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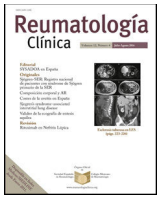

Review article

Efficacy of psychological interventions to reduce anxiety and depression in patients with lupus. A systematic review and meta-analysis

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ABSTRACT

The presence of anxiety and depression symptoms in patients with lupus is common, and some research reports that psychological interventions can reduce them, therefore we conducted a systematic review and meta-analysis of the efficacy of psychological interventions in adults with systemic lupus erythematosus. Randomized and non-randomized clinical trials with adult population diagnosed with lupus, treated with psychological intervention, and compared with similar groups were selected. Several databases were searched in July 2023. Fourteen studies were included in the meta-analysis, with moderate effect sizes for anxiety and depression in group intervention modalities. Factors such as percentage of sample with lupus, gender, medication, and interventions with relaxation components influenced the results. Group psychological intervention programs are effective in reducing symptoms in patients with lupus, although further research on treatment modulating variables is needed.

Eficacia de las intervenciones psicológicas para reducir la ansiedad y depresión en pacientes con lupus. Una revisión sistemática y metaanálisis

Palabras clave:
Intervención psicológica
Lupus
Ansiedad
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Metaanálisis

RESUMEN

La presencia de síntomas de ansiedad y depresión en pacientes con lupus es común, y algunas investigaciones informan que las intervenciones psicológicas pueden reducirlos, por ello se realizó una revisión sistemática y un metaanálisis de la eficacia de las intervenciones psicológicas en adultos con lupus eritematoso sistémico. Se seleccionaron ensayos clínicos aleatorizados y no aleatorizados con población adulta diagnosticada de lupus, tratados mediante intervención psicológica, y se compararon con grupos similares. Se buscó en diversas bases de datos en julio de 2023. Se incluyeron 14 estudios en el metaanálisis con tamaños de efecto moderados para la ansiedad y la depresión en modalidades de intervención grupales. Factores como el porcentaje de muestra con lupus, el género, la medicación y las intervenciones con componentes de relajación influyeron en los resultados. Los programas grupales de intervención psicológica son efectivos para reducir los síntomas en pacientes con lupus, aunque se necesitan más investigaciones sobre variables moduladoras del tratamiento.

Introduction

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease whose etiology is unknown and has been attributed to a variety of environmental and genetic factors.[1,2] This disease can produce a wide range of clinical manifestations and immunological disorders affecting almost all organ systems.[3] The clinical manifestations of the disease tend to change over time, although the most frequent are fatigue, fever, arthritis, exanthema, renal disorders, photosensitivity, hematological alterations, neurological alterations, hypertension or cataracts.[4,5] According to research

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conducted in Europe, Asia and America, the prevalence of SLE in the general population ranges from 0.057% to 0.091%,[6–8] being up to five times more common in women than in men.[9]

Due to changes in appearance, limitations in physical functionality, decreased health-related quality of life, subjective experience of the disease, among other factors, symptoms of anxiety and depression are common in SLE patients,[10–12] reaching prevalences between 60% and 65% for depression and anxiety respectively.[13,14] Several systematic reviews have shown that non-pharmacological interventions, such as psychological or sports interventions for the treatment of SLE, could contribute to reduce the symptomatology of anxiety, depression, and improve the quality of life in these patients.[15–17]

Regarding psychological therapies to reduce anxiety and depression in patients with SLE, there are several types of therapies which have applied different therapeutic components, such as psychoeducation, relaxation, coping strategies or cognitive restructuring, both in individual and group format,[15] although research has focused especially on cognitive-behavioral therapies, reaching moderate effect sizes for both anxiety and depression,[18,19] psychoanalytic therapies and third-generation therapies, with significant improvements in both symptomatologies,[20–23] and even play therapies for children affected by this disease, with acceptable results.[24] In these cases, it is equally important to perform an adequate psychometric assessment of anxious and depressive symptomatology,[25] and some systematic reviews[15,17,26–29] have observed that there is some homogenization in the use of self-reports to assess anxiety and depression in patients with SLE, applying in some cases specific questionnaires of anxious symptomatology, such as the State-Trait Anxiety Inventory (STAI), Perceived Stress Scale (STRESS), or Beck Anxiety Inventory (BAI) questionnaires, specific questionnaires of depressive symptomatology, such as the Beck Depression Inventory (BDI), or Center for Epidemiologic Studies Depression Scale (CES-D), or questionnaires that measure different symptomatology, such as the Symptom Checklist-90-Revised (SCL-90-R), Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29), General Health Questionnaire-28 (GHQ-28), Hospital Anxiety and Depression Scale (HADS), or Arthritis Impact Measurement Scales (AIMS).

Previous meta-analytic research related to the efficacy of psychological interventions to reduce symptoms of anxiety and depression in SLE patients (27,30), has found high effect sizes in the reduction of anxiety ($d = -.95$) and depression ($d = -1.14$). However, there are some limitations that prevent concluding that psychological interventions to reduce anxiety and depression symptomatology in SLE patients are really effective, given that these researches included a low number of studies in the analysis ($k = 3/4$), found high heterogeneity in the results of anxiety ($I^2 = 78\%$) and depression ($I^2 = 72\%/86\%$), the origin of such heterogeneity was not analyzed, and given that several psychological interventions for SLE patients have been developed in the last decade, a new meta-analysis is needed to include more research and draw firmer conclusions about the efficacy of these interventions. Therefore, the aim of this study was to answer the question: are psychological interventions effective in reducing anxiety and/or depression in adult patients diagnosed with systemic lupus erythematosus?

