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Major Depression and Adverse Patient-Reported Outcomes in Systemic Lupus Erythematosus: Results from the California Lupus Epidemiology Study

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Abstract

Objective: Health-related quality of life (HRQoL) is reduced in SLE, partly driven by comorbid depression. The association between major depression among those with SLE and HRQoL measured using the National Institutes of Health's Patient-Reported Outcomes Measurement Information System (PROMIS) is not well characterized.

Methods: Cross-sectional data were obtained from the California Lupus Epidemiology Study (CLUES), a cohort of adults in the San Francisco Bay Area with SLE. We studied the association between major depression (score ≥ 10 on Patient Health Questionnaire [PHQ-8] depression scale)

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and T-scores (scaled to population mean of 50, SD of 10) on 12 PROMIS domains representing physical, mental, and social health. Mean T-scores in depressed and non-depressed individuals were compared using multiple linear regression models, adjusting for age, sex, race/ethnicity, disease activity, damage, body mass index (BMI), and household income.

Results: Mean age of the 326 participants was 45 years; approximately 89% were women, 29% white, 23% Hispanic, 10% black, and 36% Asian. One-quarter met criteria for major depression. In multivariable analyses, major depression was independently associated with worse T-scores on all 12 PROMIS domains ($p<0.001$); compared with those without major depression, depressed individuals scored more than 10 points (1 SD) worse on Fatigue, Sleep Impairment, Negative Psychosocial Impact of Illness, Satisfaction in Discretionary Social Activities, and Satisfaction in Social Roles.

Conclusion: In individuals with SLE, major depression is associated with markedly worse PROMIS scores in physical, mental, and social domains. Diagnosing and treating depression may help improve HRQoL in individuals with SLE.

Introduction

Mortality in individuals with systemic lupus erythematosus (SLE) has declined for several decades (1), shifting the focus of care to improving health-related quality of life (HRQoL). The term “health-related quality of life” encompasses the impact of health on an individual’s physical, mental, and social functioning (2). Individuals with SLE experience reduced HRQoL, at levels comparable to other major chronic conditions (3-5). Measures of SLE disease activity such as the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI) (6), and measures of chronic damage such as the Systemic Lupus International Cooperating Clinics/American College of Rheumatology Damage Index (SDI) (7) have important roles in assessing responses to interventions and in prognostication, but they do not predict HRQoL outcomes (8-11). This suggests that HRQoL in SLE is driven by factors not measured with these physician-assessed metrics. Major depression is one such potential unmeasured factor, as it is highly prevalent in SLE (12,13), and generally manifests with symptoms which may be missed in routine assessments of disease activity (14).

Previous studies have shown a correlation between the presence of depression in SLE and reduced HRQoL as measured by the Medical Outcomes Study Short Form (SF-36) (5,14,15). This work demonstrated the importance of depression in HRQoL domains covered by the SF-36 including pain, physical function, and social functioning (5). However, the SF-36 does not cover certain domains of health relevant to SLE, such as impairment in cognition and sleep, and it has limited content related to fatigue (16). The relationship between major depression and the HRQoL domains of most importance to individuals with SLE is less well understood. The Patient-Reported Outcomes Measurement Information System (PROMIS) is a publicly available set of person-centered measures for HRQoL, developed under the National Institutes of Health (NIH) Roadmap for Medical Research Initiative. PROMIS was designed for efficiency (minimizing item number while maintaining reliability), flexibility (allowing for the use of optional domains), and precision (minimizing estimate error), and for use across a wide range of chronic conditions (17,18). PROMIS potentially allows for more comprehensive HRQoL assessments in SLE (14,19), as it has

many available domains of particular relevance to SLE and allows comparison to other conditions using the same measures. A better understanding of the contribution of major depression to these domains will improve the ability to interpret these scores and highlight the importance of screening and referral for depressive symptoms.

