# An overview of psychological functioning in systemic lupus erythematosus

This article provides an overview of the role of psychological factors and psychiatric disorders in the adjustment to systemic lupus erythematosus (SLE) and how to conceptualize their relationship with disease activity. Depression and anxiety disorders are highly prevalent in SLE. Depression poses a variety of health risks for afflicted patients and is associated with increased healthcare utilization and work disability. In addition, research has also shown that factors such as illness beliefs, coping, social support and life stress affect SLE health outcomes, highlighting the need for psychological screening and management. The contribution of psychological factors and disease activity to lupus fatigue is analyzed, emphasizing the importance of a multidimensional approach to understanding this troublesome symptom that affects the majority of SLE patients. At present, there is little behavioral intervention research in SLE. The findings suggest that a closer alliance between rheumatology, behavioral medicine and health psychology would facilitate SLE research and clinical care in the future.

KEYWORDS: behavioral = coping = depression = fatigue = helplessness = management = psychological = screening = stress = support

Systemic lupus erythematosus (SLE) is a chronic, inflammatory autoimmune disease that can potentially affect multiple organ systems, impair quality of life and lead to significant psychological distress in afflicted patients. SLE is characterized by the production of antibodies that are reactive with nuclear, cytoplasmic and cell membrane antigens [1]. SLE affects mostly women and has a high prevalence in vulnerable populations and certain ethnic groups, especially among individuals of African-American, Hispanic, Native American and Asian descent [2,3], and among those of lower socioeconomic status [4,5]. This disease can lead to lifethreatening consequences for approximately a third of diagnosed patients who may suffer impaired functioning in several organ systems, including the heart, lungs, liver and kidneys. Importantly, SLE can have profound effects on the physical and psychosocial adjustment of afflicted patients [6,7]. For many patients, SLE can contribute to work disability, functional impairments, loss of valued activities and a high prevalence of mood disturbance [8-12]. For these reasons, conceptualizing and managing the difficult symptoms and impact of SLE represents a major challenge for clinicians, researchers and patients alike.

Arthritis and inflammatory diseases pose a high risk for psychiatric comorbidity [13,14]. Researchers in the fields of behavioral medicine, health psychology and rheumatology have devoted considerable attention to the role of psychological functioning in SLE in order to understand the mechanisms underlying physical, behavioral and psychological manifestations of the disease [6.7]. Accordingly, this article will illustrate the salience of such mechanisms in the following areas: psychosocial processes and variables affecting the adjustment to SLE, the role of psychological distress in SLE health outcomes, and psychological functioning and lupus fatigue. Finally, the article will address the implications of this work for the psychological and behavioral management of SLE in rheumatology care.

### **Conceptual background**

Three scenarios provide a basis for conceptualizing the relationship between chronic illness and psychological functioning, and have served as a guide for much behavioral medicine research in arthritis. In the first scenario, SLE disease burdens (e.g., disease activity and organ damage symptoms) are postulated to create risk for mood disturbance and diminished quality of life. Organ damage and symptoms such as pain, for example, may lead to depression, anxiety and obstacles in role functioning in some patients. The second scenario examines the effects that psychological factors can have on the disease process. For example, a history of depression may create risk for inflammation or lead to maladaptive

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coping and poor adherence to treatment that, in turn, may contribute to more frequent disease flares. The third scenario, a combination of scenarios 1 and 2, describes a dynamic process in which the physical demands of SLE create psychological distress that can then lead to troublesome symptoms, poor adherence and heightened disease activity. A key assumption in each scenario is that the relationship between SLE disease activity and psychological distress may be indirect, and mediated or moderated by other physical, social and psychological factors. While behavioral medicine research in SLE has not followed a particular conceptual framework, FIGURE 1 illustrates a hypothetical model demonstrating the potential roles of factors such as illness beliefs and coping processes as mediators of the relationship between disease activity and health outcomes that is pertinent to rheumatic disease. Importantly, the model depicts the coping process as taking place in a social/cultural context, and affected by patients' personal resources such as education and selfefficacy [15]. Knowledge of mechanisms that explain the association between disease burdens and psychological outcomes can be used to inform the development of treatment plans that

target key factors affecting patient adjustment using an integrated, comprehensive approach to management.