Method

A systematic review and meta-analysis were conducted following the presentation format and guidelines proposed by the PRISMA statement.[31]

Study selection criteria

To be included in the meta-analysis, each study had to meet the following PICOS criteria: (a) population: adults over 18 years of age with a diagnosis of systemic lupus erythematosus disease. Studies with patients with other autoimmune diseases were not excluded, in case there were patients with lupus included in the study; (b) intervention: any type of psychological intervention conducted by health professionals; (c) comparison: the study had to include at least one intervention group and one comparison group with similar clinical characteristics to the intervention group; (d) outcomes: the study had to provide at least a unique and quantitative measure of anxious and/or depressive symptomatology. Priority was given to self-report measures, if these were not available, heteroinformed measures were selected; (e) design: randomized or non-randomized controlled trials.

Search strategy

Several search strategies were used to locate the studies. Firstly, the electronic databases SCOPUS, PsycINFO, PSICODOC, PsycARTICLES and Medline were consulted in July 2023, with no limit on the number of years. The following keywords were combined: [Lupus OR SLE] AND [Intervention OR Treatment OR Therapy] AND [Anxiety OR Depression] AND [Psycho* OR Relax* OR "Cognitive Behavioral"]. Secondly, the references of some meta-analyses and systematic reviews were reviewed.[15,26–30,32,33] Finally, the references of the studies located and included were reviewed. The data flow chart represented in Fig. 1 describes the bibliographic search process.

The search strategy yielded a total of 1600 references. Once duplicate references were excluded, were reviewed by two independent and blind raters. The result of the search process allowed us to select 14 studies,[18,23,34–42] providing a total of 16 treatment groups and 14 comparative groups. We had to exclude one study because it did not report the statistical data needed to calculate effect sizes and we did not receive a response to our request for additional information.[43] The degree of inter-rater agreement was satisfactory (Cohen's Kappa = .856) and disagreements were resolved by consensus.

Coding of moderator variables

To examine the possible influence of study characteristics on effect sizes, we coded the following variables:

(a) General aspects: mean age, psychometric instrument to measure anxiety and depression, percentage of women and type of comparative group; (b) socio-demographic profile (expressed in percentages): country of the sample, ethnic origin, socio-economic status (low, medium, high), educational level (low, medium, high), cohabitation (single or couple), and employment status (active or inactive); (c) clinical profile of the sample: percentage of patients with lupus disease included in the study, percentage of mental health diagnoses, mean duration of disease (in years), mean number of drugs consumed per patient, patients in period of active disease or not (when the study did not report this variable it was considered period of active disease); (d) characteristics of psychological treatments: structured therapy by manual, number of sessions, modality of intervention (individual or group), type of intervention (cognitive behavioral, psychodynamic, third generation or no specific therapeutic modality), treatment components or modules (psychoeducation, relaxation, cognitive restructuring, social skills, problem-solving training or coping training, relapse prevention, emotional regulation, behavioral activation, EMDR, mindfulness, desensitization techniques, acceptance and commitment therapy), intensity of treatment (number of hours per week),

