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Psychological, social and behavioral factors associated with disease/illness activity and adjustment to Lupus: A systematic review and meta-analysis

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Abstract

Systemic Lupus Erythematosus (SLE) bears a heavy toll on individuals' psychological wellbeing and quality of life. Despite vital to the development of effective interventions, systematic and quantifiable knowledge on modifiable factors associated with adult SLE adjustment and disease/ illness activity is currently lacking. This systematic review with meta-analysis aimed to bridge this gap, by examining the effects of modifiable psychological, social, and behavioral factors associated with SLE adjustment and disease/illness activity. Eight databases were searched for quantitative studies, using Boolean combinations of keywords on SLE adjustment, disease/illness activity and psychological, social, or behavioral correlates/predictors. Ninety studies were included in the narrative review, and fifty-four in the meta-analysis. The psychological factors more strongly associated with SLE adjustment and disease/illness activity were illness- and treatment-related beliefs, self-perceptions, resilience-related factors, and perceived stress. Avoiding sedentary behavior showed a consistent, albeit small association with better outcomes. Social factors were largely under investigated, but better perceived social support showed moderate associations with better outcomes. The meta-analysis findings, which should be considered with caution due to high risk of bias, uncovered several potentially fruitful avenues for future research and highlight potentially relevant targets for psychosocial and behavioral interventions to improve quality of life of individuals with SLE.

Keywords

Systemic Lupus Erythematosus, illness adjustment, disease/illness activity, psychosocial correlates/predictors, systematic review, meta-analysis

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Introduction

Systemic Lupus Erythematosus (SLE) is an autoimmune chronic disease, with increasing worldwide prevalence rates, ranging from 20 to 70 cases per 100.000 individuals (Arnaud & van Vollenhoven, 2018; Pons-Estel et al., 2010). SLE can affect individuals of all age groups, but its peak incidence is in middle adulthood, with 90% of diagnosed cases in women (Nusbaum, 2020; Rees et al., 2017). SLE presents a variable and unpredictable disease course, as it can affect almost any tissue or organ, and its severity can range from mild to potentially fatal (Arnaud & van Vollenhoven, 2018; Kapoor & Mahadeshwar, 2020; Pons-Estel et al., 2010). The most prevalent manifestations of SLE are systemic (e.g., fatigue and fever), musculoskeletal (e.g., arthralgias, hand deformities), cutaneous (e.g., malar rash, photosensitivity), and hematological (e.g., anemia and leukopenia) (Arnaud & van Vollenhoven, 2018; Barcia-Sixto & Isenberg, 2020; Nyman et al., 2020).

As the prognosis and course of the disease are uncertain, SLE often bears a heavy toll on individuals' psychological wellbeing and quality of life (QoL) (Sutanto et. al., 2013). Individuals with SLE have a higher prevalence of depression and anxiety than individuals with other rheumatic diseases and the general population (Zhang et al., 2017). SLE also severely interferes with individuals' physical and social functioning (Tunnicliffe et al., 2015). Its social and economic costs associated with productivity loss are significant. Direct costs alone (e.g., healthcare visits, hospitalizations, medications, diagnostic and therapeutic laboratory tests, imaging procedures, and renal replacement therapies) are estimated to range approximately between 4968€ and 10781€ annually per patient in Europe (Carter et al., 2016). These costs are even higher for those with severe SLE and/or when organ dysfunction is present.

A person living with SLE will often go through an illness adaptation process, which is a complex, idiosyncratic and dynamic journey involving behavioral, cognitive and affective changes over time in response to living with a chronic illness. This adaptation process often involves ongoing changes in multiple life domains (e.g., social, sexual, emotional, and physical; Dennison et al., 2009;

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Moss-Morris, 2013; Stanton et al., 2007). This process may, eventually, lead to good SLE adjustment, i.e., an optimal level of fit between the individual and their circumstances, which has been defined as a multidimensional construct encompassing five main dimensions: 1) good illness and treatment management; 2) absence of psychological disorder or reduced distress; 3) ability to maintain positive affect; 4) minimal illness interference on daily activities, life roles and relationships and 5) perceived quality of life in several domains (Dennison et al., 2009; Moss-Morris, 2013; Stanton et al., 2007). Poor SLE adjustment is tightly associated with disease activity, i.e., the presence of signs (e.g., cutaneous involvement, the appearance of a rash) and symptoms of the disease (e.g., pain and fatigue) (Elera-Fitzcarrald et al., 2018; Pereira et al., 2020). For example, higher levels of pain and fatigue have been associated with poorer SLE adjustment (Elera-Fitzcarrald et al., 2018; Tench et al., 2000). Thus, researchers and clinicians have come to recognize that SLE management involves preventing the onset of organ damage and controlling disease activity, as well as improving individuals' quality of life (Griffiths et al., 2005), as these are intimately interrelated.

The development of psychosocial and/or behavioral interventions as adjuncts to pharmacological interventions is paramount to optimal SLE management (Zhang et al., 2012). Indeed, previous systematic reviews showed that psychological, social, and behavioral interventions (e.g., cognitive-behavioral, psychoeducational, supportive therapies and exercise) have the potential to reduce fatigue and improve mental health and health-related quality of life of individuals with SLE (Fangtham et al., 2019; Liang et al. 2014; Neill et al., 2006; Pino-Sedeño et al., 2016; Tsoi et al., 2024; Zhang et al., 2012). However, findings do not consistently support the efficacy of such interventions, especially regarding disease activity, which seems to improve only slightly by changes in diet or harmful exposures (i.e., sun and smoke; Liang et al., 2014; Tsoi et al., 2024). This has led some authors to call for further development of evidence-based psychosocial interventions for individuals with SLE (Zhang et al., 2012), and to better understand the different impact of those interventions on disease activity/illness and SLE adjustment outcomes (Tsoi et al., 2024).

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The development of such evidence-based interventions requires systematic knowledge of the major modifiable risk and protective factors of SLE adjustment and disease/illness activity (Bartholomew et al., 2006; Craig et al., 2020; Kankaya & Karadakovan, 2020; Michie et al., 2008). To the best of our knowledge, there is currently just one literature review on psychosocial factors associated with the experience of adults with SLE, which was published 20 years ago (Seawell & Danoff-Burg, 2004). Importantly, this review was not systematic nor aimed at quantifying the effects of the main modifiable factors associated with SLE adjustment and disease/illness activity. Notwithstanding, several studies have been published in the last two decades, suggesting that various psychological, social, and behavioral features can work as either risk and/or protective factors in relation to SLE adjustment and disease/illness activity. For example, factors such as optimism, empowerment, self-control (Sutanto et. al., 2013) and physical activity (Margiotta et al., 2018) have been associated with positive SLE adjustment. Conversely, perceived stress seems to be associated with lower quality of life (Greco et al., 2004) and higher disease activity (Sumner et al., 2020). Also, social factors - such as social support - have an impact on disease activity (Schattner et al., 2010) and SLE adjustment (Sutanto et. al., 2013).

The mounting evidence exploring the role of various psychological, social, and behavioral factors on SLE adjustment and disease/illness activity, along with the lack of a systematic investigation and quantification of their effects set the stage to the present study. The purpose of this systematic review and meta-analysis was to: 1) identify modifiable psychological, social, and behavioral factors associated with illness adjustment and disease/illness activity among adults with an SLE diagnosis; and 2) investigate which factors are most strongly associated with disease/illness activity and SLE adjustment. Producing systematic and quantifiable knowledge on modifiable factors associated with adults' SLE adjustment and disease/illness activity will be crucial to inform the future development of effective psychosocial and behavioral interventions.

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Method

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Page et al., 2021). The data synthesis included a meta-analysis, carried out in accordance with American Psychological Association Meta-Analysis Reporting Methods (MARS; Appelbaum et al., 2018). All methodological procedures were specified in advance and pre-registered in PROSPERO (PROSPERO CRD42020163126).

1. Study Identification

Eight electronic databases (PsycARTICLES, Academic Search Complete, PsycINFO, Psychology and Behavioral Sciences Collection, Scopus, Web of Science, Pubmed and Cochrane library) were searched from database inception until April 2022, for studies published in English, Portuguese, or Spanish. A comprehensive search strategy (see Supplementary File 1) was used combining keywords and synonyms for: a) dimensions of chronic illness adjustment (e.g., adjustment, adaptation, function, quality of life; Moss-Morris, 2013); AND b) most prevalent SLE signs and symptoms (e.g., photosensitivity, malar rash, cutaneous) (Barcia-Sixto & Isenberg, 2020) present in the classification criteria of the American College of Rheumatology (ACR) (Aringer et al., 2019; Arnaud & van Vollenhoven, 2018) and the Systemic Lupus International Collaborating Clinics (Arnaud & van Vollenhoven, 2018); AND c) terms detailing the relation between factors and outcomes variables (e.g., predict*, determin*, correlat*); AND d) terms specifying the type of predictors/correlates/determinants (i.e., psychological, social or behavioral).

2. Study Selection

Studies were retained when they met the following inclusion criteria: a) participants were adults (i.e., over 18 years old) diagnosed with SLE; b) included at least one outcome measure of disease/illness activity (i.e., symptoms reported by individuals or clinical SLE signs reported by

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physicians or other diagnostic tools) or/and a dimension of SLE adjustment (Moss-Morris, 2013); c) reported the association between outcome variables and at least one modifiable psychological, social or behavioral factor (i.e., individuals' attitudes, beliefs, feelings and behaviors towards oneself or significant others, such as family, medical team or care service); d) used quantitative methods (e.g., randomized controlled trials, cluster-randomized controlled trials, prospective/retrospective cohort studies, correlational studies), and e) were published in peer-reviewed journals.

For each of the five dimensions of illness adjustment (Moss-Morris, 2013) different outcome variables were considered as indicators (Supplementary File 2): 1) good illness and treatment management (outcome variables - e.g., good medication adherence) ; 2) absence of psychological disorder or reduced distress (outcome variables - e.g., low depression, anxiety, distress); 3) ability to maintain positive affect (outcome variables – e.g., high positive mood); 4) minimal illness interference on daily activities, life roles and relationships (outcome variables - e.g., low work disability, high physical functioning) and 5) perceived quality of life in several domains (outcome variables – e.g., good quality of life). Disease activity was more commonly measured by global disease activity indexes, i.e., questionnaires that include the assessment of clinical and/or laboratory parameters to define the level of disease activity in a specific time frame (e.g., Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). Measures of individual symptoms (e.g., fatigue and pain) were also included as indicators of disease/illness activity (Supplementary File 2).

Studies were excluded if they: a) only reported biological outcomes (e.g., the extent of organ damage and/or mortality rates); b) only included non-modifiable factors associated with SLE adjustment and/or disease/illness activity (e.g., demographic factors); c) only measured medical treatment effects or comorbidities; d) were review articles, case reports, conference abstracts or qualitative studies; and e) were not written in English, Portuguese or Spanish.

Firstly, at the abstract screening stage, 35% of the titles and abstracts were reviewed by two authors independently (S.R. and C.Ca.), with disagreements being resolved by a third author (C.G.).