### Prevalence of psychiatric disorders in SLE

Significant research has focused on the extent and nature of psychological distress in SLE. Studies from the past decade indicate that such suffering occurs at significantly higher rates among patients with SLE than healthy controls [16]. For example, evidence suggests that as many as 65% of such patients meet criteria for a psychiatric disorder [17,18]. In particular, mood and anxiety disorders appear to be the most frequently occurring psychiatric problems [17,19]. Although research has tended to focus on depression in SLE patients, Nery et al. found that 45% of participants with SLE met criteria for an anxiety disorder [20]. The same researchers found that 69% of patients diagnosed with SLE were positive for a lifetime history of mood disorder, and 52% for lifetime anxiety disorder. There is also evidence to suggest that other forms of psychiatric disturbance are prevalent in SLE. For example, in a study of 326 patients, 47% had a history of a major depressive episode, 24%



**Figure 1. A biopsychosocial paradigm for understanding the relationship between disease activity and health outcomes in chronic illness.** In the model, the relationship between disease activity and health outcomes is characterized as indirect, explained by such factors as illness beliefs and coping. These factors may either interact with disease activity, or mediate the effects of disease activity on health outcomes. Social/cultural resources and personal resources are postulated as affecting health outcomes directly, or indirectly, through moderating/mediating variables.

had a history of specific phobia, 16% for panic disorder, 9% for obsessive–compulsive disorder and 6% for bipolar I disorder [17]. In addition, various types of cognitive dysfunction, including delirium, and psychosis have also been reported to occur in some patients with SLE [21].

# Psychosocial processes & variables affecting the adjustment to SLE

The high prevalence rate of psychiatric disorders in SLE raises the question of how psychosocial factors affect the adjustment to SLE. As reflected in Figure 1, the following factors may be postulated as either moderating or mediating variables that may explain the relationship between SLE disease burdens and psychological outcomes.

### **Illness cognition**

The field of illness cognition addresses the contribution of patients' beliefs about their disease to both mental and physical health outcomes. Several studies, for example, have focused on the role of helplessness, the perception that patients cannot manage symptoms or the disease course of SLE. Research using the Rheumatology Attitudes Index (RAI) adapted for SLE from the Arthritis Helplessness Index [22,23] has shown that greater helplessness is associated with a range of negative outcomes in SLE, including depression, physical disability and poor healthrelated quality of life (HRQOL) [11,22,24-26]. Importantly, the role of helplessness in SLE has been explored in diverse ethnic groups, including those of Asian, African-American and Hispanic descent [25-27]. The RAI has also been used in a Swedish SLE population [28].

Other aspects of illness cognition have been studied in SLE. Lotstein et al. found that high beliefs in powerful others locus of control, the view that health professionals controlled patients' health outcomes, were associated with lower socioeconomic status and greater organ damage [4], while Karlson et al. found that self-efficacy, the belief that one is effective in managing disease, correlated with lower disease activity and better health status [29]. Devins et al. reported that illness intrusiveness, the perception that SLE interfered with several different aspects of quality of life, was associated with poorer psychological well-being and mediated the effects of racial differences on their measure of adjustment [30]. More recently, in a study using the Illness Perception Questionnaire (IPQ), Philip et al. found that patients who perceived their SLE as having negative life consequences, who felt that their lupus had an unpredictable future and who possessed little understanding of lupus reported higher levels of depression [31,32]. As a test of the self-regulation model of chronic illness, these findings reflect the importance of considering the meaning and perceived significance of SLE to patients, tapping into a subjective frame of reference that is independent of the disease process.

### **Coping strategies**

Coping refers to the cognitive and behavioral responses that patients engage in to manage the various demands of their disease and/or other life stressors [33]. There is evidence to suggest that the way in which patients cope with SLE may have significant influences on their psychosocial and physical adjustment to their disease. For example, Kozora et al. found that disengaged and emotional coping styles of SLE patients were related to increased depressive symptoms [34]. Similarly, Rinaldi et al. reported that behavioral and mental disengagement coping, and venting of emotions were related to lower HRQOL, and that patients who exhibited more restraint coping and positive reinterpretation and growth had higher HRQOL scores [35]. Interestingly, the effects of coping on HRQOL were independent of the effects of pain. In a longitudinal study, McCracken et al. showed that passive coping was associated with greater mood disturbance and disability in SLE [36]. These findings converge with studies that have shown a positive correlation between passive coping and greater helplessness, mood disturbance and pain in rheumatoid arthritis [37-39].