The objective of this cross-sectional study was to determine the association between a proxy for major depression and HRQoL scores on 12 SLE-relevant health domains as measured by PROMIS. We also examined the relationship between major depression and scores on the SF-36 and its subcomponents. In addition, we compared characteristics of depressed and non-depressed individuals with SLE and tested the independent association between major depression and HRQoL by adjusting for socio-demographic factors and comorbidities.

Patients and Methods

Data Source

This was a cross-sectional analysis of individuals enrolled in the California Lupus Epidemiology Study (CLUES), a prospective longitudinal cohort of adults with SLE. The data collection method for this cohort has been described elsewhere (20) and is summarized here. Beginning in 2015, participants were recruited through the California Lupus Surveillance Project, which used medical and laboratory records to identify all individuals with SLE living in the City and County of San Francisco from 2007-2009 (21). Additional participants in the nine counties of the San Francisco Bay Area geographic region were identified through academic and community rheumatology clinics, and from earlier studies of genetic risk factors for SLE outcomes (22,23). Diagnoses were confirmed based on meeting any of three criteria: meeting at least 4 of 11 ACR revised criteria for SLE (24,25), meeting 3 ACR criteria plus confirmation of diagnosis by a study rheumatologist, or a diagnosis of lupus nephritis. The data sources for this analysis were the initial research clinic encounter with a physician specializing in SLE, which encompassed a review of medical records, a history and physical examination, and collection of biospecimens, along with a structured interview administered by research staff. The physician visit included calculation of the SLEDAI score (a physician-calculated measure of disease activity in SLE) (6) and the SDI (a physician-calculated measure of irreversible organ system damage caused by SLE) (7). The structured interview covered demographics, socioeconomic status, and completion of various patient-reported health status metrics: 12 PROMIS domains, the SF-36, and the Patient Health Questionnaire depression scale PHQ-8 (26). Study interviews were conducted in English, Spanish, Mandarin, or Cantonese according to the preferred language of the participant. PROMIS short forms are translated using the Functional Assessment of Chronic Illness Therapy (FACIT) translation methodology (27, 28), consistent with guidelines for translation of PRO metrics (29). All participants provided informed consent to participate in this study, and the research protocol was approved by the UCSF Committee on Human Research.

Of the 332 participants attending the baseline research clinic visit, six individuals were excluded from analysis (two because of incomplete interviews with multiple questions unanswered, two because of missing SLEDAI scores, one for missing race/ethnicity, and one for missing SDI score), leaving a total of 326 patients. Some PROMIS domains were not

available in all languages, so the number of completed domains varied by the language of the interview (see Table 1).

Outcomes

The primary outcomes were T-scores on each of the 12 PROMIS domains listed in Table 1, definitions of selected PROMIS domains in Supplementary Information. PROMIS domains can be tested using static interviewer-administered short form questionnaires or using computer-adaptive testing (CAT). PROMIS item banks using CAT are only available in English and Spanish, while many of the short forms are also available in Cantonese and Mandarin. CLUES used short forms to keep the method of administration consistent across the cohort. The short forms were scored and converted to T-scores, which have a general population mean of 50 and standard deviation of 10. Higher T-scores represent more of the concept being measured. For example, a higher score on the Physical Function domain would represent better functioning, while a higher score on Fatigue would represent a higher burden of fatigue. All PROMIS domains were scored using scoring documentation available at http://assessmentcenter.net (30).

Secondary outcomes included scores on the Medical Outcomes Study Short Form (SF-36) subcomponent summaries of physical HRQoL, called the Physical Component Summary (SF-36 PCS) and emotional HRQoL, called the Mental Component Summary (SF-36 MCS), scored from 0 (worst possible HRQoL) to 100 (best possible HRQoL) (15).

Additional Variables

The primary independent variable was defined as a score of ≥ 10 on the PHQ-8 depression scale during the structured interview. A PHQ-8 score ≥ 10 has been validated as a proxy for current major depression in previous population-based studies (26). In the remainder of this paper, we will use the term “major depression” to refer to a PHQ-8 score ≥ 10, for the sake of simplicity, recognizing that a positive screen is not equivalent to a clinical diagnosis of depression.