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Given that a high agreement level was obtained (91.4%), the remaining abstracts were screened by the first author (S.R.). Secondly, at the full-text eligibility stage, 30% of the articles were analyzed by two authors independently (S.R. and C.Ch.), and an agreement level of 95.5% was reached. A third element of the team (C.G.) made the final decision for disagreements. Given the high level of agreement, the first author analyzed the remaining 70% of the papers. In both screening stages, the articles were randomly distributed by the software random.org. The software Ryann QCRI was used to keep track of the decisions made.

3. Data Collection

The team developed a standardized data charting form (available upon request), identifying the main information to be extracted. The definition of the information to be extracted was based on the guidelines of the Centre for Reviews and Dissemination (Dissemination, 2009), and included: (1) *bibliographic information and study characteristics*, i.e., study ID, author, year of publication, title, the country in which the study was conducted, aim, hypothesis and study design, namely, experimental vs. observational studies (correlational/cross-sectional or longitudinal prospective/retrospective), (2) *sample characteristics*, i.e., lupus criteria classification, disease duration, sample size, participant sex/gender and age, (3) *variables of interest*, i.e., type of outcome (adjustment or disease/illness activity), dimension of adjustment or disease/illness activity, name and type of modifiable factor (psychological, social or behavioral), and instruments used to assess them; (4) *results*, i.e., descriptive results and effect sizes. Data extracted on measures of disease activity were reviewed by a physician, specialist in internal medicine (U.S.).

The data were extracted by the first author, with 30% of the references being confirmed by another researcher (A.C.) against the defined coding scheme (Supplementary File 3).

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4. **Risk of bias assessment**:

The risk of bias of the studies and respective effect sizes included in the meta-analysis was assessed by the following tools:

a) ROBINS-E (Risk Of Bias In Non-randomized Studies - of Exposures; Higgins et al., 2024) for correlational/cross-sectional or longitudinal prospective/retrospective studies. The tool provides a qualitative score of "low risk of bias", "some concerns", "high risk of bias", and "very high risk of bias" for different categories (i.e., risk of bias due to confounding, measurement of the exposure, selection of participants, post-exposure interventions, missing data, measurement of the outcome, selection of the reported result) and for the overall risk of bias.

b) ROBINS-I (Risk Of Bias In Non-randomized Studies - of Interventions; Sterne et al., 2016) to assess the risk of bias of intervention studies. Studies are classified with "low", "moderate", "serious" or "critical risk of bias" for different categories (i.e., bias due to confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, selection of the reported results) and for the overall bias.

Both instruments were applied independently by two authors (S.R. and C.C.) and discrepancies were resolved by consensus.

5. **Data Synthesis**

a. **Qualitative data synthesis.** All modifiable factors were firstly classified into broad categories of psychological, social, or behavioral, based on the definition of APA Dictionary of Psychology and Davis et al. (2015). These were subsequently classified into more specific subcategories based on conceptual similarity (see Supplementary File 4 for concept operationalization). In the results section, the term "correlate" is used when the studies were cross-sectional, and the term "predictor" is used when the studies were prospective or experimental.

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b. **Meta-analysis.** Quality of life, absence of depression and/or anxiety symptoms were conceptualized as indicators of adjustment, whereas global indexes of disease activity, fatigue and pain were conceptualized as indicators of disease/illness activity, as these were the ones for which more studies were available. These indicators were treated as the outcome variables in the meta-analysis. Pearson's correlation coefficient (*r*) was used (Rosenthal & DiMatteo, 2001), and studies were only included in the meta-analysis if they reported sufficient statistical information to calculate Pearson's *r* based on bivariate results. All extracted data were transformed into Pearson's *r* using the method and formulas proposed by Rosenthal and DiMatteo (2001), Lipsey and Wilson (2001), Ferguson (1966) and Rosenthal (1994). Small, medium, and large effects correspond to .100 <*r* < .243, .243 < *r* < .371, and *r* > .371, respectively (Rice & Harris, 2005).Ideally, an appropriate set of confounders for each association extracted from the original studies should be defined (Poppe et al., 2024). However, given the very high heterogeneity in the adjustment for confounders within and between the included primary studies, we have only extracted the unadjusted effects (Voils et al., 2011).

Prior to the meta-analysis, all *r* coefficients were transformed into Fisher's *z*-scores, which were examined for potential outliers. After the analysis, z-scores were reconverted into *r-coefficients* to facilitate interpretations (Lipsey & Wilson, 2001). When a category included several effect sizes extracted from the same study, we used multilevel meta-analytic models to analyze three different levels of variance: sample variance of all effect sizes (level 1), effect size variance within studies (level 2), and variance between studies (level 3) (Van den Noortgate et al., 2014).

The meta-analysis was performed in R (version 4.0.5, R Core Team, 2020). The function "rma" of the Metafor package (Viechtbauer, 2010) was used for simple meta-analysis. The syntax described by Assink and Wibbelink (2016), and the function "rma.mv" of the Metafor package (Viechtbauer, 2010) were used for multilevel meta-analytical models. Using the "rma" of the Metafor package (Viechtbauer, 2010), we have performed the nonparametric and funnel-plot based trim-and-fill analysis to examine different sources of bias, such as publication bias. This analysis allows not only

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to explore potential biases, but also to estimate their magnitude by calculating a bias-corrected estimate of the true effect size (Duval & Tweedie, 2000).

Results

Study Selection

The search retrieved 4515 articles, including 2182 duplicates, which were excluded. From the remaining 2333 articles, 255 were included for full-text review. Of these, 90 were included for data extraction (for the list of included references see Supplementary File 5). Of the 90 articles included in the review, 54 were included in the meta-analysis. The PRISMA 2020 flow diagram (Page et al., 2021), including reasons for exclusion in the full-text phase, is presented in Figure 1.

Studies Characteristics

Seventy-two included studies were cross-sectional (89%), followed by prospective observational (*k*= 14, 17.3%) and intervention studies (*k*= 4, 4.9%). Overall, studies' sample sizes ranged between 20 and 777 individuals with SLE (*M*= 175.76, *SD*= 158.99), mean aged between 27.9 and 44.8 years (*M*= 41.53 years, *SD*= 5.22; *k*= 81), reporting 10 years, on average, since disease onset, the mean disease duration ranged between 1.45 and 14.5 years (*M* = 10.85, *SD* = 5.2; *k*= 65). The proportion of women with SLE in the samples ranged between 82.14% and 100%, with most studies including more than 90% of women. Of the 90 included studies, 43 focused exclusively on SLE adjustment as an outcome (48%), 17 only considered disease/illness activity as an outcome (19%), and 30 focused on both types of outcomes (33%).

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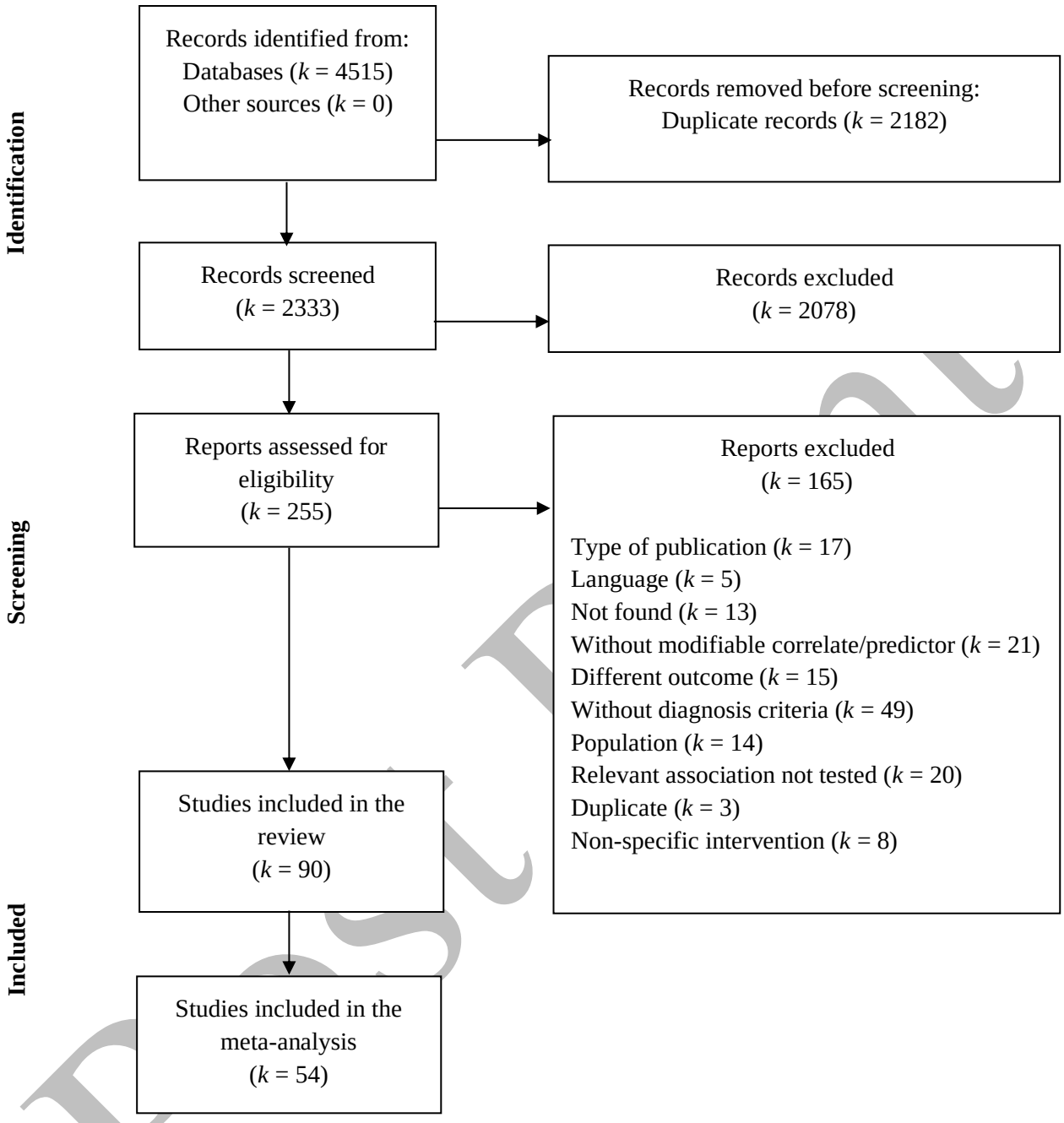


Figure 1. PRISMA 2020 flow diagram of the literature searching and screening processes

Modifiable Correlates/Predictors of SLE Adjustment and Disease/Illness Activity

A summary of the outcome variables related to the dimensions of SLE adjustment and disease/illness activity can be seen in Supplementary File 2. Overall, most studies included outcome variables associated with two main dimensions of SLE adjustment - individuals' quality of life and psychological health (i.e., low levels of depression, anxiety, or distress). The most investigated

outcome variables related to disease/illness activity were specific symptoms, such as fatigue and pain, and a general evaluation of disease activity via global indexes. Most studies investigated psychological (*k*= 57, 63.33%), followed by behavioral correlates/predictors (*k*=28; 31.11%). Social correlates/predictors were the least researched (*k*=24; 26.67%). A list of the instruments/measures used to assess each correlate/predictor and respective study references can be found in Supplementary File 3. Table 1 presents an overview of all associations. The categories of correlates/predictors more frequently investigated and with more consistent findings are described in detail in the following sections. The less investigated and/or consistent categories are presented in supplementary file 6.