Other research has shown that SLE patients who reported finding benefits in facing the vicissitudes of SLE had less pain and psychological distress than patients who felt demoralized by their illness [40]. Abu-Shakra et al. found that a greater sense of coherence correlated strongly with the mental health component of HRQOL [41]. The data from these studies suggest that patients who can transcend the demands of SLE and find meaning in their life circumstances are able to achieve a more positive adaptation to their disease. Importantly, in a review of coping research in SLE, Bricou et al. concluded that coping strategies in SLE were more strongly and consistently associated with indices of functional adaptation and quality of life than with lupus disease activity [42].

### Social support

Extensive research is available showing the salutary effects of social support on health outcomes in persons with a variety of health conditions, including arthritis [43]. Theoretically, social support may affect health outcomes directly, or indirectly, through other factors such as coping (see FIGURE 1). Studies in SLE have demonstrated that higher availability of social support is associated with better HRQOL [44,45]. However, the role of social support in SLE health outcomes is quite limited, and further research is needed to clarify its impact on the long-term adjustment to SLE.

### Life stress

Research has investigated whether life stress is related to physical and emotional functioning in SLE. Studies have focused on the role of both major life events stress (e.g., divorce and job loss) and daily stress (e.g., interpersonal conflict and role strain). Da Costa et al. showed that greater negative major life events stress predicted adverse changes in functional disability over an 8-month interval independently of depressive symptomatology [46], while Kozora et al. reported that major life-threatening events were related to a greater current depressed mood [34]. Pawlak et al. found that daily interpersonal stress was positively associated with SLE disease flares [47], while a study by Peralta-Ramirez et al. showed that daily stress contributed to the worsening of SLE symptoms in 74% of their patients either a day or two later, and that the effects of stress were especially pronounced in patients with higher SLE disease activity [48]. Greco et al. found that an improvement in perceived stress, the feeling of being stressed or burdened, was related to reductions in lupus disease activity in patients receiving psychosocial interventions [49]. Earlier studies demonstrated a contribution of daily stress to psychological distress and a worsening of SLE symptoms [50,51]. The review by Bricou et al. emphasized the importance of taking into account the role of coping as potentially mitigating or exacerbating the effects of stress on SLE health outcomes [42]. Collectively, these studies indicate that heightened stress may have a detrimental effect on symptoms and emotional functioning in SLE, but studies to date have not addressed the effect of stress on immunological mechanisms that contribute to lupus disease activity.

## The role of psychological distress in SLE health outcomes

Research has addressed the link between psychological distress, particularly depression, and SLE disease activity. Segui *et al.* evaluated patients for depression and anxiety during both active and inactive stages of SLE [18]. Whereas 40% of participants were diagnosed with a psychological disorder during the acute phase, only 10% met criteria a year later when the participants no longer displayed disease activity associated with SLE. While these findings indicated that psychological disorders covaried with the severity of disease activity, they did not substantiate directionality between disease activity and psychological processes, that is, whether disease activity predicted the onset of a psychiatric disorder, or vice versa. In a recent study, Carr et al. showed that, in both cross-sectional and longitudinal analyses, depression predicted higher subjective disease activity, measured by the Systemic Lupus Erythematosus Activity Questionnaire (SLAQ) among a cohort of 125 patients with SLE [52,53]. However, this study did not find a significant relationship between depression and objectively measured disease activity using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). Similar results were found in a study by Nerv et al. who did not find a significant relationship between psychological distress and the presence of anti-ribosomal P antibodies [20].

Considerable interest exists in the relationship between depression and the inflammatory response in SLE. Depression in patients diagnosed with SLE has been associated with other illnesses involving chronic inflammation, including diabetes mellitus, hypertension, cardiovascular disease (CVD), fibromyalgia (FM) and inflammatory bowel disease [54-57]. Compared with healthy controls, patients with rheumatic disease (both rheumatoid arthritis and SLE) reported a higher prevalence of gastrointestinal symptoms, headache and backache, somatic complaints that are often associated with increased muscle tension, anxiety and depression [57]. These data correspond with other evidence suggesting that local inflammation, when left unchecked, can often become systemic and result in greater health problems [58].