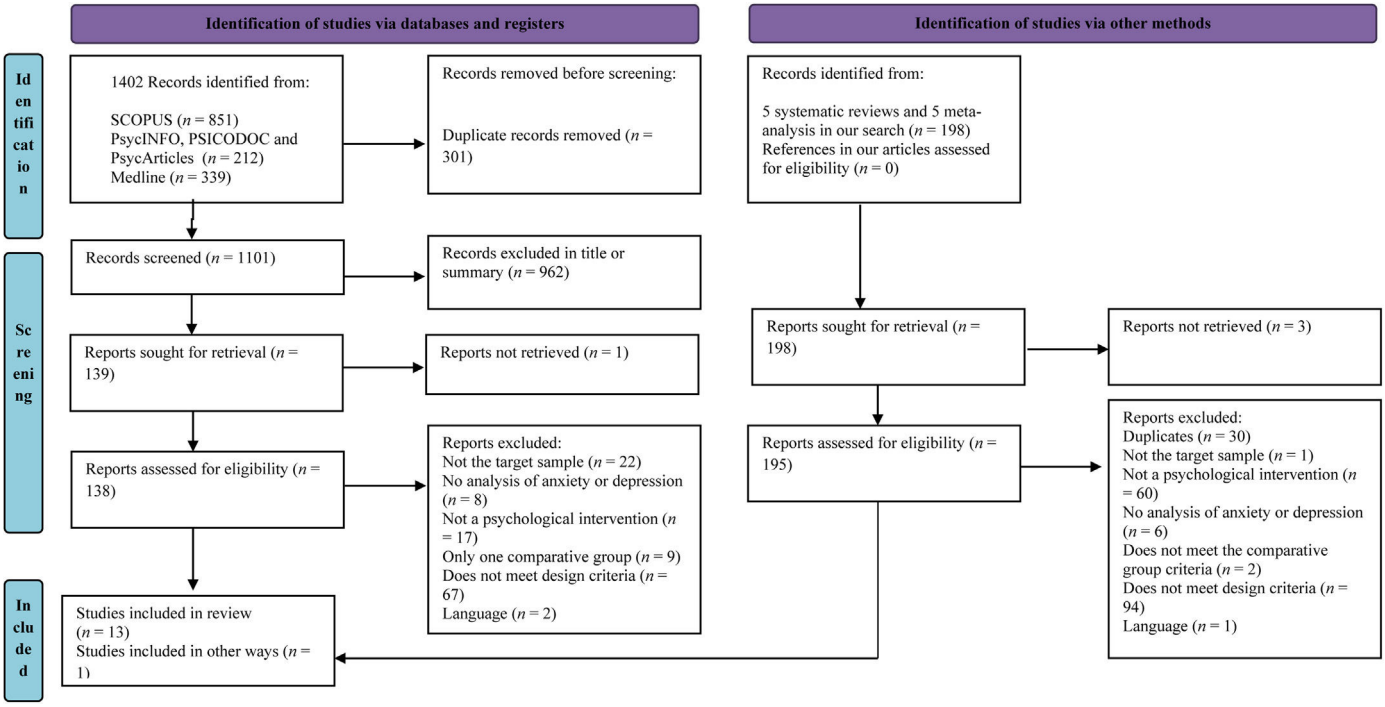

Fig. 1. PRISMA 2020 flow diagram.

duration of treatment (in weeks), and magnitude of treatment (total hours per participant).

The average degree of agreement among coders was 97% and inconsistencies were resolved by consensus.

The methodological quality of the included studies was coded using an adaptation of the PEDro scale[44] to 9 dichotomously items (1 meets criteria; 0 does not meet criteria). The items were:

(a) Clearly specified selection criteria; (b) randomisation to groups; (c) treatment masking; (d) similar groups at baseline, in relation to the most important prognostic indicators; (e) blinding of raters; (f) experimental mortality did not reach 15%; (g) results of all subjects were presented, or if there were losses, an intention-to-treat (ITT) analysis was applied; (h) absence of reporting bias; (i) psychometrically validated instruments.

The average degree of agreement among coders was 90% and inconsistencies were resolved by consensus.

Data analysis

The effect size index used for the results of anxiety and depression was Cohen's *d* index. To calculate it, means, standard deviations and *n* of subjects in the post-test were used, comparing the response variables of the treatment group with the comparative group.

A descriptive analysis of the characteristics of the studies was performed. The mean effect size with its 95% confidence interval was calculated for each individual study, and according to the therapeutic modality of the interventions (individual or group), for each response variable. Analyses were conducted assuming a random-effects model, as these are considered more realistic than fixed-effects[45] and high heterogeneity between studies was expected.

To examine the heterogeneity of effect sizes, Cochran's *Q* and index I^2 were calculated. To assess whether publication bias could threaten the validity of the overall effect size found for each response variable, Egger's test was applied.

The possible influence of qualitative and quantitative moderating variables was examined. For qualitative variables, mixed-effects ANOVAs were applied, and for continuous variables, linear regression models were used, assuming mixed effects. A meta-regression model was applied, including one by one the moderating variables that were significant, and a multiple meta-regression model was applied when more than one individual moderating variable managed to significantly reduce the heterogeneity in the individual meta-regression model. Statistical analyses were performed with IBM SPSS v. 28 for Windows.

Results

Regarding the descriptive characteristics of the studies (Table 1), the sample consisted of 741 participants in the post-test, with a mean sample size of 26.46 participants (*SD* = 14.06) and a mean age of 42.57 years (*SD* = 9.92). The samples came from the USA (40%), Spain (13.3%), Egypt, Italy, China, Iran, South Korea, UK and Brazil (6.7% each), so 46.7% of the sample was from America, 26.7% from Europe, 20% from Asia, and 6.7% from Africa. Of the studies included in this review, 81.3% of the interventions were compared to a waiting list and 18.8% to an active control group and all comparative groups were receiving usual medical care for disease management. Regarding the different instruments used to evaluate anxiety and depression symptomatology, to measure anxiety, 23.1% of the studies used the STAI[46] and HADS[47] questionnaires, 15.4% the SCL-90-R[48] and STRESS,[49] and 7.7% the PROMIS-29,[50] GHQ-28[51] and AIMS,[52] all questionnaires obtained high reliability scores in their original version (α = .79–.93). To measure depression, 31.3% used the CES-D,[53] 18.8% the BDI[54] and HADS,[47] 12.5% the SCL-90-R,[48] and 6.3% the PROMIS-29,[50] GHQ-9[51] and AIMS,[52] all questionnaires obtained high reliability scores in their original version (α = .77–.90).

With respect to the socio-demographic characteristics reported by the studies on their samples, 50% provided information on the ethnic origin of the participants, 18.8% provided information on the socio-economic status of the subjects, 43.8% provided

Table 1
Description of the characteristics of the studies included in the meta-analysis.