Covariates were age, sex, race/ethnicity (white, Hispanic, black, Asian), language of interview (English, Spanish, Mandarin, Cantonese), disease duration in years, household income (less than 125% of the Federal Poverty Level for the year of the interview, equal to or greater than this threshold, or not answered), body mass index (BMI), two comorbid conditions (diabetes mellitus, malignancy), and education level (less than or at least high school graduate). Two physician-reported measures, the SLEDAI and the SDI, were completed as part of the research clinic visit.

Statistical Analysis

Descriptive statistics were calculated for the entire cohort and separately for those with and without major depression, with differences in characteristics tested using *t*-tests for continuous variables and *chi*-squared tests for categorical variables, with statistical significance defined as $p<0.05$. We initially compared PROMIS T-scores for subjects with and without major depression using t-tests. We then used multiple linear regression models to estimate the magnitude of the difference in PROMIS T-scores by major depression status,

controlling for age, sex, race/ethnicity, SLEDAI score, SDI score, BMI, and household income. Age, BMI, SLEDAI, and SDI were modelled as continuous variables, after determining that the linear form of these variables adequately fit the data when tested using standard regression diagnostics including augmented partial residual plots (31). Sex, race/ethnicity, and household income were modelled as categorical variables. Household income was missing for 10.3% of the sample; to avoid reducing the sample size by excluding all participants with missing data for this variable, we included a third category – missing household income. In alternate models, we controlled for the language of the interview rather than for race/ethnicity, and educational attainment in lieu of household income.

All analyses were conducted using Stata 15.1 (College Station, TX).

Results

Among the 326 participants in the analysis, mean age was 45 years, approximately 89% were women, 29% identified as white, 23% as Hispanic, 10% as black, and 36% as Asian. One quarter met the PHQ-8 criteria for major depression, as shown in Table 2. In addition, 35% of the participants reported a past medical history of depression. Other reported neuropsychiatric past medical histories were as follows: 8% had a history of stroke, 7% seizure, 6% peripheral or cranial neuropathy, 4% psychosis or delirium, 1% mononeuritis multiplex, 1% myelitis, and 6% cognitive impairment.

Depressed participants, as defined by the PHQ-8 criteria, had higher mean BMI (28.8 and 25.6 among those with and without major depression, respectively; $p<0.001$). Depressed patients were more likely to have household income below 125% of the Federal Poverty Level, but this did not reach statistical significance (26% and 14% of those with and without major depression had low household income, respectively; $p=0.057$). Age, sex, race/ethnicity, educational attainment, comorbid diabetes, malignancy, hypertension, disease duration, SLEDI and SDI scores were statistically similar in those with and without major depression.

The PROMIS T-scale scores of the entire sample were slightly worse than the general population in all the Physical Health and Mental Health domains, and slightly better than the general population in Social Health domain (Table 3). Specifically, T-scores were within 5 points (0.5 SD) of the general population means (i.e., 50.0) for all tested domains. In unadjusted analyses, major depression was associated with significantly worse T-scores on each of the 12 PROMIS domains tested ($p<0.001$ for all domains), as presented in Table 3. Participants with major depression also had significantly worse scores on the SF-36 Physical Component Summary (mean of 34.6 +/− 1.2 for those with major depression versus 45.4 +/− 0.7 for those without, $p<0.001$) and SF-36 Mental Component Summary (mean of 38.1 +/− 1.2 for those with major depression versus 52.1 +/− 0.5 for those without, $p<0.001$). Those with active arthritis, as determined by the SLEDAI, scored significantly worse on Fatigue (mean of 57.0 +/− 2.1 for those with arthritis versus 51.8 +/− 0.7 for those without, $p=0.02$), Pain Interference (mean of 57.0 +/− 1.8 for those with arthritis versus 51.6 +/− 0.6 for those without, $p<0.01$), and the SF-36 Physical Component Summary (mean of 36.3 +/− 2.1 for those with arthritis versus 43.3 +/− 0.7 for those without, $p<0.01$).