One of the main causes of mortality in SLE, particularly for women, is CVD. Patients diagnosed with SLE face a risk of cardiac events that is more than 50-times greater that of their non-SLE peers [59]. There is evidence that mood disturbance may be an important mediator within the complex relationship between CVD and SLE. Greco *et al.* examined the associations between depression, CVD risk factors and coronary artery calcification (CAC) in both women with SLE and controls [60]. Women with SLE were more likely to have CAC, as well

as more severe CAC, compared with non-SLE peers. Importantly, depression was associated with greater CAC in the SLE group. Depression has been linked to increased levels of C-reactive protein and IL-6, as well as higher weight, which, itself, has been associated with the production of proinflammatory cytokines [61,62].

Depression in SLE and the presence of comorbid illnesses can also lead to secondary issues, such as problems with medication compliance, work disability, increased service utilization and higher healthcare costs [63]. Work disability is prevalent among patients with SLE and has been found to be significantly associated with fatigue, depression and disease activity [56]. Utset et al. found that neurocognitive impairment in patients with SLE was also associated with work disability, and that those who were formally disabled had higher fatigue and anxiety scores than their nondisabled peers [64]. Sleep disturbance is another common issue experienced by patients with SLE. According to one recent study, depression, disease activity and functional disability were all significant predictors of sleep disturbance in SLE [65].

In sum, these studies demonstrate that difficulties in psychological functioning, and depression in particular, pose a significant risk for negative health outcomes in SLE that are both far-reaching from a clinical standpoint and costly for patients, the healthcare system and society as a whole. While anxiety is common in SLE patients, there is little research on the role of anxiety in the SLE disease course. Additional longitudinal research that examines more sophisticated theoretical frameworks would advance our understanding of the dynamic interplay between disease processes and psychological functioning over time (see TABLE 1).

### Psychological functioning & lupus fatigue

Fatigue is one of the major factors influencing HRQOL in lupus and therefore deserving of special mention in this article [66]. Among the multitude of symptoms that characterize SLE, fatigue is the most common complaint, affecting anywhere from 50 to over 80% of patients in some studies [67]. Despite the high prevalence of fatigue in lupus, the mechanisms underlying fatigue are generally poorly understood. Various explanations have been proposed for the association between lupus and fatigue. One theory links fatigue to the disease process itself and the pathophysiological mechanisms associated with it. This theory is supported by the observation that fatigue increases during disease flares. However, this theory cannot explain the persistence of fatigue beyond the time of the disease flare. A contrasting theory links psychological factors, including mood disturbances, and poor sleep to fatigue in SLE. A third hypothesis suggests that while fatigue may start as a physiologic process linked to disease activity, psychological factors may either exacerbate it or contribute to its persistence [11]. The high prevalence of FM in lupus and the strong association of FM with fatigue could yet provide another explanation regarding the relationship of fatigue in SLE with FM and pain in general.

### The relative importance of disease activity & psychological factors to fatigue

The contribution of disease activity versus psychological determinants in lupus fatigue has been analyzed in several studies. A study by Tayer *et al.* investigated the relative contributions of disease status, helplessness and depression to

Variable	Related to
Helplessness	Increased depression, disability and poor quality of life
Self-efficacy	Lower disease activity and better health status
Passive coping	Higher mood disturbance and disability
Sense of coherence	Better mental health HRQOL
High availability of social support	Higher HRQOL
Life events stress	Higher disability and depression
Daily stress	Higher mood disturbance and more lupus symptoms
Depression	Higher self-reported disease activity, higher prevalence of other inflammatory illnesses, higher coronary artery calcification, higher work disability, greater sleep disturbance and greater medical utilization
HROOL: Health-related quality of life	

Table 1. The role of psychological factors in systemic lupus erythematosus:highlights.

fatigue in patients with SLE [11]. Their crosssectional analysis found both direct and indirect relationships between disease status and fatigue, with helplessness and depression as mediating variables. However, disease status was the only predictor of fatigue over time.

An interesting theory linking disease activity to fatigue in lupus involves the contribution of neuropsychiatric SLE (NPSLE) [68]. In a study by Kozora et al., the relationship between cognitive functioning, measured by a cognitive impairment index derived from the American College of Rheumatology neuropsychology research battery of tests for SLE (ACR-SLE battery), and other disease aspects including depression, pain, fatigue and sleep disturbances, as well as the impact on HRQOL and functional capacity was examined [16]. Within the NPSLE group, significant correlations between cognitive impairment index and depression, fatigue and pain were found. In general, patients with SLE reported higher levels of cognitive difficulties, depression, pain and fatigue compared with controls. The results suggested that cognitive dysfunction, pain, fatigue and depression in patients with NPSLE may reflect global changes in the CNS.