	Sakr et al. (2022)[39]	Allen et al. (2021)[18]	Corsetti et al. (2020)[21]	Xu et al. (2021)[42]	Solati et al. (2017)[23]	Jolly et al. (2014)[37]	Navarrete-Navarrete et al. 2010[19]	Danoff-Burg et al. 2006 DTh[35]	Danoff-Burg et al. 2006 PT[35]	Sohng et al. 2003[40]	Greco et al. 2004 CBT[36]	Greco et al. 2004 AL[36]	Arjol et al. 2022[34]	Tench et al. 2003[41]	Peterson et al. 1993[38]	Conceição et al. 2019[20]
Type comparative group	WL	WL	WL	WL	AC	WL	WL	AC	AC	WL	WL	WL	WL	WL	WL	WL
n pre	80	60	45	85	46	15	45	51	48	56	59	60	15	60	29	80
n post	80	44	38	85	46	15	45	46	42	41	51	51	12	40	29	76
M age (*DT*)	33.1 (7.4)	51 (14)	47.7	37.58 (5.28)	38 (13.6)	43.2 (12.2)	43.77 (9.88)	51.2 (13.25)	51.2 (13.25)	32.9 (11.8)	48.2 (9.1)	46.7 (11.7)	46.89 (11.94)	39 (0.8)	37 (8)	42 (12.3)
% women	96.25	95	93	95.4	67.35	90	88.8	82.7	82.7	96	93.5	95	100	100	93	100
Anxiety Questionnaire	SCL-90-R	PROMIS-29	SCL-90-R	STAI	GHQ-28	STAI	STAI	–	–	–	STRESS	STRESS	HADS	HADS	AIMS	HADS
Depression Questionnaire	SCL-90-R	PROMIS-29	SCL-90-R	BDI	GHQ-28	CES-D	BDI	CES-D	CES-D	BDI	CES-D	CES-D	HADS	HADS	AIMS	HADS
Country	Egypt	EEUU	Italy	China	Iran	EEUU	Spain	EEUU	EEUU	South Korea	EEUU	EEUU	Spain	UK	EEUU	Brazil
Ethnicity	–	35% C; 65% OT	–	–	–	85% AF; 15% H	–	86.7% C; 13.3% OT	86.7% C; 13.3% OT	–	76.7% C; 23.3% AF	80.15% C; 18.35% AF; 1.5% AS	–	–	58.6% C; 27.5% AF; 13.7% H	50.05% C; 49.95% AF
Employment	17.5% active	30% active	–	100% active	47.9% active	–	–	47% active	47% active	43.5% active	–	–	–	–	51.7% active	–
Educational level	21.25 H; 33.75% M; 45% L	82% H; 18% M	–	20% H; 60% M; 20% L	32.55% H; 49.95% M; 17.35% L	–	20% H; 60% M; 20% L	–	–	–	–	–	57.2% H; 30.5% M; 13.85 L	–	–	3.85% H; 54.1% M; 41.95% L
Socio-economic status	100% L	77.5% M; 22.5% L	–	–	–	–	–	–	–	–	–	–	–	–	–	87.45% M; 12.55% L
Cohabitation	–	–	–	75.25% couple	–	–	–	68% couple	68% couple	46.5% couple	–	–	–	–	44.8% couple	–

Table 1 (*Continued*)

	Sakr et al. (2022)[39]	Allen et al. (2021)[18]	Corsetti et al. (2020)[21]	Xu et al. (2021)[42]	Solati et al. (2017)[23]	Jolly et al. (2014)[37]	Navarrete-Navarrete et al. 2010[19]	Danoff-Burg et al. 2006 DTh[35]	Danoff-Burg et al. 2006 PT[35]	Sohng et al. 2003[40]	Greco et al. 2004 CBT[36]	Greco et al. 2004 AL[36]	Arjol et al. 2022[34]	Tench et al. 2003[41]	Peterson et al. 1993[38]	Conceição et al. 2019[20]
Active disease	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No
% sample with lupus	100%	100%	2.5%	100%	100%	100%	79.5%	28%	28%	100%	100%	100%	100%	100%	89.6%	100%
% comorbidity	–	–	80% mental disorder	–	–	–	–	–	–	–	–	–	–	–	–	–
M years duration disease	7.5	15	9.8	5.92	7.66	6	–	15	15	4.12	10.8	10.4	12.75	2.5	12	12
M drugs per patient	2.98	–	–	–	–	1.9	1	–	–	–	–	–	–	1.1	9	1.77
Manualized	No	Yes	No	No	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	No	No	No
n sessions	9	8	20	–	8	8	10	4	4	6	6	6	9	12	8	20
Intervention modality	G	I	G	I	I	G	G	I	I	G	I	I	G	I	G	G
Type of intervention	TCC	TCC	TP	TCC	TG	TCC	TCC	TCC	TCC	TCC	TCC	N	TG	TCC	N	TP
Modules	P; R; CR; SS; PS; RP; ER	R; BA; CR; PS; RP	R; ER; E	P	R; RP; M	P; CR; ER; RP; M; D	P; R; CR; SS; PS	–	–	P; SS; PS	P; R; CR; SS; PS	–	P; M; ACT	R	–	PS; ER
Intensity	1	0.75	1.25	1	1	2	2	0.33	0.33	2	1	1	1	1.5	2.5	1.5
Duration	9	8	20	12	8	8	10	3	3	6	6	6	9	12	8	20
Magnitude	9	6	25	12	8	16	20	1	1	12	6	6	9	18	20	30

Note: DTh: deep thought writing; PT: writing positive thoughts; AL: active listening by the doctor; CBT: cognitive-behavioral therapy; WL: waiting list; AC: active control; C: Caucasian; OT: others; AF: African Americans; H: Hispanics; AS: Asiatics; H: high; M: medium; L: low; G: group intervention; I: individual intervention; TP: psychodynamic therapy; TG: third-generation therapy; N: no specific therapeutic model; P: psychoeducation; R: relaxation; CR: cognitive restructuring; SS: social skills; PS: problem-solving or coping training; RP: relapse prevention; ER: emotional regulation; BA: behavioral activation; E: EMDR; M: mindfulness; D: desensitization techniques; ACT: acceptance and commitment therapy.

information on the educational level reached by the participants, 31.3% provided information on whether the participants were living alone or with a partner, and 50% provided information on whether or not the participants were working at the time of the study. In reference to the clinical characteristics of the participants, 75% of the study samples were in the period of active disease, 83.16% of the total sample had lupus disease and the rest had other autoimmune diseases, and 4.6% had comorbidity with mental health problems diagnosed according to the DSM-IV-TR. The mean disease duration of the total sample was 10.3 years ($SD = 4.19$) and the mean number of drugs per patient was 3.02 drugs ($SD = 3.01$).

