE studies with some specifically captured by the current Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) damage index (SDI) [16].

A limitation of the survey is that only 18 domains were included. For this reason, we included open-ended questions to allow respondents to elaborate on their responses. This is why we had a qualitative component to allow respondents to elaborate on the domains and suggest additional domains. Both groups suggested life-impact domains and concepts as well as more clinical domains and concepts. The suggested domains and concepts from this survey will be taken into consideration along with other domains generated by the ongoing scoping literature review and focus group interviews with SLE patients. There were no definitions for domains provided as agreed-upon definitions for SLE domains have not been established limiting the study and contributing to the misunderstanding of domains. This may be a contributing factor to the higher proportion of "I don't know" responses provided by the patients. Agreed upon definitions for the candidate domains are in development. Another limitation could be the diversity of the sample surveyed. The survey was only administered to an English-speaking population. The patient group was recruited from the University of Toronto Lupus Clinic, which does have a diverse population, though it may not have captured a substantial global representation of patients. The collaborator group consisted of a diverse group of 145 members of the OMERACT SLE Working Group representing 6 continents and over 26 countries, thus, although having a diverse global representation, it does not represent the same geographical region as the patient group. Though this study may not have a worldwide population of patients participating, other projects that are part of the initiative to update the OMERACT SLE COS had and will have a global population of patients participating.

The findings of this study along with the other initiatives by the OMERACT SLE working group will produce a final list of candidate domains [17]. These candidate domains will be put forth into a Delphi consensus exercise, an exercise to update the SLE COS where collaborators, including patients, will vote in multiple rounds on the importance of domains and review scores from each round. Definitions for domains will be prepared through literature review and assessed with a survey of domain definitions to achieve an agreement on definitions.

Conclusion

In conclusion, this study generated a large list of potential candidate domains that will be utilized for the update of the SLE COS. Although some of these domains are currently being utilized in different clinical trials and longitudinal studies, the survey also identified new important domains for patients and collaborators. Patients and collaborators emphasized different domains, supporting the importance of updating the SLE COS by engaging patients, clinicians, researchers, pharmaceutical representatives, and more in the process.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.semarthrit.2024.152520.

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