Another interesting theory examining the possible relationship between fatigue and the neuroendocrine disturbances observed in SLE and other autoimmune disorders has also been proposed [69]. For example, defects in the hypothalamus-pituitary-adrenal axis have been reported in lupus and Sjogren syndrome, and could be an effect of the hypersecretion of cytokines on the neuroendocrine system [70]. Thus, the presence of fatigue in autoimmune diseases could be explained by mechanisms related to dysfunction of the neuroendocrine system.

In contrast to the studies presented above, several other studies have found psychological factors to be stronger predictors of fatigue than disease activity. In the LUMINA cohort, the investigators reported a correlation between increased levels of fatigue and the presence of pain, abnormal illness-related behaviors, helplessness and constitutional manifestations; however, no correlation was found with lupusspecific measures, such as disease activity and damage [71]. In a study by Tench et al., patients during active disease states had fatigue scores 33% higher than during inactive disease states (p < 0.5) [67]. However, significant correlations between fatigue, disease activity, sleep quality, anxiety and depression were also found. The study concluded that, apart from treating the disease, it is important to treat mood disorders and insomnia in order to improve fatigue and quality of life.

The relationship between disease activity and fatigue was examined in several studies from the University of Toronto Lupus Clinic [72,73]. In a first study from this group of researchers, no significant correlation was found between the Fatigue Severity Score (FSS) and the SLEDAI [72]. By contrast, fatigue was highly correlated with the presence of FM (p < 0.05) and depression (p < 0.01). In addition, fatigue was significantly associated with lower performance in all six domains of the SF-20 (p < 0.001); disease activity correlated with decreases in social functioning, mental health functioning and health perception areas of the SF-20. Their results indicated that fatigue in patients with SLE did not correlate with disease activity but was associated with FM, depression and lower overall health status. The authors concluded that fatigue is a manifestation of these conditions, which are commonly coexpressed in SLE, and may reflect a diminished capacity to cope rather than a product of the disease itself.

In a follow-up study, the authors attempted to define which dimensions of disease in SLE would be most closely associated with fatigue [73]. Two indices of disease activity were used, one that included fatigue Systemic Lupus Activity Measure-Revised (SLAM-R) and one that excluded (SLEDAI) fatigue. Severity of fatigue correlated strongly with poor health status, as measured by the SF-36, and higher tender point counts. No significant correlation was found with disease activity, measured by the SLEDAI or SLAM-R, or disease damage, as measured by the Systemic Lupus International Collaborative Clinics/American College of Rheumatology (SLICC/ACR) damage index. The authors concluded that factors associated with quality of life and FM seem to have a greater influence on the severity of reported fatigue in SLE than the level of current disease activity.

These findings were supported by Kozora *et al.* using the FSS scoring system [16]. In this study, the FSS did not correlate with the SLEDAI, the SLAM-R or the SLICC damage index. Fatigue severity correlated with the tender point count and negatively correlated with all domains of the SF-36. Disease activity and damage accounted for only 4.8 and 4%, respectively, of the variance in fatigue. The authors concluded that fatigue severity correlated with poor health status and a higher tender point count.

In a systematic review by an *ad hoc* committee on SLE response criteria for fatigue, the FSS scoring system was recommended for evaluating fatigue in SLE [74]. However, the committee acknowledged the limitations of the FSS and stressed the importance of taking into consideration confounding factors such as presence of sleep disturbances, FM, depression and anemia when evaluating fatigue in lupus. The review found that the SLAM was correlated with fatigue, but the SLEDAI was not, fatigue was also found to correlate with pain, poor sleep, depression and all the components of the SF-36.

A study by Da Costa et al. characterized the experience of fatigue in lupus patients using a multidimensional assessment and delineated contributors to physical and mental dimensions of fatigue [75]. The participants scored high on all five Multidimensional Fatigue Inventory (MFI)-20 fatigue dimensions, with the highest scores in general and physical fatigue. Using hierarchical multiple regression, greater disease damage and disease activity, the presence of FM, depressed mood, sleep disturbance and less participation in leisure-time physical activity were found to contribute to higher physical fatigue scores. Depressed mood was the strongest determinant of mental fatigue, while disease-related variables were not associated with mental fatigue.