Psychological correlates/predictors

Psychological correlates/predictors were organized into nine categories. The categories with more studies were illness and treatment-related beliefs (33.33%), self-perception (13.3%), resilience (11.11%) and perceived stress (8.89%) (see Table 1). The findings on these four main categories are described in detail below. Six other categories of psychological correlates/predictors were also identified, but less frequently investigated, namely: illness-related attitudes and affect (7.78%), knowledge/literacy (5.56%), general control perceptions (4.44%), coping (3.33%), worrying (2.22%).

Table 1
Summary of the associations between psychological, social and behavioral correlates/predictors and disease/illness activity and SLE adjustment outcomes and study quality.

Factor Type	Category	Factor	N studies	Design	Disease/ Illness activity	Adjustment
Psychological	Illness and treatment-related beliefs (*n*= 30)	Threatening Illness perceptions	5	C	§	- (4/5)
		Illness severity	1	C	NT	-
		Concerns about medicines	3	C	NT	- (2/3)
		Negative attitude towards SLE	1	C	NT	-

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		Illness uncertainty	3	C	+	-
		Perception of control over disease	2	C	-	+ (1/2)
		Perceived Helplessness	14	C, L	+ (2/4)	-
	Perceived illness control	Pain-related self-efficacy	1	C	NS	+
		Self-efficacy regarding medication use	1	C	NT	+
		Illness related-self-efficacy	3	C, L	-	+
Self-Perception (*n*= 12)	Body image		6	C	- (1/3)	+ (5/6)
	Self-esteem		2	C	NS	+
	Self-criticism		1	L	NS	-
	Cognitive bias		1	C	NS	NT
	Self-illness separation		1	C	NS	§
	Perception of physical capacity		1	C	NT	§
Resilience-related factors (*n*=10)	Sense of coherence		3	C	NS	+
	Resilience		4	C	- (1/2)	+(2/3)
	Hope		1	C	§	+
	Optimism		2	C	NS	+
	Hostility		1	C	NT	-
Perceived stress			8	C, L	+ (4/6)	-
Illness-related attitudes and affect			7	C, L	+	-

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	Knowledge/ Literacy (*n*= 5)	Disease and treatment understanding	2	C	NT	+ (1/2)
		Health literacy	2	C	-	+ (1/2)
		Knowledge of when to seek treatment	1	C	NT	+
	General Control perception (*n*= 4)	Self-efficacy	1	C	NT	NS
		Personal Mastery	2	C	-	+
		Self-control	1	C	NT	+
	Coping (*n*= 3)	Coping method	1	C	NT	§
		Emotion-oriented coping strategies	1	C	NT	§
		Task-oriented coping strategies			NT	§
		Defense mechanisms	1	C	NT	§
	Worrying (*n*= 2)	Pain-related worrying	1	C	§	-
		Lupus flare-related worrying	1	C	NT	-
Behavioral	Physical activity (*n*= 14)	Physical activity (PA)	12	C, L, I	- (8/11)	+ (3/6)
		Sedentary behavior	3	C	+	-
	Addictive behaviors (*n*= 12)	Smoking	11	C, L	+ (1/3)	- (5/9)
		Alcohol consumption	7	C, L	+ (1/3)	+ (2/5)
		Recreational drug use	1	L	NS	NT
	Diet (*n*= 3)	Dietary Intake	2	C	NT	+
					+	NT
		Caffeine intake	1	C	-	NT
	Sunlight exposure and no use of sun protection (*n*= 2)		2	C	+ (1/2)	NT
	Health-promoting Lifestyle (n=1)		1	C	NT	+
Social	Interaction with others/groups (*n*= 20)	Social Support	18	C, L	- (9/11)	+ (11/12)
		Social Capital	1	C	NT	+
		Social stress and Support	1	C	NT	-
	Relation with	Negative physician-patient interactions	4	C, L	+ (1/2)	- (3/4)

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healthcare system and professionals (*n*= 6)	Satisfaction with care	3	C	NS	+
	Illness Stigma (*n*= 1)	1	C	NT	-

Note: Design - C = cross-sectional; L = Longitudinal; I = Intervention Disease activity/Adjustment: (+) positive consistent association; (-) negative consistent association; (e.g., 2/3) two out of three studies found a significant association; § = only one study with inconsistent results; NS = no significant associations; NT = associations not tested.

Illness and treatment-related beliefs. Twenty-one studies (23.33%) investigated the relation between illness and treatment-related beliefs and SLE adjustment. Most of these studies focused on *illness control perceptions*. Only two out of 21 studies reported non-significant associations (Chehab et al., 2018; Moldovan et al., 2011) and most studies consistently showed that worse illness- and treatment-related beliefs were associated with poorer SLE adjustment. Fourteen studies (15.56%) investigated the association between *illness and treatment-related beliefs* and disease/illness activity. Higher pain or fatigue were consistently associated with worse illness and treatment-related beliefs (Burgos et al., 2009; Engle et al., 1990; Moldovan et al., 2013; Nowicka-Sauer et al., 2018; Somers et al., 2012; Tayer et al., 2001; Zonana-Nacach et al., 2000). Although some studies using the global index of disease activity showed no significant associations with these beliefs (Azizoddin et al., 2017; Bertoli et al., 2006; Kim et al., 2015; Nowicka-Sauer et al., 2018; Somers et al., 2012), other studies showed that increased disease activity was associated with worse illness and treatment-related beliefs (Alarcon et al., 2006; Cui et al., 2020; Karlson et al., 1997; Kim et al., 2015; Li et al., 2020; Tayer et al., 2001).

Perceptions of greater *illness uncertainty and severity* were associated with increased perceived limitations in daily activities, worse quality of life and poorer self-help performance (i.e., increased difficulties in accomplishing various roles, such as work, recreation, social activity, family, and self-

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care, as part of their health self-management process; Chuang et al., 2010). Illness uncertainty was also associated with more anxiety and depression symptoms (Cui et al., 2020), and higher global disease activity (Cui et al., 2020; Li et al., 2020).

Greater perceived *helplessness* (i.e., the overall belief in one's own inability to control SLE outcomes) was associated with more anxiety and depression symptoms (Azizoddin et al., 2017; Gholizadeh et al., 2018), and lower quality of life in one (Burckhardt et al., 1993) of two studies (Moldovan et al., 2011), significantly predicting the latter three months after baseline (Alarcón et al., 2004; Sanchez et al., 2009; Tayer et al., 2001). Perceived helplessness was also associated with worse psychosocial adjustment to illness, evaluated in several domains: 1) health care orientation, 2) vocational environment, 3) domestic environment, 4) sexual relationship, 5) extended family relationship, 6) social environment, and 7) psychological distress (Engle et al., 1990), increased difficulty, dissatisfaction, and pain in performing activities of daily living (Engle et al., 1990), and predicted work disability six months after baseline (Bertoli et a., 2007). Perceived helplessness was associated with more fatigue and pain (Burgos et al., 2009; Engle et al., 1990; Moldovan et al., 2013; Tayer et al., 2001; Zonana-Nacach et al., 2000), but its association with the global index of disease activity was only found in two (Alarcon et al., 2006; Tayer et al., 2001) out of four studies (Azizoddin et al., 2017; Bertoli et al., 2006). A *negative attitude towards SLE* was associated with a higher risk of nonadherence to treatment (Sae-lim et al., 2021).

Threatening illness perceptions, increased *concerns about medications* and a weaker illness-related *internal locus of control* showed inconsistent associations with SLE adjustment and disease/illness activity. More specifically, although some studies did not find a significant association between *threatening illness perceptions* and medication adherence (Chehab et al., 2018) and the global index of disease activity (Nowicka-Sauer et al., 2018), four studies showed that threatening illness perceptions were associated with lower medication adherence (Daleboudt et al., 2011), poorer quality of life (Kotsi et al., 2014) and function in different areas of life (Sharpe et al., 2004), higher depression

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and anxiety symptoms, and more fatigue and pain (Nowicka-Sauer et al., 2018). *Increased concerns about medication* were also associated with lower treatment adherence in two out of three studies (Chehab et al., 2018; Daleboudt et al., 2011; Georgopoulou et al., 2020). A *lower illness-related internal locus of control* was associated with poorer mental and physical functioning and lower global disease activity (Karlson et al., 1997). Although internal locus of control was not associated with treatment adherence (Chehab et al., 2018), individuals with SLE who considered their physician to be the main responsible for their health reported higher adherence rates (Chehab et al., 2018).

Conversely, higher *self-efficacy* regarding different domains such as pain, medication use, and illness demands, was associated with different indicators of adjustment. Self-efficacy regarding medication use was associated with better treatment adherence (Flower et al., 2016), pain-related self-efficacy was associated with better mood, and less fatigue and pain (Somers et al., 2012), and self-efficacy regarding illness demands was associated with lower work disability (Bertoli et al., 2007), better physical and mental functioning (Karlson et al., 1997). Whereas some studies found that greater illness-related self-efficacy was associated with lower global disease activity (Karlson et al., 1997; Kim et al., 2015), pain-related self-efficacy showed no association with the global index of disease activity in one study (Somers et al., 2012).

In sum, there is evidence generally suggesting that more positive beliefs about SLE and its treatment, including perceptions of control over the illness, are associated with better SLE adjustment and lower disease/illness activity.

Self-perception. The relation between self-perceptions and SLE adjustment and disease/illness activity was investigated in twelve studies. *Self-esteem* and positive *body image* showed a consistent association with SLE adjustment (Azizoddin et al., 2017; Jolly et al., 2012a, 2012b; Narupan, Seeherunwong, & Pumpuang, 2022; Shen et al., 2015; Zamora-Racaza et al., 2018; Zhao et al., 2018). Better body image was associated with lower anxiety (Zhao et al., 2018) and depression symptoms

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(Jolly et al., 2012; Narupan, Seeherunwong, & Pumpuang, 2022; Zhao et al., 2018), better quality of life (Jolly et al., 2012a, 2012b), and sexual functioning in one (Shen et al., 2015) of the two studies investigating these associations (Curry et al., 1993). Higher self-esteem was also consistently associated with lower symptoms of anxiety and depression (Azizoddin et al., 2017; Zamora-Racaza et al., 2018). The associations between body image and disease activity were not as consistent (Azizoddin et al., 2017; Jolly et al., 2012b; Zhao et al., 2018), with only one study reporting that better body image was associated with less SLE rash and flares (Jolly et al., 2012b).