In multivariable adjusted models, there were statistically significant worse T-scores for all 12 PROMIS domains between those with and without major depression (average T-score difference between depressed and non-depressed of 10.0, $p<0.001$ for all domains) after adjustment for age, sex, race/ethnicity, SLEDAI score, SDI score, BMI, and household income (table 3). Depressed participants scored more than 10 points, approximately 1 SD, worse on Fatigue, Sleep Impairment, Satisfaction in Discretionary Social Activities, and Satisfaction in Social Roles. As in unadjusted analyses, depressed individuals had worse scores on the SF-36 Physical Component Summary (36.2 in major depression versus 44.9 without major depression, $p<0.001$) and the SF-36 Mental Component Summary (37.9 in major depression versus 52.2 without major depression, $p<0.001$). Participant race/ethnicity and the language of the completed interview were correlated with each other (for example, Hispanic ethnicity and Spanish language of interview; R=0.49, $p<0.001$), as were household income and educational attainment (R=0.46, $p<0.001$). An alternative model adjusting for language of interview, rather than for race/ethnicity led to similar results, with significantly worse T-scores for depressed compared to non-depressed participants in all 12 PROMIS domains (average T-score difference between major depression and non-major depression participants in all domains of 10.2; $p<0.001$ for all).

Discussion

Understanding the relationship between major depression and a wide range of HRQoL domains can help clinicians interpret PROMIS scores and better target interventions to meaningfully improve the HRQoL of individuals with SLE. We found that major depression was associated with markedly worse scores across all 12 PROMIS domains tested, and scores in those who were depressed were more than 10 points or 1 SD worse than in non-depressed in domains of particular relevance to SLE, for example in Fatigue and in Satisfaction in Social Roles.

The associations between major depression and worse scores on every tested PROMIS domain remained even after controlling for age, sex, race/ethnicity, educational attainment, BMI, SLEDAI, and SDI. These findings suggest that major depression may be a major factor contributing to reduced HRQoL in SLE patients, and that its impact is both broad and deep, as it is associated with all measured health domains from physical function to social roles to sleep and self-perception. The average lupus disease activity for the sample was low, as measured by the SLEDAI. There was no statistically significant difference in lupus disease activity between individuals with and without major depression, highlighting the independence of the depression and HRQoL relationship from disease activity.

These findings are generally in agreement with prior research on quality of life in SLE, which has emphasized the role of psychological factors in HRQoL outcomes. In a Southern California SLE cohort, depression was the major factor correlated with lower scores on all SF-36 domains, while physician-measured disease activity via the SLEDAI had no such correlation (5). Another study of an Italian SLE cohort found that worse scores on the Hamilton Depression Rating Scale were independently associated with poorer SF-36 scores in SLE (32). Similarly, a study of a Chinese cohort found depression and anxiety to be independently associated with lower physical and mental component scores on the SF-36

after adjustment for disease activity, demographics, household income and education in multivariate regression models (33). Research focusing on fatigue and reduced energy level, common complaints among SLE patients, has shown that depression and pain, rather than disease activity scores, are the major predictors of these symptoms in SLE (34). Previous work has largely utilized legacy HRQoL instruments, such as the SF-36. Our study builds on this foundation by extending the association of major depression with adverse outcomes on a broader array of SLE-relevant health domains using the PROMIS system.

Universal screening for depression in the general population is recommended by the United States Preventive Services Task Force, as detecting clinical depression, and referring for treatment with antidepressants or psychotherapy improves morbidity (35). In individuals with arthritis, a previous randomized controlled trial demonstrated that treatment of depression can improve depressive symptoms, pain, and functional status (36). In addition, self-management approaches such as regular physical activity and attending a self-management education program (e.g. Chronic Disease Self-Management Program), are two evidence-based strategies for improving mental health among individuals with arthritis, including SLE, that complement clinical care (37). Extrapolating from this literature, treatment of depression in SLE with antidepressants, psychotherapy, and self-management strategies could both alleviate depressive symptoms and have a positive impact on HRQoL. Specific studies on the effectiveness and outcomes of depression treatments in SLE are an important area for future study, but there is a strong argument for universal screening and referral for treatment in this population given the high prevalence and association with markedly worse HRQoL.