### Contribution of pain, FM, sleep & mood disturbance to lupus fatigue

The role of FM in lupus-related fatigue has been further investigated in a study by Taylor *et al.* [76]. In the study 50% of patients complained of fatigue, but only 10% of these patients fulfilled criteria for FM. FM did not correlate with any measure of disease activity, although patients with FM had lower mean DNA antibody titers and mean SLICC/ACR damage scores. The authors concluded that, in their cohort, a minority of lupus patients with fatigue fulfilled the ACR criteria for FM, and therefore, other possible factors contributing to fatigue should be considered.

Research by Jump *et al.* examined the relative contribution of pain in general, as well as disease activity and social support, to fatigue in lupus [77]. As with some of the other studies presented in this article, disease activity, as measured by SLEDAI, did not predict fatigue. Pain and depression were both positive predictors of fatigue, while perceived social support was negatively related to fatigue scores, The researchers concluded that understanding the effect of psychosocial factors on fatigue in SLE may improve patient outcomes through psychosocial interventions aimed at reducing pain and increasing coping skills and social support.

Researchers have addressed the role of sleep disturbance in SLE-related fatigue [78,79]. One of the studies examined the course of fatigue within the first hour after awakening and during the day, as well as the contribution of sleep disturbance to fatigue in patients with primary Sjögren's syndrome, SLE and rheumatoid arthritis [78]. The patients reported significantly increased fatigue compared with healthy subjects. While fatigue levels decreased in the first hour after awakening in patients with SLE and rheumatoid arthritis, they remained unchanged or increased in patients with primary Sjögren's syndrome. Fatigue progressively increased during the remainder of the day for all patient groups. The presence of sleep disturbances was correlated overall with fatigue levels, although weakly with the change of fatigue within the first hour after awakening.

Iaboni et al. studied the impact of sleep disorders, sleepiness and depression on fatigue in patients with SLE [79]. The authors found no association between sleepiness and SLE disease features such as disease activity, medications, presence of NPSLE or a diagnosis of FM. The patients reported overall mild-to-moderate depression. The patients reporting sleepiness had lower depression scores than the nonsleepy patients (p < 0.02), and fewer of the sleepy patients were depressed (p < 0.04). The conclusion of the study was that fatigue in SLE was associated with primary sleep disorders, sleepiness and depression, and that fatigue resulting from excessive daytime sleepiness could be distinguished from the fatigue associated with depression.

Considerable evidence indicates that fatigue in SLE is multifactorial and is largely mediated by psychosocial factors such as depression and helplessness, as well as by sleep quality. Fatigue has the greatest effect on HRQOL in lupus [66]. Fatigue does not, however, consistently correlate with lupus disease activity and damage [80]. FM and pain have also been identified as contributors to fatigue in SLE (see Box 1).

### Box 1. Lupus fatigue: highlights.

- Disease activity and damage inconsistently related to fatigue
- Greater fatigue significantly associated with poorer health-related quality of life
- Pain and depression consistently related to higher fatigue
- Sleep disturbance related to higher fatigue
- Existence of fibromyalgia and higher tender point count contribute to higher fatigue
- Helplessness and abnormal illness behavior associated with higher fatigue

## Importance of psychological management in SLE

Owing to the high prevalence of psychological distress in SLE and its contribution to symptoms of the disease, the identification of patients who are in need of adjunctive psychological treatment represents a significant clinical challenge. However, the constraints of medical practice and the focus of rheumatology care on mitigating the disease process and controlling symptoms may interfere with the task of identifying SLE patients who may benefit from psychological treatment. Despite the burden of depression, research in arthritis has shown that rheumatologists may not inquire about depression during clinic visits, increasing the risk that depressed patients will not be diagnosed or treated [81]. Despite its prevalence and impact, psychological distress in SLE may similarly go unaddressed unless appropriate screening and evaluation mechanisms are in place in the medical clinic.