Other factors related to self-perceptions were investigated in relation to SLE adjustment and disease activity but less frequently. More specifically, increased *self-criticism* was associated with higher illness intrusiveness on routines, activities, and interests (Schattner et al., 2010), and predicted depression one month after baseline (Schattner et al., 2010), although it was not significantly associated with disease activity (Schattner et al., 2010). A lower *self-illness separation* (i.e., perceived distance between self and the disease) was associated with decreased physical quality of life, but no relation was found with mental quality of life (Büchi et al., 2000) or disease activity (Büchi et al., 2000). Perceptions of *low physical capacity* were associated with increased symptoms of depression and worse quality of life in some domains but showed no association with anxiety symptoms (Kinikli et al., 2021). *Cognitive bias* also showed no association with disease activity (Denton et al., 2005).

Overall, there is some evidence showing that better perceptions of the self were associated with better SLE adjustment, but no significant associations were found with disease activity.

Resilience-related factors. Resilience (i.e., the process of successfully adapting to adverse life experiences) and some related factors (i.e., optimism, sense of coherence and hope) were studied in ten studies. These factors showed an association with SLE adjustment in nine studies. Higher *resilience* was associated with higher treatment adherence (Mendoza-Pinto et al., 2021) and lower symptoms of depression in one out of two studies (Cal et al., 2013; García-Carrasco et al., 2019). The association

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between resilience and global disease activity was inconsistent, with only one of two studies reporting a significant negative association (García-Carrasco et al., 2019; Li et al., 2020).

Higher *optimism* (Azizoddin et al., 2017; Zamora-Racaza et al., 2018) and *hope* (Cui et al., 2020) were associated with lower levels of depression and anxiety symptoms, and an increased *sense of coherence* was associated with higher quality of life (Abu-Shakra et al., 2006; Büchi et al., 2000; Hyphantis et al., 2011). Optimism and sense of coherence did not show, however, an association with disease activity (Abu-Shakra et al., 2006; Azizoddin et al., 2019; Büchi et al, 2000). The association between hope and disease activity was investigated by just one study and the results diverged depending on the way disease activity was evaluated. Higher levels of hope were associated with lower ratings in the global index of disease activity, but no significant associations were found with laboratory parameters of disease activity (e.g., erythrocyte sedimentation rate, concentration of C-reactive protein, complement 3 and 4; Cui et al., 2020). *Hostility* was also associated with lower quality of life (Hyphantis et al., 2011).

Overall, there is some evidence suggesting that resilience-related factors are associated with better SLE adjustment, but their association with disease activity is less consistent.

Perceived stress. Six studies investigated the association between perceived stress (e.g., subjective measures of the degree to which one's life situations are appraised as taxing one's resources) and adjustment. Higher perceived stress consistently showed an association with poorer SLE adjustment, such as increased depression (Azizoddin et al., 2019; Greco et al., 2004; Mills et al., 2017; Sumner et al., 2020), anxiety (Mills et al., 2017), symptoms of psychiatric disorders (Peralta-Ramírez et al., 2018), affective distress (i.e., anxiety, tension, and irritability in the past week) (Greco et al., 2004), interference on activities of daily living (Sumner et al., 2020), and lower treatment adherence (Prados-Moreno et al., 2018) and quality of life (Greco et al., 2004).

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There was also a clear association between perceived stress and specific measures of SLE symptoms (i.e., pain and fatigue; Azizoddin et al., 2019; Greco et al., 2004; Sumner et al., 2020), but when a global index of disease activity or other disease markers (e.g., Leukocyte, ESR, Anti-dsDNA Ab, Complement 3) were considered, the association with perceived stress was inconsistent, i.e., only reported in two (i.e., Greco et al., 2004; Plantinga et al., 2017) out of five studies (Azizoddin et al., 2019; Jung et al., 2015; Mills et al., 2017). In one of these studies, perceived stress significantly predicted disease activity four to five months after baseline (Jung et al., 2015).

In sum, there is some evidence showing that perceived stress is a risk factor for SLE adjustment, but besides its more consistent association with pain and fatigue, its role on disease activity has been less investigated.

Other categories. Seven of the included studies used a measure of illness-related attitudes and affect (including subscales on general hypochondriasis, disease conviction, psychological versus somatic functioning, denial, affective inhibition and disturbance, and irritability; e.g., Bertoli et al., 2007), finding a consistent association with poorer adjustment and increased disease/illness activity (e.g., Alarcon et al., 2006).

Three out of five studies found a negative association between poor knowledge/literacy and different adjustment outcomes (e.g., Sae-lim et al., 2021). One study found that worse health literacy was associated with increased disease activity (Katz et al., 2021).

General control perceptions (i.e., not specifically related to the disease or its treatments) showed significant associations with better SLE adjustment and lower disease activity (*e.g.*, Azizoddin et al., 2017; Zamora-Racaza et al., 2018).

Lupus flare-related worrying (Dhanhani et al., 2014) and pain-related worrying (Somers et al., 2012) were associated with worse adjustment and increased pain and fatigue.

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Only three studies focused on the association between coping and adjustment, and none focused on the relation between coping and disease/illness activity. Those three studies tapped into different coping strategies, so comparisons are unwarranted and the results are inconsistent (e.g., Dobkin et al., 1999).

Behavioral correlates/predictors.

Behavioral correlates/predictors were organized into five categories, with physical activity (15.56%) being the most frequent and with more consistent findings, which are described in detail below. Four other categories of behavioral correlates/predictors were also identified, but less frequently investigated and/or with more inconsistent findings, namely: addictive behaviors (13.33%) diet (3.33%), sunlight exposure and sun protection behaviors (2.22%), health-promoting lifestyle (1.11%).

***Physical activity*.** A total of 12 studies investigated the role of physical activity on SLE adjustment and disease/illness activity, and 3 studies focused on sedentary behaviors.

Sedentary behaviors were consistently associated with increased levels of anxiety, depression, work disabilities and worse quality of life (Margiotta et al., 2018; Patterson et al., 2021; Pisoni et al., 2018; Sanchez et al., 2009), predicting lower quality of life six months after baseline (Sanchez et al., 2009). They were also associated with increased global disease activity (Margiotta et al., 2018), higher levels of fatigue (Margiotta et al., 2018; Zonana-Nacach et al., 2000), and more SLE flares (Margiotta et al., 2018).

The role of physical activity in adjustment and disease/illness activity was less consistent. Some studies found no significant associations between physical activity (Gavilán-Carrera et al., 2019; Mahieu et al., 2016), or training programs without supervision (Gavilán-Carrera et al., 2020; Robb-Nicholson et al., 1989) on SLE adjustment. However, some studies showed that higher physical activity was associated with lower depression and anxiety (Margiotta et al., 2018) and higher physical

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functioning (Mahieu et al., 2016). One supervised training program significantly contributed to the improvement of physical functioning, depression and quality of life (Carvalho et al., 2005). Regarding disease/illness activity, some studies found no significant associations between physical activity and a global index of disease activity (Barnes et al., 2014; Gavilán-Carrera et al., 2019; Kinikli et al., 2021), nor of effects of physical activity interventions on global disease activity (Reis-Neto et al., 2013; Robb-Nicholson et al., 1989), or on specific symptoms, such as pain (Carvalho et al., 2005). However, other studies found that increased physical activity levels were associated with lower scores of a global index of disease activity (Margiotta et al., 2018), lower levels of C-reactive protein and sICAM-1 (Barnes et al., 2014), less fatigue (Mahieu et al., 2016; Burgos et al., 2009; Da Costa et al., 2006), SLE flares (Margiotta et al., 2018), and pain (Mahieu et al., 2016). Two physical activity programs improved fatigue (Carvalho et al., 2005; Robb-Nicholson et al., 1989), and another improved individuals' general and physical (but not mental) fatigue (Gavilán-Carrera et al., 2020).

These findings suggest that avoiding sedentary behavior may improve adjustment and reduce disease/illness whereas the role physical activity is less consistent.

***Other categories*.** Addictive behaviors (i.e., smoking, drinking alcohol and recreation drugs) showed an inconsistent pattern of associations with adjustment and disease/illness activity (Barta et al., 2010; Burgos et al., 2009; Huang et al., 2007; Ishikura et al, 2000; Karlson et al., 1997; Kim et al., 2017; Knight et al., 2018; Pisoni et al., 2018; Sanchez et al., 2009; Seguier et al., 2020; Zhu et al., 2012; Zonana-Nacach et al., 2000).

Diet was the focus of only three studies. As the effects of different ingredients on quality of life and disease activity were tested (e.g., green vegetables, soybean, fish, omega-6 and caffeine), overall conclusions are unwarranted (Elkan et al., 2012; Furukawa et al., 2015; Orefice et al., 2020).

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Two studies investigated the role of sunlight exposure and photoprotection behaviors, showing no association with disease activity (Kadir et al., 2018), with the exception of one study showing a higher frequency of thrombocytopenia among those who did not use sunscreen (Vilá et al., 2014).

One study showed that higher ratings on a composite score of health-promoting behaviors were associated with better quality of life (Huang et al., 2007).

Social correlates/predictors

Social correlates/predictors were organized in three categories, with interaction with others/groups being the more frequently investigated and showing more consistent findings (22.22%), which are presented in detail below. The other two categories, i.e., relation with healthcare system and professionals (6.67%) and stigma (1.11%), are presented in the supplementary file 6.

***Interaction with others/groups*.** Most studies showed that higher *perceived social support* (i.e., social resources that are perceived to be available and the quality of support in case of need) was associated with better adjustment outcomes, such as lower depression (Azizoddin et al., 2017; Jump et al., 2005; Narupan, Seeherunwong, & Pumpuang, 2022; Schattner et al., 2010; Zamora-Racaza et al., 2018), with social support predicting depression after one month (Schattner et al., 2010). Perceived social support was also associated with lower anxiety (Azizoddin et al., 2017; Zamora-Racaza et al., 2018), lower levels of disability (Bertoli et al., 2007), better mental health (Dobkin et al., 1999) and higher quality of life (Alarcón et al., 2004; Karlson et al., 1997; Sanchez et al., 2009; Zheng et al., 2009), predicting the latter after six months (Sanchez et al., 2009). However, perceived social support showed no significant association with intrusiveness on routines, activities, and interests (Schattner et al., 2010), nor with medication adherence (Marengo et al., 2012). Some studies showed that higher perceived social support was associated with lower global disease activity (Alarcon et al., 2006; Bertoli et al., 2006; Karlson et al., 1997; Schattner et al., 2010), and less fatigue (Burgos et al., 2009; Da Costa

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et al., 2006; Jump et al., 2005; Zonana-Nacach et al., 2000), although others showed no significant association between social support and a global index of disease activity (Azizoddin et al., 2017; Jump et al., 2005; Kim et al., 2015, 2017; Schattner et al., 2010), and pain (Jump et al., 2005).

Higher *social capital* (i.e., higher actual or perceived connection and trust in institutions or groups in the community) was also associated with lower levels of depression (Kim et al., 2015), whereas higher *social stress* (i.e., individuals' experience of social stress in relation to occupation, marriage, family, housing, finance, and social life) was associated with the presence of psychiatric disorders among individuals with SLE (Hay et al., 1992). Also, daily hassles with social relationships predicted an exacerbation of global disease activity after one month (Pawlak et al., 2003).

Overall, results point to dual effects of social relations on adjustment and disease/illness activity, with perceived social support and stress associated with social relations being protective and risk factors, respectively.