Regarding the characteristics of the interventions (Table 1), 43.8% of the studies followed a treatment manual, in 50% of the studies the intervention modality was group-based intervention and in the rest individual, in 62.5% the theoretical aspect of the treatment was cognitive behavioral, and in 12.5% the therapy was psychodynamic, third generation or of no type. As for the components of the treatment programs, 43.8% contained a Psychoeducation and a relaxation module, 37.5% problem-solving training or coping skills, 31.3% cognitive restructuring, 25% social skills, relapse prevention and emotional regulation, 18.8% mindfulness, 6.3% behavioral activation techniques, desensitization techniques, EMDR and acceptance and commitment therapy. The mean intensity of the treatments was 1.26 h/week ($SD = 0.61$), the mean duration was 9.25 weeks ($SD = 4.91$) and the mean magnitude was 12.43 h ($SD = 8.38$).

Concerning the methodological quality of the studies analyzed, most of the studies met the criterion of using psychometrically validated instruments (92.9%), followed by specifying the criteria for subject selection and the criterion of equality of groups at baseline in relevant characteristics (85.7%), followed by the criterion of no reporting bias (78.6%), intention-to-treat analysis (71.4%), followed by the criterion that experimental mortality was less than 15% (64.3%), the criterion of randomization of subjects (57.1%), the criterion of masking (35.7%), and the criterion of blinding (21.4%). The total quality score of the studies had a mean of 5.93 (SD = 1.73), with a range between 3 and 9 points (Table 2).

After analyzing the overall effect size (Table 3), significant effect sizes of medium magnitude were found for anxiety ($d = -.530$; $Z = -3.184$; $p < .001$; $k = 13$), and of low magnitude and not significant for depression ($d = -.381$; $Z = -1.748$; $p = .080$; $k = 16$). High heterogeneity was observed for anxiety ($Q\ (12) = 42.405$; $p < .001$; $I^2 = 74.7\%$) and depression ($Q\ (15) = 108.909$; $p < .001$; $I^2 = 87.8\%$), and Egger's test allowed us to rule out publication bias as a threat to the validity of the results for anxiety ($t\ (12) = -.530$; $p = .606$), and depression ($t\ (15) = -.196$; $p = .848$). On analyzing the effect size by subgroups (Table 3), according to the intervention modality (individual or group), it was observed that for anxiety, the effect sizes were significant and of moderate magnitude when the interventions were in group format ($d = -.636$; $Z = -2.834$; $p < .005$; $k = 7$), with moderate heterogeneity ($Q(6) = 15.065$; $p < .05$; $I^2 = 65.7\%$) and no publication bias was observed ($t\ (6) = -.916$; $p = .402$). In the same way, for depression, significant effect sizes were only observed when the interventions were in group format, finding effect sizes of moderate magnitude ($d = -.573$; $Z = -3.015$; $p < .005$; $k = 8$), with moderate heterogeneity ($Q\ (7) = 15.730$; $p < .05$; $I^2 = 59.8\%$) and no publication bias ($t\ (7) = -1.079$; $p = .322$).

Due to the high heterogeneity found in the results, we examined the possible influence of moderating variables for the overall effect size in anxiety, and for the effect size when the intervention was group modality in anxiety and depression. All variables related to (a) general aspects; (b) socio-demographic profile; (c) clinical profile; (d) treatment characteristics; (e) methodological quality, were analyzed as potential moderators. ANOVAs were used for qualitative variables and regression models for quantitative variables.

For the overall effect size of anxiety ($k = 13$), statistical significance was observed for the variables: percentage of women who participated in the study ($F = 4.775$; $p < .05$) with a moderate percentage of variance explained ($R^2 = 30.30\%$); percentage of sample with lupus participating in the study ($F = 5.328$; $p < .05$) with a moderate percentage of variance explained ($R^2 = 32.60\%$). For the effect size of anxiety when the interventions were in group format ($k = 7$), statistical significance was observed for the variables: percentage of the sample with lupus ($F = 8.504$; $p < .05$) with a moderate percentage of variance explained ($R^2 = 55.60\%$); mean number of drugs consumed per patient ($F = 62.562$; $p < .005$) with a high percentage of variance explained ($R^2 = 93.90\%$). For the effect size of depression when the interventions were in group format ($k = 8$), statistical significance was observed for the variables: percentage of sample with lupus ($F = 8.108$; $p < .05$) with a moderate percentage of variance explained ($R^2 = 50.40\%$); mean number of drugs consumed per patient ($F = 20.746$; $p < .05$) with a high percentage of variance explained ($R^2 = 87.40\%$); it was also significant that the interventions contained a relaxation module ($F = 8.577$; $p < .05$) and higher effect sizes were found when the interventions contained a relaxation module ($d = -.985$; $Z = -4.365$; $p < .001$; $k = 3$) than when they did not ($d = -.257$; $Z = -1.455$; $p = .146$; $k = 5$).