This study has several limitations. First, in an observational, cross-sectional study, the association between major depression and worse PROMIS scores does not prove a causal relationship. Reverse causation, such as severe fatigue leading to or exacerbating major depression, is also a consideration, though the association of major depression with every tested domain of health outcome makes reverse causation less plausible. Second, the studied cohort was limited to patients able and willing to attend a research clinic visit, raising the possibility of selection or non-response bias; specifically, individuals who were severely ill or depressed may have declined to participate. However, this would be expected to create a bias toward null results. Third, despite adjusting for several likely confounders in the multivariable analysis, unmeasured confounders may influence both major depression and patient-reported outcomes. For example, unmeasured aspects of socioeconomic adversity beyond race, income, and education, such as lack of social support, work and relationship stress, or poor access to medical care, are unknown and likely influence both the presence of major depression and patient-reported outcomes. Fourth, a score ≥ 10 on PHQ-8 depression scale denotes a high likelihood of major depression (26), but it is not equivalent to a clinical diagnosis. This score cutoff also does not account for individuals with more mild depressive symptoms. Lastly, this study did not have data on fibromyalgia, which is common in those with SLE and is associated with worse HRQoL outcomes (38).

The association of major depression with adverse HRQoL outcomes in SLE is striking and consistent in this study and across the literature. Further study could explore a potential causal relationship of major depression and adverse HRQoL, such as distinguishing whether

major depression itself is a manifestation of SLE, an independent co-morbidity, or a reaction to other elements of chronic illness. Regardless, there is good evidence that treatment of depression through antidepressants and psychotherapy improves depressive and HRQoL symptoms in patients with other rheumatic conditions (36), so targeted intervention on depressive symptoms appears to be a worthy use of clinical resources in SLE. The efficacy of antidepressants and psychotherapy in improving HRQoL outcomes in depressed individuals with SLE is an important area for further research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Urowitz MB, Gladman DD, Tom BD, Ibañez D, Farewell VT. Changing patterns in mortality and disease outcomes for patients with systemic lupus erythematosus. J Rheumatol 2008; 35:2152–8. [PubMed: 18793004]
2. Centers for Disease Control and Prevention. Measuring healthy days: Population assessment of health-related quality of life. Centers for Disease Control and Prevention, Atlanta, Georgia 2000.
3. Jolly M How does quality of life of patients with systemic lupus erythematosus compare with that of other common chronic illnesses? J Rheumatol 2005; 32:1706–8. [PubMed: 16142864]
4. McElhone K, Abbott J, Teh LS. A review of health related quality of life in systemic lupus erythematosus. Lupus 2006; 15:633–43. [PubMed: 17120589]
5. Moldovan I, Katsaros E, Carr FN, Cooray D, Torralba K, Shinada S, et al. The Patient Reported Outcomes in Lupus (PATROL) study: role of depression in health-related quality of life in a Southern California lupus cohort. Lupus 2011; 20:1285–92. [PubMed: 21813589]
6. Gladman D, Ibañez D, Urowitz MB. Systemic Lupus Erythematosus Disease Activity Index 2000. J Rheumatol 2002; 29:288–91. [PubMed: 11838846]
7. Gladman D, Ginzler E, Goldsmith C, Fortin P, Liang M, Urowitz M, et al. The development and initial validation of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index for systemic lupus erythematosus. Arthritis Rheum 1996; 39:363–69. [PubMed: 8607884]
8. Gladman DD, Urowitz MB, Ong A, Gough J, MacKinnon A. A comparison of five health status instruments in patients with systemic lupus erythematosus (SLE). Lupus 1996; 5:190–95. [PubMed: 8803889]
9. Hanly JG. Disease activity, cumulative damage and quality of life in systematic lupus erythematosus: results of a cross-sectional study. Lupus 1997; 6:243–7. [PubMed: 9104730]
10. Jolly M, Utset TO. Can disease specific measures for systemic lupus erythematosus predict patients' health related quality of life? Lupus 2004; 13:924–6. [PubMed: 15645747]
11. Kasturi S, Szymonifka J, Burket JC, Berman JR, Kirou KA, Levine AB, et al. Validity and reliability of Patient Reported Outcomes Measurement Information System computerized adaptive tests in systemic lupus erythematosus. J Rheumatol 2017; 44:1024–31. [PubMed: 28412708]
12. Palagini L, Mosca M, Tani C, Gemignani A, Mauri M, Bombardieri S. Depression and systemic lupus erythematosus: a systematic review. Lupus 2013; 22:409–16. [PubMed: 23427220]