Other categories. Better physician-patient interactions and higher satisfaction with the healthcare system showed a positive association with adjustment in the majority of studies, however only better physician-patient relations were associated with lower global disease activity in one of two studies (Da Costa et al., 1999; Drenkard et al., 2019; Georgopoulou et al., 2020; Heiman et al., 2018; Karlson et al., 1997; Schattner et al., 2010).

One study showed that higher illness stigma was associated with higher depression (Sehlo et al., 2013).

Meta-Analysis

Studies Characteristics. In total, 222 effect sizes were extracted from 54 studies included in the meta-analysis. An overview of the overall effects of each category of correlates/predictors on quality of life, depression and anxiety symptoms and disease/illness activity (global index, fatigue and pain)

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are presented in Table 2. Adjusted overall effects from trim and fill analyses by categories for all outcomes are presented in Table 3.

Risk of bias assessment. Due to the low number of studies with adjusted effect sizes for the studied relationships, and to tackle the high heterogeneity within and between primary studies, all extracted effect sizes from correlational/cross-sectional or longitudinal prospective/retrospective studies were total effects (i.e., without controlling for confounders). Therefore, according to the preliminary considerations of the ROBINS-E assessment tool, all of these effect sizes have a high risk of bias, with no further assessment being required. Regarding the four intervention studies included in the meta-analyses, one was classified with a low risk of bias (Carvalho et al., 2005); two with moderate risk of bias - one because of confounding factors (i.e., significant differences between the control and treatment groups on depression symptoms and quality of life at baseline; Gavilán-Carrera et al., 2020) and another due to the classification of interventions (i.e., group allocation according to the willingness of participants to exercise or not; Reis-Neto et al., 2013); and another study with serious risk of bias due to no clearly defined intervention and control groups in the report of the results (Robb-Nicholon, et al., 1989) (full details are presented in the supplementary file 7).

Quality of life. Four out of eight categories of correlates/predictors showed significant overall effects. Specifically, less threatening illness and treatment-related beliefs (r= -.622), better self-perceptions (r= .334), higher resilience (r= .464) and more physical activity (r= .194) were associated with higher quality of life of individuals with SLE.

Absence of depression and anxiety symptoms. Eight categories showed significant overall effects over depression and anxiety symptoms. Specifically, less threatening illness and treatment-related beliefs (r= -.636), lower perceived stress (r= -.572), better self-perceptions (r= .464), more resilience

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(*r*= .482), higher knowledge/literacy (*r*= .394), better general perceived control (*r*= .446), more physical activity (*r*= .209), and more positive interactions with others/groups (*r*= .337) were associated with less anxiety and depression symptoms.

Global index of disease activity. Only threatening illness and treatment-related beliefs showed a positive significant but small overall effect over disease activity (*r*= .225).

Fatigue and pain. Four out of seven categories of correlates/predictors showed significant overall effects. Specifically, more threatening illness and treatment-related beliefs (*r*= .445), higher perceived stress (*r*= .366), less physical activity (*r*= -.223) and poorer interactions with others/groups (*r*= -.270) were associated with more fatigue and pain among individuals with SLE.

Trim and fill analyses. The trim and fill analyses (Table 3) suggested that bias was present in some of the categories of correlates/ predictors, given the asymmetrical funnel plot distributions. The overall effects of these were thus adjusted considering the missing effect sizes. Regarding quality of life, two categories revealed higher adjusted effects (threatening illness and treatment-related beliefs, and physical activity). For the absence of depression and anxiety symptoms, two categories revealed lower adjusted effect sizes (self-perception and positive relation with healthcare system and professionals). For disease activity, seven categories revealed higher adjusted effects (self-perception, resilience, perceived stress, physical activity, diet, and sunlight exposure), and two categories showed lower adjusted effects (threatening illness- and treatment related-beliefs, and interactions with others/ groups). Regarding fatigue and pain, two categories showed higher adjusted effects (perceived stress, and illness-related attitudes and affect), and two categories revealed lower adjusted effects (illness- and treatment-related beliefs, and interaction with others/groups). For the remaining categories, the

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distribution of effect sizes was symmetrical, so the overall adjusted effects of those categories did not change.

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Table 2

Overall mean effect sizes of predictors/correlates over adjustment (quality of life, absence of depression and anxiety symptoms), and disease/illness activity (global index, fatigue, and pain).

	# Studies	# ES	Fisher's *z* (SE)	95% CI	Sig. mean z (*p*)	Mean *r*	% Var. level 1	Level 2 variance	% Var. level 2	Level 3 variance	% Var. level 3
Outcome: SLE adjustment											
Quality of life											
Psychological correlates/predictors											
Threatening illness and treatment-related beliefs	4	6	-.729 (.201)	-1.245, -0.212	.015*	-.622	1.58	.199***	98.42	.000	1.64
Self-perception	4	7	.347 (.084)	0.142, 0.552	.006**	.334	22.07	.103^{+}	35.51	.112	42.41
Resilience-related factors	2	3	.503 (.076)	0.174, 0.833	.022*	.464	100	.000	5.64	.000	0
Perceived stress	1	1	-	-	-	-.260	-	-	-	-	-
Illness-related attitudes and affect	2	3	-.589 (.262)	-1.718, 0.540	.154	-.529	1.23	.093***	56.48	.070	42.30
Knowledge/literacy	1	2	.161 (.040)	-0.341, 0.664	.153	.160	-	-	-	-	-
General control perception	1	1	-	-	-	.421	-	-	-	-	-
Behavioral correlates/predictors											
Physical activity	5	8	.197 (.067)	0.039, 0.355	.022*	.194	31.01	.000	9.13	.014	68.99
Addictive behavior	3	6	-.234 (.096)	-0.482, 0.013	.059	-.230	8.73	.000	2.37	.024**	91.27
Social correlates/predictors											
Interaction with others/groups	3	4	.321 (.124)	-0.073, 0.716	.081	.310	5.06	.014**	29.81	.032	65.12

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Positive relation with healthcare system and professionals	1	1	-	-	-	.185	-	-	-	-	-
Absence of depression and anxiety											
Psychological correlates/predictors											
Threatening illness and treatment-related beliefs	5	11	-.752 (.059)	-0.884, -0.621	<.001***	-.636	39.00	.000	4.23	.013*	60.99
Self-perception	6	14	.503 (.120)	0.244, 0.762	.001***	.464	10.39	.025**	28.99	.053***	60.61
Resilience-related factors	5	10	.526 (.129)	0.233, 0.818	.003**	.482	8.87	.036**	40.14	.046***	50.99
Perceived stress	4	6	-.650 (.095)	-0.895, -0.405	.001**	-.572	22.47	.003	8.09	.027	69.45
Knowledge/literacy	1	2	.416 (.079)	0.262, 0.569	<.0001***	.394	-	-	-	-	-
General control perception	2	6	.480 (.107)	0.205, 0.755	.006**	.446	16.78	.038**	75.03	.004	8.19
Behavioral correlates/predictors											
Physical activity	5	15	.212 (.086)	0.028, 0.396	.027*	.209	27.07	.028	1.98	.396***	72.93
Addictive behavior	1	1	-	-	-	-.128	-	-	-	-	-
Social correlates/predictors											
Interaction with others/groups	5	10	.351 (.092)	0.144, 0.559	.004**	.337	21.20	.025**	51.37	.014	27.42
Positive Relation with healthcare system and professionals	1	2	.218 (.136)	-0.048, 0.485	.189	.215	-	-	-	-	-
Illness stigma	1	1	-	-	-	-.730	-	-	-	-	-
Outcome: Disease/Illness activity											
Global Index of disease activity											
Psychological correlates/predictors											
Threatening illness and treatment-related beliefs	6	8	.229 (.076)	0.050, 0.409	.019*	.225	22.52	.014	48.81	.008	28.67

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Self-perception	6	6	-.106 (.055)	-0.248, 0.036	.113	-.106	75.99	.000	24.01	.003	3.04
Resilience-related factors	6	6	-.203 (.100)	-0.460, 0.055	.099	-.200	20.76	.012	29.22	.020	50.01
Perceived stress	5	8	.195 (.087)	-0.011, 0.401	.060	.193	17.15	.000	3.43	.033***	82.85
Illness-related attitudes and affect	1	1	-	-	-	.017	-	-	-	-	-
Knowledge/literacy	1	3	-.332 (.332)	-1.761, 1.097	.423	-.320	-	-	-	-	-
General control perception	1	1	-	-	-	-.248	-	-	-	-	-
Worrying	1	1	-	-	-	.110	-	-	-	-	-
Behavioral correlates/predictors											
Physical activity	4	7	-.296 (.170)	-0.711, 0.119	.131	-.288	14.46	.000	1.15	.097**	85.53
Diet	2	2	-.118 (.101)	-1.406, 1.170	.452	-.117	49.99	.000	0	.010	50.00
Sunlight exposure	1	2	.024 (.048)	-0.584, 0.631	.709	.024	-	-	-	-	-
Social correlates/predictors											
Interaction with others/groups	4	4	-.072 (.035)	-0.183, 0.039	.130	-.072	100	.000	1.84	.000	1.84
Positive Relation with healthcare system and professionals	2	2	-.095 (.064)	-0.909, 0.718	.377	-.095	100	.000	1.01	.000	1.01
Fatigue and pain											
Psychological correlates/predictors											
Threatening Illness and treatment-related beliefs	6	10	.478 (.037)	0.394, 0.563	<.001***	.445	71.38	.002	13.83	.002	14.79
Perceived stress	3	7	.384 (.037)	0.292, 0.475	<.001***	.366	100	.000	1.11	.000	0
Illness-related attitudes and affect	2	2	.438 (.037)	-0.031, 0.908	.054	.412	100	.000	5.63	.000	5.64
Worrying	1	2	.481 (.084)	-0.586, 1.547	.110	.447	-	-	-	-	-
Behavioral correlates/predictors											

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Physical activity	9	19	-.227 (.054)	-0.340, -0.114	<.001***	-.223	34.43	.000	3.78	.016	65.57
Addictive behavior	2	5	.073 (.029)	-0.008, 0.155	.067	.073	61.66	.002	38.38	.000	8.44
Social correlates/predictors											
Interaction with others/groups	4	5	-.277 (.030)	-0.311, -0.144	.002**	-.270	100	.000	3.66	.000	6.60

Note. # Studies = number of studies; # ES = number of effect sizes; SE = standard error; CI = confidence interval for Fisher's *z*; Sig. mean *z* = level of significance of mean effect size; Mean *r* = mean effect size (Pearson's correlation); % var = percentage of variance; Level 2 variance = variance between effect sizes within studies; Level 3 variance = variance between studies.

* $p < .05$; ** $p < .01$; *** $p < .001$

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Table 3

Overall mean effect sizes of the predictors/correlates over adjustment (quality of life, absence of depression and anxiety symptoms), and disease/illness activity (global index, fatigue and pain).