An individual and multiple meta-regression models was applied to analyze part of the variability found (Table 4) and the predictors selected were the variables that proved to be significant in the regression and ANOVA models. For the anxiety variable, the percentage of women ($k = 13$) reached statistical significance ($t = 2.216$; $p < .05$) and managed to reduce heterogeneity to a moderate level ($Q\ (12) = 30.716$; $p <$v.001; $I^2 = 66\%$). The percentage of the sample with lupus ($k = 13$) did not reach statistical significance ($t = 2.177$; $p = .052$), but reduced heterogeneity to a moderate level ($Q\ (12) = 31.388$; $p < .001$; $I^2 = 67.3\%$). When the two variables were entered into the meta-regression model, heterogeneity was reduced to a moderate level ($Q\ (12) = 23.482$; $p < .01$; $I^2 = 58.2\%$). For the anxiety variable when the interventions were in group modality, the percentage of the sample with lupus ($k = 7$) reached statistical significance ($t = 3.057$; $p < .05$) and eliminated heterogeneity ($Q\ (6) = 5.722$; $p = .334$; $I^2 = 0\%$). The mean number of drugs consumed per patient ($k = 5$) did not reach statistical significance ($t = 2.296$; $p = .105$) and eliminated heterogeneity ($Q\ (4) = .455$; $p = .929$; $I^2 = 0\%$). For the depression variable when the interventions were in group modality, the percentage of the sample with lupus ($k = 8$) did not reach statistical significance ($t = 2.428$; $p = .051$), but managed to reduce heterogeneity to a low level ($Q\ (7) = 7.98$; $p = .240$; $I^2 = 31.4\%$). Having or not a relaxation component in the intervention ($k = 8$) reached statistical significance ($t = 2.609$; $p < .05$) and reduced heterogeneity to a low level ($Q\ (7) = 7.143$; $p = .308$; $I^2 = 24.6\%$). The mean number of drugs consumed per patient ($k = 5$) did not reach statistical significance ($t = 2.022$; $p = .136$) and eliminated heterogeneity ($Q\ (4) = 1.232$; $p = .736$; $I^2 = 0\%$). Introducing the variables "percentage of sample with lupus" and "having or not a relaxation component in the intervention" in the meta-regression model, the heterogeneity was reduced to almost null ($Q\ (7) = 4.205$; $p < .520$; $I^2 = 6.9\%$).

Discussion

The purpose of this study was to analyze if psychological interventions to reduce anxiety and/or depression in adult patients diagnosed with systemic lupus erythematosus are effective in reducing symptoms of anxiety and/or depression. This purpose was motivated by the fact that current meta-analytical research includes a scarce number of studies analyzing the efficacy of these interventions, and due to their rise in the last decade, it was decided to carry out this study.

Table 2
Analysis of the methodological quality of the studies included in the meta-analysis.

Study	Specified criteria	Randomisation	Masking	Similar groups	Blinding	Mortality lower than 15%.	ITT	Absence bias report	Validated instruments	Total quality
Sakr et al. (2022)[39]	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	6
Allen et al. (2021)[18]	Yes	Yes	Yes	Yes	No	No	No	No*	Yes	5
Corsetti et al. (2020)[21]	No	No	No	Yes	No	No	No	Yes	Yes	3
Xu et al. (2021)[42]	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	7
Solati et al. (2017)[23]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
Jolly et al. (2014)[37]	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	6
Navarrete-Navarrete et al. (2010)[19]	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	7
Danoff-Burg et al. (2006)[35]	Yes	Yes	Yes	Yes	No	Yes	No	No**	Yes	6
Sohng et al. (2003)[40]	Yes	No	No	No	No	Yes	No	Yes	Yes	4
Greco et al. (2004)[36]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	8
Arjol et al. (2022)[34]	Yes	No	No	Yes	No	No	Yes	Yes	Yes	5
Tench et al. (2003)[41]	Yes	Yes	No	No	No	No	Yes	Yes	Yes	5
Peterson et al. (1993)[38]	No	No	No	Yes	No	Yes	Yes	Yes	No	4
Conceição et al. (2019)[20]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No*	Yes	8

* Data needed to calculate effect sizes were not provided and were requested from the corresponding author.
** Depression results were presented clustered by subjects with high and low anxiety, so the mean score between the two groups was calculated.

In general terms, only the interventions to reduce anxiety were effective, since the efficacy results for the depression variable were not significant. Other similar meta-analyses[27,30] although with a low number of included studies, found these interventions to be effective in reducing depression ($d = -1.14/-.44$; $k = 3/4$) and anxiety ($d = -.95$; $k = 3$). This discrepancy in efficacy for depression between our study and other meta-analyses could be due to the number of studies included in the analyses, as our study includes $k = 16$ intervention groups for the depression variable, and the rest range between $k = 3/4$ groups. A possible explanation for the lack of efficacy of interventions for depression could be that due to the influence of variables not reported in the studies analyzed, such as the participants' concern about the negative consequences of the disease for their lives, the unpredictable nature of the disease, or the level of knowledge that patients have about lupus, the results of depression could be modulated[55] and this may be more resistant to therapeutic change.