13. Zhang L, Fu T, Yin R, Zhang Q, Shen B. Prevalence of depression and anxiety in systemic lupus erythematosus: a systematic review and meta-analysis. BMC Psychiatry 2017; 17:70. [PubMed: 28196529]
14. Fonseca R, Bernardes M, Terroso G, de Sousa M, Figueiredo-Braga M. Silent burdens in disease: fatigue and depression in SLE. Autoimmune Dis 2014; 2014:790724. [PubMed: 24592329]
15. Ware JE, Kosinski MA, Gandek B. SF-36 health survey: manual and interpretation guide. Lincoln(RI): Quality Metric; 2005.
16. Stamm TA, Bauernfeind B, Coenen M, Feierl E, Mathis M, Stucki G, et al. Concepts important to persons with systemic lupus erythematosus and their coverage by standard measures of disease activity and health status. Arthritis Rheum 2007; 57:1287–95. [PubMed: 17907225]
17. Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, et al. Initial adult health item banks and first wave testing of the Patient Reported Outcomes Measurement Information System (PROMIS) Network: 2005-2008. J Clin Epidemiol 2010; 63:1179–94. [PubMed: 20685078]
18. Cella D, Yount S, Rothrock N, Gershon R, Cook K, Reeve B, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH Roadmap Cooperative Group During its First Two Years. Med Care 2007; 45:S3–S11.
19. Witter JP. The promise of Patient-Reported Outcomes Measurement Information System - turning theory into reality: a uniform approach to patient-reported outcomes across rheumatic disease. Rheum Dis Clin North Am 2016; 42:377–94. [PubMed: 27133496]
20. DeQuattro K, Trupin L, Li J, Katz PP, Murphy LB, Yelin EH, et al. Relationships between adverse childhood experiences and health status in systemic lupus erythematosus. Arthritis Care Res 2019; Epub ahead of print. doi: 10.1002/acr.23878
21. Dall'Era M, Cisternas MG, Snipes K, Herrinton LJ, Gordon C, Helmick CG. The incidence and prevalence of systemic lupus erythematosus in San Francisco County, California: The California Lupus Surveillance Project. Arthritis Rheumatol 2017; 69:1996–2005. [PubMed: 28891237]
22. Freemer MM, King TE Jr, Criswell LA. Association of smoking with dsDNA autoantibody production in systemic lupus erythematosus. Ann Rheum Dis 2006; 65:581–84. [PubMed: 16150789]
23. Parsa A, Lovett DH, Peden EA, Zhu L, Seldin MF, Criswell LA. Renin-angiotensin system gene polymorphisms predict the progression to renal insufficiency among Asians with lupus nephritis. Genes Immun 2005; 6:217–24. [PubMed: 15789057]
24. Tan EM, Cohen AS, Fries JF, Masi AT, Mcshane DJ, Rothfield NF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982; 25:1271–7. [PubMed: 7138600]
25. Hochberg M Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1997; 40:1725.
26. Kroenke K, Strine TW, Spitzer RL, Williams J, Berry JT, Mokdad AH. The PHQ-8 as a measure of current depression in the general population. J Affective Disorders 2009; 114:163–73.
27. Ermenco SL, Cella D, Arnold BJ. A comprehensive method for translation and cross-cultural validation of health status questionnaires. Eval Health Prof 2005; 28:212–32. [PubMed: 15851774]
28. Available translations. HealthMeasures. http://www.healthmeasures.net/explore-measurement-systems/promis/intro-to-promis/available-translations . Accessed April 2020.
29. Wild D, Grove A, Martin ML, Ermenco S, McElroy S, Verjee-Lorenz A, et al. Principles of good practice for the translation and cultural adaptation process for patient-reported outcomes (PRO) measures: report of the ISPOR task force for translation and cultural adaptation. Value Health 2005; 8:94–104. [PubMed: 15804318]
30. Cella D, Gershon R, Bass M, Rothrock N. Assessment Center. 2007 https://assessmentcenter.net/
31. Mallows CL Augmented partial residuals. Technometrics 1986 28: 313–319.
32. Doria A, Rinaldi S, Ermani M, Salaffi F, Iaccarino L, Ghirardello A, et al. Health-related quality of life in Italian patients with systemic lupus erythematosus. II. Role of clinical, immunological and psychological determinants. Rheumatology 2004; 43:1580–6. [PubMed: 15367746]
33. Mok CC, Chan KL, Ho LY. Association of depressive/anxiety symptoms with quality of life and work ability in patients with systemic lupus erythematosus. Clin Exp Rheumatol 2016; 34:389–95. [PubMed: 27049836]