	# Studies	# ES	Fisher's z (SE)	95% CI	Sig. mean z (*p*)	Mean *r*
Outcome: SLE adjustment						
Quality of life						
Psychological correlates/predictors						
Threatening illness and treatment-related beliefs	5	7	-.730 (.167)	-1.057, -0.402	<.0001***	-.623
Self-perception	-	-	-	-	-	-
Resilience-related factors	-	-	-	-	-	-
Illness-related attitudes and affect	-	-	-	-	-	-
Knowledge/literacy	-	-	-	-	-	-
Behavioral correlates/predictors						
Physical activity	8	11	.222 (.041)	0.141, 0.303	<.0001***	.218
Addictive behavior	-	-	-	-	-	-
Social correlates/predictors						
Interaction with others/groups	-	-	-	-	-	-
Absence of depression and anxiety						
Psychological correlates/predictors						
Threatening illness and treatment-related beliefs	-	-	-	-	-	-
Self-perception	8	16	.475 (.069)	0.340, 0.609	<.0001***	.422

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Resilience-related factors	-	-	-	-	-	-
Perceived stress	-	-	-	-	-	-
Knowledge/literacy	-	-	-	-	-	-
General control perception	-	-	-	-	-	-
Behavioral correlates/predictors						
Physical activity	-	-	-	-	-	-
Social correlates/predictors						
Interaction with others/groups	-	-	-	-	-	-
Positive relation with healthcare system and professionals	2	3	.216 (.111)	-0.002, 0.434	.052	.213
Outcome: Disease/Illness activity						
Global Index of disease activity						
Psychological correlates/predictors						
Threatening illness and treatment-related beliefs	9	11	.173 (.067)	0.041, 0.305	.010*	.171
Self-perception	8	8	-.049 (.037)	-0.123, 0.024	.185	-.454
Resilience-related factors	7	7	-.277 (.076)	-0.426, -0.127	<.0001***	-.270
Perceived stress	7	10	.221 (.058)	0.108, 0.334	<.0001***	.217
Knowledge/literacy	-	-	-	-	-	-
Behavioral correlates/predictors						
Physical activity	6	9	-.299 (.089)	-0.473, -0.124	<.0001***	-.290
Diet	3	3	-.213 (.115)	-0.438, 0.012	.063	-.210
Sunlight exposure	2	3	.037 (.039)	-0.039, 0.114	.343	.037
Social correlates/predictors						

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Interaction with others/groups	6	6	-.050 (.032)	-0.113, 0.012	.115	-.050
Positive relation with healthcare system and professionals	3	3	-.080 (.061)	-0.199, 0.039	.187	-.080
Fatigue and pain						
Psychological correlates/predictors						
Threatening illness and treatment-related beliefs	9	13	.444 (.034)	0.377, 0.512	<.0001***	.417
Perceived stress	4	8	.402 (.035)	0.334, 0.469	<.0001***	.382
Illness-related attitudes and affect	3	3	.459 (.032)	0.396, 0.523	<.0001***	.429
Worrying	-	-	-	-	-	-
Behavioral correlates/predictors						
Physical activity	-	-	-	-	-	-
Addictive behavior	-	-	-	-	-	-
Social correlates/predictors						
Interaction with others/groups	5	6	-.219 (.029)	-0.275, -0.163	<.0001***	-.216

Note. # Studies = number of studies; # ES = number of effect sizes; SE = standard error; CI = confidence interval for Fisher's *z*; Sig. mean *z* = level of significance of mean effect size; Mean *r* = mean effect size (Pearson's correlation).
* $p < .05$; ** $p < .01$; *** $p < .001$

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Discussion

This systematic review of 90 articles aimed to: (1) identify modifiable psychological, behavioral and social factors associated with illness adjustment and disease/illness activity among adults with SLE, and (2) quantify the individual contributions of those factors via a meta-analysis, which included findings from over 9200 individuals across 54 articles. In the next section, we will first highlight and discuss the main findings and research trends on predictors/correlates of adjustment to SLE and disease/illness activity. Then, we will pinpoint major gaps in the literature, as to inform novel directions for future research. Finally, we discuss the study limitations and its clinical implications.

Predictors/correlates of SLE adjustment and disease/illness activity: Main trends and findings

Figure 2 illustrates the current state of knowledge on the main psychological, behavioral and social predictors/correlates of SLE adjustment and disease/illness activity. Most of the included studies (> 60%) focused on psychological factors, reflecting a dominance of intraindividual psychological theoretical models on psychosocial research on SLE adjustment and disease/illness activity (Walker, Jackson, & Littlejohn, 2004).

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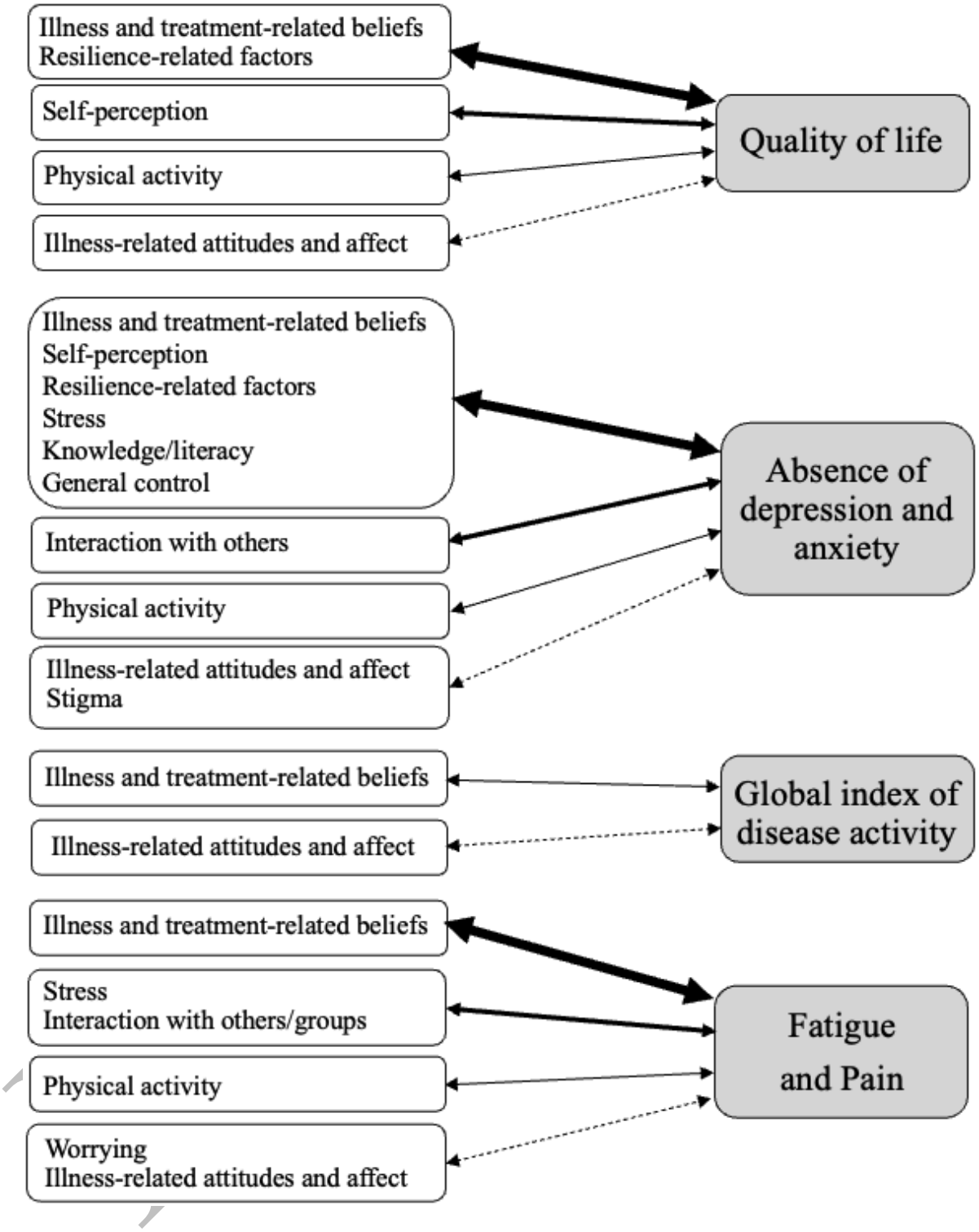


Figure 2. Illustration of the main psychological, physical and social correlates/predictors of SLE adjustment and disease/illness activity. Note:

- Large associations ($r > .371$)
- Moderate associations ($.243 < r < .371$)
- Small associations ($.100 < r < .243$)
- Association found in narrative review but not in meta-analysis.

Three main categories of psychological correlates/predictors showed consistent associations with SLE adjustment and disease/illness activity. First, a bulk of research on the role of *illness- and treatment-related cognitions and affect*, supports their relevance in self-regulation processes underlying illness adjustment (Leventhal et al., 1992; Leventhal & Brissette, 2002). Better illness- and treatment-related beliefs (*i.e.*, low perceived illness threat and severity, low medication-related concerns and high perceived illness control) were strongly and consistently associated with better SLE adjustment and lower pain and fatigue. Conversely, *maladaptive illness-related attitudes and affect* (e.g., denial, hypochondriac beliefs) were consistently (albeit less strongly) associated with poorer SLE adjustment and higher disease/illness activity (in the narrative review only). These findings are aligned with previous systematic reviews on the predictors/correlates of adjustment to other autoimmune and/or rheumatological diseases, such as multiple sclerosis (Dennison et al., 2009) and rheumatoid arthritis (Matcham et al., 2015). They also concur on stressing the central role of cognitions in shaping pain and fatigue, and their inherently biopsychosocial nature (Cleanthous et al., 2012; Jensen et al., 2011; Nichilatti, et al., 2020).

A second trend of findings, showed that *positive self-perceptions* (e.g., good body image, self-esteem, self-illness separation) and stronger *resilience-related factors* (e.g., optimism, hope, resilience) were consistently associated with better SLE adjustment, supporting the contention that maintaining positive perceptions of the self, the world, and the future are central coping tasks when dealing with stressors imposed by chronic diseases (Helgeson & Zajdel, 2017; Walker et al., 2004). This is especially the case when a disease, such as SLE, bears visible signs that may threaten public appearance (Ribeiro et al., 2017). Although certain self-perceptions (e.g., body image) have been less investigated in relation to adjustment to other chronic conditions (Dennison et al., 2009; Jensen et al., 2011; Matcham et al., 2015), self-esteem has also been associated with better adjustment to inflammatory bowel disease (Jordan et al., 2016). Resilience-related factors, such as hope or optimism,

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have also been shown to play a significant role in the adjustment to other chronic conditions (Dennison et al., 2009; De Ridder et al., 2008).

In line with previous studies, a third and final trend in research on psychological correlates/predictors showed that higher *perceived stress* (i.e., the degree to which one's life situations are appraised as taxing one's resources) was strongly associated with higher symptoms of depression and anxiety (Dennison et al., 2009; Jordan et al., 2016) and moderately associated with increased pain and fatigue (Druce & Basu, 2019; Hannibal & Bishop, 2014; Matcham et al., 2015).