Interesting results have been observed in analyzing the efficacy of the interventions according to their delivery modality (individual or group), finding that only the effect sizes for anxiety and depression are significant and of moderate magnitude when the delivery modality is group-based. These results are consistent with previous meta-analytic research, which has shown that group-based interventions for anxious and depressive disorders are effective,[56,57] making this type of intervention a good choice for community care settings, where emotional support, social learning and group cohesion are key elements, with group-based therapy showing equivalent results to individual therapy.[58] In patients with lupus, some studies have shown that group-based interventions improve self-efficacy, coping skills and depressive symptomatology,[40] being social support, coping skills and emotional regulation key elements of treatment,[59,60] although other studies suggest that group-based interventions do not improve medical symptoms or quality of life in these patients.[61]

To our knowledge, this study is the first meta-analysis to analyze the heterogeneity found among the effect sizes of psychological interventions to reduce symptoms of anxiety and depression in adult patients with lupus, and as happened in other meta-analyses with a lower number of included articles,[27,30] which found high heterogeneity for depression ($I^2 = 72\%/86\%$; $k = 3/4$) and anxiety ($I^2 = 78\%$; $k = 3$), our study also found high heterogeneity. For the overall effect size of anxiety ($k = 13$), the percentage of women and the percentage of sample with lupus reduced the heterogeneity to moderate levels. These results reflect that for anxiety, a greater number of women included in the studies explain part of the variability found in the effect sizes, in addition, the percentage of the sample with a diagnosis of lupus also explains this variability. These results are consistent with the increased inclusion of women in clinical trials given the higher prevalence of lupus in women[6,9,62] and reflect the need for clinical trials with more balanced male-female samples and with participants diagnosed exclusively with lupus. However, heterogeneity remains moderate, suggesting that other variables not taken into account, such as resilience, subjective experience of the disease, perceived social support or knowledge that patients have about their disease[58,60,63] may be modulating the effect sizes. For anxiety when the interventions were group-based, the heterogeneity was moderate, and the percentage of the sample with a diagnosis of lupus and the mean number of drugs consumed per patient ($k = 5$), were shown to be moderators that eliminated the heterogeneity of the effect sizes, however, due to the small number of articles that provided information on the mean number of drugs consumed per patient, it cannot be concluded that this is really a factor that explains the variability observed. For depression when the interventions were group-based, heterogeneity was

Table 3
Overall effect size, by intervention modality and by individual studies included in the meta-analysis.

Group/study	Anxiety								Depression							
	k	*d*	*SE*	95% CI		*Q* (*p*)	I^2 (%)	Egger's test	*k*	*d*	*SE*	95% CI		*Q* (*p*)	I^2 (%)	Egger's test
				d−	*d*+			*t* (*p*)				*d*−	*d*+			*t* (*p*)
Overall effect size	13	−.530	.1663	−.856	−.204	42.405 (.001)	74 .7%	−.530 (.606)	16	−.381	.2179	−.808	.046	108.909 (.001)	87 .8%	−.196 (.848)
Intervention modality																
Individual	6	−.430	.2571	−.934	.074	25.631 (.001)	82 .3%	.951 (.395)	8	−.211	.3880	−.972	.549	87.187 (.001)	93 .4%	.351 (.737)
Group	7	−.636	.2244	−1.076	−.196	15.065 (.020)	65 .7%	.916 (.402)	8	−.573	.1902	−.946	−.201	15.730 (.028)	59 .8%	−1.079 (.322)
Individual studies																
Sakr et al. (2022)[39]		−.492	.227	−.937	−.047	–	–	–	–	−.734	.231	−1.187	−.282	–	–	–
Allen et al. (2021)[18]		.253	.2637	−.264	.77	–	–	–	–	.036	.2626	−.479	.551	–	–	–
Corsetti et al. (2020)[21]		−1.709	.3795	−2.453	−.965	–	–	–	–	−1.547	.3702	−2.273	−.821	–	–	–
Xu et al. (2021)[42]		−.887	.2274	−1.333	−.441	–	–	–	–	−.961	.2291	−1.41	−.512	–	–	–
Solati et al. (2017)[23]		−1.514	.3345	−2.17	−.859	–	–	–	–	−2.147	.3702	−2.872	−1.421	–	–	–
Jolly et al. (2014)[37]		−.597	.5584	−1.691	.498	–	–	–	–	−.522	.556	−1.612	.567	–	–	–

Table 3 (*Continued*)

Group/study	Anxiety							Depression						
k	*d*	*SE*	95% CI		Q (*p*)	I^2 (%)	Egger's test	*k*	*d*	*SE*	95% CI		Q (*p*)	I^2 (%)	Egger's test
			d−	*d*+			*t* (*p*)				*d*−	*d*+			*t* (*p*)
Navarrete-Navarrete et al. (2010)[19]	−.878	.3128	−1.491	−.265	–	–	–	–	−.879	.3128	−1.492	−.265	–	–	–
Danoff-Burg et al. (2006) DTh[35]	–	–	–	–	–	–	–	–	−.319	.2979	−.903	.265	–	–	–
Danoff-Burg et al. (2006) PT[35]	–	–	–	–	–	–	–	–	.821	.3214	.191	1.451	–	–	–
Sohng et al. (2003)[40]	–	–	–	–	–	–	–	–	.006	.3124	−.607	.618	–	–	–
Greco et al. (2004) TCC[36]	−.398	.2639	−.915	.119	–	–	–	–	−.452	.2646	−.971	.066	–	–	–
Greco et al. (2004) AL[36]	−.176	.26	−.685	.334	–	–	–	–	−.298	.2609	−.81	.213	–	–	–
Arjol et al. (2022)[34]	−.496	.6743	−1.818	.825	–	–	–	–	−.472	.6736	−1.792	.848	–	–	–
Tench et al. (2003)[41]	.053	.2588	−.454	.561	–	–	–	–	1.59	.2967	1.009	2.172	–	–	–
Peterson et al. (1993)[38]	.267	.3733	−.464	.999	–	–	–	–	.159	.3722	−.571	.888	–	–	–
Conceição et al. (2019)[20]	−.532	.2281	−.979	−.085	–	–	–	–	−.522	.228	−.969	−.075	–	–	–