34. Moldovan I, Cooray D, Carr F, Katsaros E, Torralba K, Shinada S, et al. Pain and depression predict self-reported fatigue/energy in lupus. Lupus 2013; 22:684–9. [PubMed: 23660302]

35. Siu A, US Preventive Services Task Force (USPSTF). Screening for depression in adults. JAMA 2016; 315:380–7. [PubMed: 26813211]

36. Lin EH, Katon W, Von Korff M, Tang L, Williams JW Jr., Kroenke K, et al. Effect of improving depression care on pain and functional outcomes among older adults with arthritis: a randomized controlled trial. JAMA 2003; 290:2428–9. [PubMed: 14612479]

37. Brady TJ, Murphy L, O'Colmain BJ, Beauchesne D, Daniels B, Greenberg M, et al. A meta-analysis of health status, health behaviors, and health utilization outcomes of the Chronic Disease Self-Management Program. Prev Chronic Dis 2013; 10:120112 [PubMed: 23327828]

38. El-Rabbat MS, Mahmoud NK, Gheita TA. Clinical significance of fibromyalgia syndrome in different rheumatic diseases: relation to disease activity and quality of life. Reumatol Clin 2018; 14:285–289. [PubMed: 28411133]

Significance and Innovations

- This is the first study examining the association between major depression and patient-reported outcomes using PROMIS in SLE
- Major depression was independently associated with worse patient-reported outcomes on all 12 tested domains of PROMIS, encompassing physical, mental and social health
- The degree to which depressed individuals scored lower on five of the tested PROMIS domains was at least 1 SD lower than non-depressed individuals, highlighting domains for which comorbid depression may be especially relevant
- Screening and treatment of major depression in those with SLE may help address a major component of poor HRQoL across multiple domains

Table 1.

PROMIS Short Form Domains Administered in CLUES

PROMIS Domain	English (N=281)	Spanish (N=20)	Chinese (N=25)
Physical Function	✓	✓	✓
Pain Interference	✓	✓	✓
Fatigue	✓	✓	✓
Sleep Disturbance	✓	✓	✓
Sleep Impairment	✓	✓	
Applied Cognitive Abilities	✓	✓	
Psychosocial illness impact, negative	✓		
Psychosocial illness impact, positive	✓		
Ability to Participate in Social Roles and Activities	✓	✓	
Satisfaction with Participation in Discretionary Social Activities	✓	✓	
Satisfaction with Participation in Social Roles	✓	✓	
Social Isolation	✓	✓	

Table 2.