Although Figure 2 shows a predominance of psychological factors, around one third of the studies investigated the role of behavioral factors. These studies showed that *physical activity*, and especially *avoiding sedentary behavior*, was slightly but consistently associated with higher quality of life, lower depression, anxiety, fatigue, and pain. Although the study of the role of physical activity on autoimmune diseases is relatively recent, these findings are in line with previous evidence showing that staying active brings better health and illness adjustment outcomes (Sharif et al., 2018; Wu et al., 2017).

Finally, although only a quarter of the included studies focused on social factors, our review included more references on this topic than systematic reviews on other chronic conditions (e.g., Dennison et al., 2009; Jensen, et al., 2011; Jordan et al., 2016). Evidence showed that *positive interactions with others* (mostly higher *perceived social support*) were associated with better mental health and less fatigue and pain. These findings are in line with previous systematic reviews on the role of social support in chronic pain (Bernardes et al., 2017; Che et al., 2018) and other illness adjustment processes (Dennison et al., 2009). Our findings also indirectly confirm the social support stress buffering hypothesis, which states that perceived availability of support in case of need is a major health protective factor when facing stressful events (Lakey & Cohen, 2000).

In sum, current evidence suggests that to improve SLE adjustment and/or reduce disease/illness activity (mostly fatigue and pain) interventions may target illness- and treatment-related cognitions,

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self-perceptions and resilience-related factors, perceived stress, sedentary behaviors and perceived social support.

Gaps and future directions for research on SLE adjustment and disease/illness activity

Our findings uncovered several gaps in the literature, which may inform future research on SLE adjustment and disease/illness activity. Although most current evidence stressed the role of psychological correlates/predictors, research is still needed to further investigate the role of several potentially relevant cognitive and affective processes. First, we have found an *unexpected lack of studies on stress and coping from a cognitive-transactional perspective* (Lazarus & Folkman, 1984; Lazarus, 1991). Only three studies addressed coping processes. These studies measured different ways of coping, neglecting their underlying action tendencies and their role on self and action regulation processes (Skinner et al., 2003). These studies also did not investigate the extent to which coping efficacy may be modulated by individual and situational factors (Marroquín, Tennen, & Stanton, 2017). This gap may partially account for the inconsistent associations between perceived stress and global indexes of disease (only significant in 2 out 5 studies), which were unexpected, given the well-known long-term impact of stress on health (O'Connor et al., 2021). As such, the role of stress and coping processes on SLE adjustment and disease/illness activity is currently unclear. This gap is somewhat surprising, considering the centrality of the Transactional Model of Stress (Lazarus & Folkman, 1984) in research on chronic illness adjustment (Helgeson & Zajdel, 2017; Moss-Morris, 2013). Indeed, previous systematic reviews confirm the central role of stress and coping on adjustment to other chronic and/or autoimmune conditions (Dennison et al., 2009; Jordan et al., 2016), pain (Peres & Lucchetti, 2010) and fatigue (Matcham et al., 2015). Future research should address the role of stress and coping from a transactional perspective, examining the longitudinal relationships between challenge and threat appraisals, coping action tendencies (e.g., to reestablish control, relatedness and/or

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autonomy, Skinner et al., 2003) and their differential effects on SLE adjustment as to better understand which coping processes may lead to better outcomes, for whom and in which situations.

Second, there is a *striking lack of research on the role of emotion regulation and affective processes* on SLE adjustment and disease/illness activity. Living with a chronic disease is often emotionally challenging and the use of emotion regulation strategies is a central process in illness self-regulation (Hagger & Orbell, 2022; Leventhal et al., 1992). Indeed, evidence suggests that emotion regulation - the ability to modulate emotional states and their expression – can include adaptive or maladaptive strategies that impact the adjustment to chronic illnesses (Koechlin et al., 2018; Wierenga et al., 2017). Future research is needed to investigate the role of emotions and emotion regulation on SLE adjustment and disease/illness activity.

Third, although (chronic) pain is often a central aspect of the experience of living with SLE (Franco et al., 2014), most of the reviewed studies were *not informed by current psychosocial theories on chronic pain adjustment*, e.g., the Fear Avoidance Model of Pain (Vlaeyen et al., 2016) or the Psychological Flexibility Model (McCracken & Morley, 2014). Consequently, there is lack of evidence on specific pain-related adjustment processes and how these may contribute to SLE adjustment and disease/illness activity. For example, although pain-related worrying is a main predictor of poor adjustment to chronic pain conditions (Jensen et al., 2011; Petrini & Arendt-Nielsen, 2020), this cognitive process was one of the least investigated in our study. By drawing upon pain-related psychosocial theoretical models, future research may uncover other relevant disease-specific correlates/predictors of SLE adjustment and disease/illness activity (e.g., fear-avoidance beliefs, acceptance, and psychological flexibility).

Fourth, despite its strong associations with mental health (as show in Figure 2), *only a few studies focused on the role of knowledge/literacy*. Disease-related knowledge and health literacy can shape illness adjustment by influencing, for example, illness representations, coping strategies repertoires or the ability to navigate in the healthcare system (Sorensen et al., 2012). Consistent with reviews on

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other chronic conditions (Rottmann et al., 2010; Vélez-Vélez & Bosch, 2016), *knowledge/literacy* is a promising factor to promote SLE adjustment and may inform the development of psychoeducational interventions.

Our findings on behavioral correlates/predictors have also uncovered a few gaps in the literature, suggesting that *less attention has been paid to the role of self-management in SLE* adjustment and disease/illness activity. Adherence to effective self-management practices is a central behavioral predictor of chronic illness adjustment (Anekwe, & Rahkovsly, 2018; Moss-Morris, 2013; Schulman-Green et al., 2012). Diet, sun exposure or photoprotection and health-promoting lifestyle were the least studied behavioral categories. Considering that *nutrition* has a key influence on the immune system (Childs, Calder & Miles, 2019), and that *sun exposure* is considered a risk factor for SLE flares (Fanouriakis, 2019; Mosca, 2010), further investigation on the possible influence of these factors is needed. These connections could be explored using a combination of different measures (e.g., frequency questionnaires, dietary recall, microtopography of sun-exposed skin; Shim et al., 2014; King et al., 2015). Moreover, other important self-management behaviors, such as treatment adherence (Conthe et al., 2014) or the reduction of risky addictive behaviors (e.g., smoking; Barlow et al., 2002) should also be considered, given their well-known association with illness adjustment and disease/illness activity among individuals with other chronic conditions.

Still under *behavioral correlates/predictors*, the inconsistent findings on the *role of physical activity* (especially concerning disease/illness activity) suggest that further research is needed. As the ability to maintain regular physical activity levels is central to good illness adjustment (Moss-Morris, 2013; Sharif et al., 2018), randomized controlled trials testing the type and volume of physical activity that have better results for individuals with SLE, considering different levels of disease/illness activity could be conducted (Ayán & Martín, 2007). Furthermore, the investigation of physical activity patterns (i.e., regular and consistent behavioral patterns that occur in daily activities or occupations; Bendixen, 2006) among individuals with SLE may be an important avenue for future research. Patterns of activity

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avoidance or excessive activity are often associated with poorer physical and psychological function among individuals with chronic pain conditions (Andrews et al., 2012). Conversely, activity pacing to achieve an adaptive goal (Esteve et al., 2017; McCracken & Samuel, 2007) has shown promising results as a strategy to decrease the fluctuation between peaks of overactivity and sedentary behavior (Guy et al., 2019).

Only around one quarter of the included studies focused on the role of *social correlates/predictors in SLE* adjustment and disease/illness activity, showing *a limited use of psychosocial and/or socioecological approaches* to understand SLE adaptation (Chan, Cardoso & Chronister, 2009). Furthermore, research on social factors goes *little beyond perceived social support* (an intraindividual factor), falling short from uncovering the complexities of the social roots of chronic illness adaptation processes (Smedema, Bakken-Gillen, & Dalton, 2009). Social integration, received/provided social support, social control, social constraints on disclosure, relationship quality, enacted stigma, dyadic coping are just a few examples of processes characterizing interpersonal relationships, which shape (and are shaped by) chronic illness experiences (Helgeson & Zajdel, 2017; Martire & Helgeson, 2017; Marroquín, Tennen, & Stanton, 2017; Pietromonaco & Collins, 2017; Stanton, Revenson & Tennen, 2007). Our findings also suggest that the relationship with *health professionals and the healthcare system may also deserve further attention*, as these may influence satisfaction with healthcare and treatment adherence (Polinski et al., 2014). Beyond interpersonal relationships, other modifiable social factors can influence chronic illness adaptation. Individuals with SLE may identify with different social groups (gender, culture/ethnicity, religion), whose norms and values often inform their health and illness beliefs and behaviors (Jetten et al., 2017; Jettem, Haslam, & Haslam, 2011). These individuals live in different communities with different environmental and social resources (e.g., social capital; Ehsan et al., 2019), and in different societies with different legal, health and socioeconomic systems. All these social factors trickle down and influence interpersonal and individual processes of chronic illness adaptation (Chan, Cardoso & Chronister, 2009; Helgeson & Zajdel, 2017; Kapos et al.,

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2024; Taylor, Repetti & Seaman, 1997). The extent to which different layers of our social lives shape chronic illness adaptation, in general, and SLE adjustment and disease/illness activity, in particular, is a very rich and promising avenue for future research.

If the interconnections between social and psychological factors have been underexplored, the same could be said about research on the links between psychosocial and biological factors. *SLE research is still barely informed by biopsychosocial models of adjustment* (Walker et al., 2004). Most of the studies including biological measures of disease activity did not assess psychological or social correlates/predictors. A growing field of research suggests that psychosocial variables can influence disease activity and physical adjustment via several physiological pathways (Walker, Jackson & Littlejohn, 2004), so future investigation should investigate biological correlates (e.g., neuroendocrine responses, immune system functioning) of psychological and social predictors of disease activity.

Finally, some methodological gaps in research can be highlighted. First, most study participants were young or middle-aged women from Europe or USA, with SLE for 10 years on average, which *hampers the generalization of our findings to more diverse clinical populations*. Recent intersectionality approaches to health (Giritli-Nygren, & Olofsson, 2014; Schulz, & Mullings, 2006) may inform future research on SLE adjustment and disease/illness activity among men and/or individuals with different cultural backgrounds. Whether predictors of SLE adjustment and disease/illness activity change throughout the course of the disease should also be investigated. Indeed, such temporal perspective on SLE adjustment and disease/illness activity, along with inferences on causality, are curtailed by the *cross-sectional design of most of the studies*. Also, most studies used self-report measures for both correlates/predictors and outcomes, hence, their results may be influenced by *shared-method variance*.

Overall, these methodological gaps urge some caution when interpreting our previously mentioned trends in the current literature, especially when it comes to making causal inferences and establishing temporal relationships. More high-quality prospective and intervention studies, making use of

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experimental designs as well as having, whenever possible, self-report and objective measures of predictors and outcomes are sorely needed to provide the required evidence to allow causal inference in future studies. Also, the more widespread use of causal directed acyclic graphs (DAGs) to guide study design, data collection and statistical analysis in observational studies is recommended (Poppe et al., 2024).