Note: *k*: number of groups; *d*: Cohen's effect size; *SE*: standard error; CI: confidence interval.

Table 4
Meta-regression analysis.

Variable	Model	Moderators	*b*	*SE*	*t* (*p*)	*Q* (*p*)	I^2 (%)
Overall anxiety	Individual (*k* = 13)						
		Intersection	−3.634	1.410	−2.576 (.026)	30.716 (.001)	66%
		Percentage of women	3.313	1.495	2.216 (.049)		
	Individual (*k* = 13)						
		Intersection	−1.735	.574	−3.019 (.012)	31.388 (.001)	67.3%
		Percentage of sample with lupus	1.325	.608	2.177 (.052)		
	Combined (*k* = 13)						
		Intersection	−4.219	1.305	−3.231 (.009)	23.482 (.009)	58.2%
		Percentage of women	2.832	1.366	2.072 (.065)		
		Percentage of sample with lupus	1.133	.557	2.033 (.070)		
Anxiety. group intervention	Individual (*k* = 7)						
		Intersection	−1.738	.3883	−4.475 (.007)	5.722 (.334)	0%
		Percentage of sample with lupus	1.308	.4278	3.057 (.028)		
	Individual (*k* = 5)						
		Intersection	−.851	.205	−4.138 (.026)	.455 (.929)	0%
		Mean number of drugs	.126	.055	2.296 (.105)		
Depression. group intervention	Individual (*k* = 8)						
		Intersection	−1.594	.4427	−3.602 (.011)	7.98 (.240)	31.4%
		Percentage of sample with lupus	1.188	.4893	2.428 (.051)		
	Individual (*k* = 8)						
		Intersection	−.972	.2042	−4.761 (.003)	7.143 (.308)	24.6%
		No relaxation component	.720	.2759	2.609 (.040)		
	Individual (*k* = 5)						
		Intersection	−.891	.2060	−4.322 (.023)	1.273 (.736)	0%
		Mean number of drugs	.111	.0548	2.022 (.136)		
	Combined (*k* = 8)						
		Intersection	−1.526	.3929	−3.883 (.012)	4.205 (.520)	6.9%
		Percentage of sample with lupus	.780	.4746	1.643 (.161)		
		No relaxation component	.494	.2655	1.860 (.122)		

moderate, and the percentage of the sample with a diagnosis of lupus and the fact that the interventions had or did not have a relaxation component managed to reduce heterogeneity to a low level. This again reflects the importance of conducting clinical trials with diagnostically homogeneous samples and the need to incorporate relaxation components in group therapy sessions, as higher effect sizes were observed when interventions included this component. Reviews of previous scientific literature[64–66] have observed that group therapies with relaxation components are effective and more cost-effective than individual therapies, and it is likely that the efficacy of relaxation in group therapies lies in its ability to influence the physiological and psychological processes that modulate anxiety and depression.[67–69] The mean number of drugs consumed per patient was also able to reduce the heterogeneity of depression when the interventions were group-based, with the same problem as in the interventions for anxiety, so more clinical trials are needed to provide information on this variable, as it is likely to be a significant factor.

Regarding the limitations of our study, we first report that our results are focused on the reduction of anxiety and depression symptoms and not on the reduction of clinical diagnoses, which could be of greater interest to those responsible for the implementation of psychological interventions. Secondly, no criteria were established to screen the papers included in the review related to the lupus activity or damage index using validated instruments such as the SLEDAI-2K or SLICC. Thirdly, the inclusion of studies with participants with different diagnoses of lupus could compromise the results obtained.

Concerning the strengths of our study, it is difficult to find relevant studies without locating them due to the exhaustive systematic review through five databases, covering a wide range of years. Second, the studies were screened and coded by two independent evaluators, following an updated coding manual, which enhances the objectivity and rigor of the study. Thirdly, the studies came from four different continents (Europe, America, Asia and Africa), which may favor the generalization of our results to different geographical locations. Fourthly, most of the articles included met numerous criteria of methodological quality.

We conclude that the best option to reduce anxiety and depression symptoms in patients with systemic lupus erythematosus are group-based interventions. Therapists in charge of providing such interventions should keep in mind when preparing interventions that therapeutic groups should be as homogeneous as possible in terms of diagnosis, and interventions should incorporate relaxation components to be most effective. However, more clinical trials are required to provide further evidence for these conclusions, in which the mean number of drugs consumed per patient should be reported, in order to firmly conclude whether it is a factor that modulates treatment effects or not.

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Conflict of interest

None declared.

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