Distribution of Characteristics of CLUES Cohort, Overall and by Major Depression Status

	All individuals (n=326)	Major Depression 82 (25%)	No major depression 244 (75%)	*p*
Age, years (mean ± sd)	45 ± 14	46 ± 13	44 ± 14	*0.28*
Women	290 (89%)	77 (94%)	213 (87%)	*0.10*
Race/Ethnicity				*0.68*
White	95 (29%)	26 (32%)	69 (28%)	
Hispanic	75 (23%)	20 (24%)	55 (23%)	
Black	34 (10%)	9 (11%)	25 (10%)	
Asian	117 (36%)	27 (33%)	90 (37%)	
Other race/ethnicity	5 (2%)	0 (0%)	5 (2%)	
Household income				*0.057*
Below 125% FPL	56 (17%)	21 (26%)	35 (14%)	
At least 125% FPL	238 (73%)	55 (67%)	183 (75%)	
Unknown income	32 (10%)	6 (7%)	26 (11%)	
Did not graduate high school	30 (9%)	8 (10%)	22 (9%)	*0.84*
BMI (mean ± sd)	26.4 ± 6.7	28.8 ± 7.4	25.6 ± 6.3	*<0.001*
Comorbid Diabetes	24 (7%)	7 (9%)	17 (7%)	*0.65*
Comorbid Malignancy	24 (7%)	6 (7%)	18 (7%)	*0.99*
Comorbid Hypertension	83 (25%)	24 (29%)	59 (24%)	*0.36*
Disease Duration, Years (mean ± sd)	16 ± 10	16 ± 11	16 ± 10	*0.91*
SLEDAI (mean ± sd)	2.95 ± 3.1	2.89 ± 3.2	2.98 ± 3.1	*0.83*
SDI (mean ± sd)	1.83	1.89	1.81	*0.759*

CLUES = California Lupus Epidemiology Study

sd = standard deviation

SLEDAI = SLE Disease Activity Index 2000

SDI = Systemic Lupus International Cooperating Clinics Damage Index

FPL = Federal Poverty Level based on Household Size for year of interview

BMI = body mass index

p calculated by chi-squared statistic comparing major depression and no major depression.

Table 3.

Association of PROMIS Domain T-Scores with Major Depression, by unadjusted and adjusted

PROMIS Domain	N	Mean T-Score	Unadjusted Mean T-Scores			Adjusted Mean T-Scores		
		Overall	No Depression	Depression	p	No Depression	Depression	p
Physical Health								
Physical Function	326	48.0	50.3	41.3	<0.001	49.8	42.7	<0.001
Pain Interference	323	52.1	49.4	60.0	<0.001	49.7	59.1	<0.001
Fatigue	323	52.3	48.4	63.6	<0.001	48.5	63.3	<0.001
Sleep Disturbance	325	52.5	50.3	59.2	<0.001	50.5	58.6	<0.001
Sleep Impairment	301	53.0	49.5	63.7	<0.001	49.7	63.1	<0.001
Mental Health								
Cognitive Abilities	299	48.5	50.3	42.8	<0.001	50.1	43.5	<0.001
Negative Psychosocial Impact	269	52.2	49.9	60.1	<0.001	49.9	59.8	<0.001
Positive Psychosocial Impact	267	48.3	50.4	41.5	<0.001	50.2	42.2	<0.001
Social Health								
Participation in Social Roles	286	50.9	53.3	42.8	<0.001	53.0	44.0	<0.001
Satisfaction in Discretionary Social Activities	301	52.9	55.9	43.7	<0.001	55.6	44.6	<0.001
Satisfaction in Social Roles	299	51.1	54.2	41.6	<0.001	53.9	42.7	<0.001
Social Isolation	296	46.2	43.7	54.3	<0.001	43.9	53.6	<0.001

PROMIS = Patient-Reported Outcomes Measurement Information System

N for each PROMIS domain varies based on number of participants who responded to the questions in that domain

Higher T-scores represent more of the concept being measured. For example, a higher score on the Physical Function domain would represent better functioning, while a higher score on Fatigue would represent a higher burden of fatigue.

Adjustment for age, sex, race/ethnicity, SLEDAI score, SDI score, BMI, and household income