### Screening for psychological distress

While standard interviewing methods such as the Structured Clinical Interview for Mental Disorders (SCID-I) are essential for definitively evaluating psychiatric disorders for clinical trials and epidemiological research, the length and complexity of such measures make them impractical for use in medical practice [82]. Since the major objective of screening is to identify quickly and efficiently the existence of psychological disturbances for further evaluation and management, a more viable and efficient alternative is to implement a screening mechanism that focuses on the psychological disturbances that have been most commonly found in SLE clinical studies and that pose the greatest risk for interfering with disease management and/or quality of life. Importantly, the establishment of screening mechanisms should be complemented by the existence of resources for accurately diagnosing, treating, referring and following up patients to provide continuity of clinical care.

While a range of psychiatric problems may be found in SLE, the screening for depression is a critical component in the care of patients with SLE, and measures are available to accomplish this goal. The Beck Depression Inventory – Fast Screen (BDI-FS) is a seven-item inventory that assesses the cognitive and affective criteria for depression specified in the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV [83]. Derived from the 21-item Beck Depression Inventory that has been widely adopted in psychiatric populations for several decades, the measure omits somatic criteria that may be confounded with medical problems that can artificially inflate the depression score. This is particularly crucial for SLE since symptoms such as sleep disturbance, inertia and poor motivation may reflect inflammation and disease complications. The BDI-FS has adequate to good sensitivity and specificity in diagnosing depression using a cutoff of 4. Importantly, the BDI-FS can be used with a range of populations, including adolescents, adults and geriatric patients.

Another validated measure for screening depression is the Patient Health Questionnaire (PHO-9) [84]. Based on the nine symptoms used for the diagnosis of depression in the DSM-IV, the PHQ-9 has been extensively used in primary care settings and with a variety of medical conditions. A cutoff score of 10 has proven to have optimal sensitivity and specificity for detecting depression in clinical samples [85]. The PHQ-2 is comprised of the first two items of the PHQ-9 that assess depressed mood and anhedonia [86]. A cutoff score of 2 has yielded sensitivity and specificity that is comparable to the PHQ-9 in a primary care population [87]. While the PHQ-9 has been used with SLE patients, there is no literature on the use of the PHQ-2 in SLE [52]. Although sufficiently sensitive to the presence of depression, briefer measures tend to have poor specificity and high rates of false positives. Some patients may be identified as depressed when they, in fact, do not have a depressive disorder. However, these instruments may still be helpful if the goal is to identify patients for referral to a clinician for further diagnosis and evaluation, but are not appropriate as diagnostic tools when they are used alone.

Owing to the prevalence of anxiety disorders in SLE and the fact that many patients report worry and states of tension in the face of their disease, screening for anxiety is also recommended, although there is less research in this area. However, a newly developed screening measure, the Generalized Anxiety Disorder-7 scale (GAD-7) and its two core items (GAD-2) has shown promise as an effective screening tool [88,89]. Using a cutoff score of 10, the GAD-7 has recently demonstrated appropriate sensitivity and specificity for detection of the four most prevalent anxiety disorders [89]. Importantly, the GAD-7 has been shown to correlate with higher disability and healthcare use in primary care [88] settings and to be a valid measure of anxiety in Hispanic populations [90,91]. As of yet, there is no research literature on the use of the GAD-7 in SLE.

# The need for behavioral interventions & psychotherapy

The existence of a high degree of psychiatric comorbidity and psychological distress in SLE illustrates an important clinical need and provides a rationale for the use of adjunctive psychological and/or behavioral interventions. While significant research has documented the efficacy of behavioral interventions in contributing to improvement in psychological and physical outcomes for patients with arthritis, relatively little controlled research has been conducted on the use of behavioral interventions in SLE [92,93]. The dearth of behavioral intervention research, coupled with the high prevalence of psychological distress in SLE, represents a troubling paradox in lupus care and contributes to an unmet clinical need.

However, some initial studies have been conducted that have shown promising results. Greco et al. found that a 6-week pain management intervention led to improvement in pain and psychological functioning in patients with SLE [94], and a study by Karlson *et al.* found that a one-session behavioral intervention based on self-efficacy principles contributed to similar salutary physical and psychological outcomes [95]. More recently, Navarrete-Navarrete et al. reported that a behavioral intervention led to reduced anxiety, depression and daily stress in 45 patients with SLE [96]. These studies suggest that behavioral interventions may lead to improved psychological functioning in patients with SLE. An important goal would to be integrate behavioral interventions with conventional medical care in the lupus clinic in order to increase patients' management skills and sense of control in the face of this disease.