Study limitations

The conclusions of this review should be considered in light of several limitations. First, given the large number of included articles, unpublished studies and grey literature were excluded; this may be a potential source of bias, as these are more likely to report non-significant results. Publication bias was rare for SLE adjustment outcomes, but somewhat meaningful for disease/illness activity outcomes. Thus, missing studies may have impacted results regarding the latter. Second, also due to the large number of available studies, this review did not include qualitative studies, which may have curtailed insights regarding the topic of research. Third, the term "lifestyle" or related terms (e.g., diet, physical activity) were not included in the search string, which might have hampered the identification of studies on behavioral factors. While the decision of not mentioning specific behavioral, social and psychological factors on the search string was made to prevent valuing some factors over others, this strategy may have contributed to leaving out a few potentially relevant studies. Fourth, although 60% of the studies were included in the narrative review and the meta-analysis, the remaining studies did not provide appropriate statistical information to be included in the latter. The high heterogeneity of factors and measures across studies and lack of statistical information prevented the quantification of the effects of three correlates/predictors categories (out of 17; i.e., coping, diet and knowledge) on SLE adjustment and disease/illness activity. Fifth, this review has only considered the total effects of correlates/predictors over outcomes, not providing information on the mechanisms accounting for those relationships (i.e., mediators) nor the conditions that may modulate them (i.e., moderators). The

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meta-analysis results showed a significant variance of some correlate/predictor effect sizes within the same study and between different studies. This suggests that some of the studies' (e.g., design, country) or samples' characteristics (i.e., age, age of diagnosis) may explain this variance. However, because of the reduced number of studies in each category, it was not possible to conduct moderation analyses. Sixth, high risk of bias due to study design and confounding should be considered when interpreting the findings of our meta-analysis. Given the low number of experimental and prospective primary studies, it was not possible to run a separate meta-analysis only including these. By synthesizing findings from experimental, prospective and (mostly) cross-sectional studies, our meta-analysis has an increased risk of bias due to study design. Thus, the current strength of evidence for the tested relationships is low/insufficient, limiting the goal of informing intervention development. As intervention development requires causal inference, future meta-analyses supporting such a goal should exclude cross-sectional studies, which do not allow to establish the direction of causation between exposure and outcome nor allow adequate control of confounding (Mathur & VanderWeele, 2022). Furthermore, due to the low number of studies with adjusted effect sizes for the studied relationships, and to tackle the high heterogeneity within and between primary studies in the adjustment for confounders, only the unadjusted effects were extracted. This increased the risk of bias due to confounding, with all extracted effect sizes from observational studies having high risk of bias, and only one of the four included intervention studies having a low risk of bias.

Given the impossibility of running sensitivity analyses to quantify the level of bias in our meta-analysis estimates (Mathur & VanderWeele, 2022), our results of our meta-analysis should be interpreted with caution. To decrease the risk of bias due to confounding, future meta-analyses should, whenever possible, use adjusted effect sizes, and ensure the original studies have controlled for the correct set of confounders. This requires defining an appropriate set of confounders for each association extracted from the original studies and causal DAG development might be a useful tool to do it (Poppe et al., 2024). Although some demographic or socioeconomic variables should be

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controlled for all associations, some factors might be specific to certain predictor-outcome associations. For example, if the association between self-perception and depression is being considered, factors such as the level of skin visible signs should be controlled for, whereas if the association between physical activity and quality of life is being considered, a different set of confounders should be used, such as stiffness or joint pain.

Implications for clinical practice

Despite the previous limitations, our main trends and findings may have important implications for clinical practice. It is important to highlight that, as our results do not allow drawing firm causal inferences, the following implications are mainly informed by current empirically-supported theoretical models and some of our findings from experimental and prospective studies. We start by reflecting on clinical practice implications for addressing potential risk or protective factors as specific targets of psychosocial and/or behavioral interventions. Given the wide variety of SLE manifestations, we then reflect on the extent to which such interventions programmes could be tailored to individuals' needs.

Although many of the current interventions to improve the quality of life of individuals with SLE have mainly focused on lifestyle changes (e.g., diet, exercise; Chang et al., 2021; Geertsema-Hoeve et al., 2024), future interventions to improve SLE adjustment and reduce illness activity (pain and fatigue) should address the psychological factors that showed consistent and robust associations with these outcomes, namely, *illness and treatment-related beliefs*. Indeed, helping individuals explore the personal meanings of their chronic disease is a common rehabilitation intervention (Livneh, 2022). Psychoeducation, identifying and challenging negative automatic thoughts and beliefs regarding SLE identity, causes, consequences, timeline and control/cure are useful cognitive-behavioral techniques (Goodman et al., 2005), that have shown promising results in promoting better illness representations with individuals with other chronic diseases (e.g., atrial fibrillation; Shan et al., 2022). Improving self-

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management skills such as providing symptom-monitoring support can also promote self-efficacy regarding SLE management (Greco et al., 2004; Sohng, 2003). Such interventions, by potentially replacing SLE threat appraisals may ultimately foster more adaptive coping action tendencies (Skinner et al., 2003) leading to reduced levels of distress.

Indeed, reducing *perceived stress* is also an important objective to include in future interventions to foster better stress management among individuals with SLE. Aside from restructuring SLE-related beliefs, mindfulness-based (Taub et al., 2021) or cognitive-behavioral stress reduction programs (Greco et al., 2004) may be useful. For example, a program including muscle relaxation and cognitive-behavioral pain and stress management training (e.g., problem-solving strategies for coping with SLE symptoms and interpersonal challenges) predicted short term improvements on pain and psychological and physical function, and reduced long term perceived stress (Greco et al., 2004).

Due to the self-perception impact on SLE adjustment and the poor body image of some women with SLE (Jolly et al., 2012a), future interventions could also target these factors. However, specific psychosocial interventions for adults with visible SLE manifestations are lacking, hampering conclusions regarding the optimal contents, setting, length or intensity of such interventions (Norman & Moss, 2015). Nevertheless, combining education, CBT and cosmetic training showed promising results on improving body image and well-being among individuals with SLE (Jolly et al., 2014).

Overall, psychological interventions restructuring SLE representations, improving symptom and stress management skills and promoting better self- and body- image, will ultimately increase individuals' psychological resilience, which is also an important predictor of good SLE adjustment (Joyce et al., 2018).

Although our findings are less consistent regarding the role of behavioral and social predictors of SLE adjustment and disease/illness activity, we believe that integrating intervention components targeting some of these predictors, such as activity engagement and (perceived) social support may be useful. Despite the reduced number of studies regarding exercise in SLE contexts and the lower

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physical fitness of many individuals with SLE, physical training can have potential advantages in fatigue and pain reduction and quality of life improvement (Ayán & Martín, 2007; Bogdanovic et al., 2015; Boström et al., 2016; Wu et al., 2017). More importantly, avoiding sedentary behavior was a factor consistently associated with adjustment. Thus, activity pacing (e.g., resting, activity grading, alternating/spreading activities, prioritizing and grading levels of activity) could be considered in future interventions to stabilize individuals' levels of engagement in valued life activities and, hence, reduce pain, fatigue and improve their quality of life (Guy et al., 2019). Activity pacing interventions can also easily integrate behavior change or self-enactable techniques (e.g., goal setting, action and coping planning, self-monitoring; Michie et al., 2013, Knittle et al., 2020) to improve their efficacy (Antcliff et al., 2021).

Except for the consistent association between perceived social support and better health outcomes, the role of social factors in SLE adjustment is still underexplored. It could be important to help individuals with SLE to acknowledge others as a source of support and to consider different ways of seeking the needed support. In fact, a randomized clinical trial of a psychoeducational intervention to promote social support showed positive results with individuals with SLE (Karlson et al., 2004).

Overall, it is worth noting that our findings showed a wider range of psychosocial correlates/predictors with a moderate/strong association with SLE adjustment than to disease/illness activity. Although disease/illness activity may influence SLE adjustment, this pattern of findings may suggest that psychosocial interventions might be more effective if directly aiming to improve individuals' SLE instead of directly aiming to reduce levels of disease/illness activity. Indeed, the few existing psychosocial interventions that were effective in reducing fatigue have done so by increasing engagement in activities despite it (Tsoi et al., 2024). In other words, although these interventions' primary outcomes were to reduce illness activity, they have done so by changing a dimension of SLE adjustment, namely reducing illness interference in daily activities.

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The extent to which these different types of interventions would be effective with individuals with different SLE-related needs and concerns is currently unknown. SLE has a huge variation of manifestations (e.g., neuropsychiatric, mucocutaneous, musculoskeletal), which may lead to different interindividual illness-related needs and concerns but also intraindividual changes over time in SLE adaptation challenges. Therefore, tailoring interventions to SLE-related manifestations, needs and concerns should be considered in the future. For example, if an individual with SLE, at some point in their journey, has more severe visible mucocutaneous symptoms (e.g., malar rash, alopecia, cutaneous lesions), body image, self-esteem or social stigma might be relevant intervention targets (Jolly et al., 2014). Addressing relatedness threat appraisals and promoting coping action tendencies towards relatedness challenges (e.g., self-reliance, seeking social support; Skinner et al., 2003) could be some of the vital common ingredients in these interventions. However, if an individual with SLE has as more preeminent fatigue or other musculoskeletal symptoms (e.g., join stiffness or pain) interventions promoting activity engagement in valued life activities (e.g., exercise, activity pacing) can be a more relevant intervention approach (Guy et al., 2019). Addressing competence and autonomy threat appraisals and promoting coping action tendencies towards effective and self-determined action (e.g., problem solving, negotiation, accommodation; Skinner et al, 2003) may be more important ingredients in these interventions. For individuals with life threatening symptoms (e.g., pericarditis or nephritis), illness representations, perceived stress or existential anxiety can be relevant intervention targets (e.g., Goodman et al., 2005).

Finally, digital interventions that target some of the factors that we found to be associated with adjustment (e.g., physical activity, emotional distress) seem to have positive outcomes on self-management of other chronic diseases (Lee et al., 2018). However, there is a dearth of digital non-pharmacological interventions for individuals with SLE (Chang et al., 2021). Such digital interventions can, then, be an important avenue for future research and development, as these allow reaching bigger samples, can be scalable and are cost-effective (Gentili et al., 2022).

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Conclusion

This systematic review identified important modifiable psychological, social, and behavioral factors associated with SLE adjustment and disease/illness activity, which may be targeted in future intervention development. Evidence supported the protective role of adaptive illness- and treatment-related beliefs, positive self-perceptions and resilience-related factors, and high perceived social support. Conversely, high perceived stress and sedentary behaviors are identified as risk factors. Furthermore, this study uncovers several gaps in the literature that point to fruitful directions for future research. Regarding psychological factors, more research is needed drawing upon theoretical models on stress and coping from a transactional perspective, affective processes and emotion regulation, psychological predictors of chronic pain development and health literacy. Risk and protection behaviors may be uncovered by research based on illness self-management approaches and/or focused on physical activity (patterns). Finally, socio-ecological perspectives are needed to unpack the potential multiple and complex social influences on SLE adjustment and disease/illness activity, and more high-quality prospective and intervention studies with more diverse clinical populations are in order.

Disclosure statement: The authors report there are no competing interests to declare.

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