While most patients may benefit from strategies that help them manage their disease, other patients with SLE may need specialized care that focuses directly on the treatment of depression and other psychological problems. Psychotherapy may be an effective treatment strategy for depressed patients with SLE. An abundant research literature exists on the behavioral and psychotherapeutic treatment of depression. A meta-analysis of 25 randomized controlled trials showed that psychotherapy led to improvement in depression for patients with depressive disorder and that the combination of psychotherapy and medication was superior to medication alone [97]. Behavioral treatment by itself for disease management is not likely to be sufficient for such patients, and a referral to a mental health specialist with a behavioral medicine background would be recommended. Currently, however, there is no published literature on the psychological treatment of depression in patients with SLE. The psychological treatment of SLE patients with anxiety disorders also warrants attention (see Box 2).

### Future perspective & conclusion

Systemic lupus erythematosus is a difficult disease with a range of potentially harmful physical and emotional consequences for patients. In particular, this article has highlighted the role and prevalence of depression and anxiety disorders in patients with SLE and has described how psychological factors may contribute to fatigue, a highly common symptom of this disease that greatly impacts sufferers. Significant research has demonstrated the potential deleterious effects of depression in the management of SLE, while sparse research has been conducted on the determinants and effects of anxiety. Several studies have demonstrated the importance of adopting a comprehensive model for understanding the association between disease activity and psychosocial functioning in SLE. Additional longitudinal research analyzing the interplay between psychological factors and the disease process would further illuminate the nature of the adjustment process, and, hopefully, would give rise to novel treatment approaches. Clinical trials evaluating the efficacy of behavioral interventions are also needed that would provide a broader empirical basis for management and a foundation for more comprehensive clinical care. This research suggests that a closer partnership between the fields of behavioral medicine, rheumatology and health psychology would

Box 2. Recommendations for the psychological management of systemic lupus erythematosus: highights.

- Adopt interdisciplinary model of care in rheumatology practice
- Establish liaison with behavioral medicine professionals
- Screen for depression and anxiety
- Use behavioral interventions for management of pain, stress and disability
- Use psychotherapy and cognitive behavior therapy for severely depressed patients and for patients with anxiety disorders

facilitate the accomplishment of this work and lead to new insights regarding the management of this burdensome disease. financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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### **Executive summary**

#### Conceptual model

- There are three scenarios for conceptualizing the relationship between disease burdens and psychological distress.
- Disease burdens can lead to psychological distress; psychological distress can affect disease; disease burdens can lead to psychological distress that, in turn, can affect disease.
- The relationship between psychological distress and disease can be mediated or moderated by other psychological or biological variables.

#### Psychological factors affecting the adjustment to systemic lupus erythematosus

- As many as 69% of systemic lupus erythematosus (SLE) patients have been found to have a lifetime history of mood disorder and 52% a lifetime history of anxiety disorder.
- Illness beliefs such as helplessness and intrusiveness are related to mood disturbance and poor health functioning.
- Disengagement coping contributes to depression, while finding benefits and meaning in life is related to better quality of life.
- Greater life stress is related to mood disturbance and lupus symptoms.
- Depression has been found to predict higher self-reported disease activity, higher healthcare utilization and greater work disability.

#### The problem of lupus fatigue

- The majority of SLE patients have significant difficulty with fatigue and low energy.
- Fatigue has been considered to be the product of both disease activity and psychological factors.
- Studies have shown that depression, helplessness, sleep disturbance, pain and fibromyalgia all contribute to fatigue.

#### Approaches for psychological management

- Procedures for psychological screening of depression and anxiety are highly recommended in the SLE clinic.
- Some initial behavioral intervention research has shown promise in alleviating lupus symptoms and improving health functioning in SLE.
- There is a need for more aggressive treatment approaches for the treatment of depression and mood disturbance.

#### Future perspective & conclusion

- Research has demonstrated the value of adopting a comprehensive biopsychosocial model in examining the adjustment of SLE patients.
- Additional longitudinal research and clinical trials would enhance our understanding of the psychosocial adaptation of SLE patients and the efficacy of behavioral treatments.
- A closer alliance between rheumatology, behavioral medicine and health psychology will provide the foundation for advances in research and clinical care in the future.

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