

## PAPER

# Effects of psychological interventions for patients with systemic lupus erythematosus: a systematic review and meta-analysis

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The purpose of this systematic review was to quantify the effects of psychological interventions on psychological health, physical health and disease activity in patients with systemic lupus erythematosus (SLE). Studies were identified through a systematic search of six electronic databases and were included if they used a randomized controlled trial designed to explore the effects of psychological interventions in patients with SLE. Two authors independently assessed the methodological quality of included studies using a quality-scoring instrument developed by Jadad et al. and extracted relevant information according to a pre-designed extraction form. Data was analysed using the Cochrane Collaboration's Revman5.1. Finally, six studies involving 537 patients were included. Meta-analysis showed that psychological interventions could reduce the levels of anxiety (standard mean difference (SMD)  $-0.95$ , 95% confidence interval (CI)  $-1.57, -0.34$ ,  $p$ -value 0.00), depression (SMD  $-1.14$ , 95% CI  $-1.84, -0.44$ ,  $p$ -value 0.00), stress (SMD  $-0.63$ , 95% CI  $-1.02, -0.23$ ,  $p$ -value 0.00), and disease activity (SMD  $-0.34$ , 95% CI  $-0.57, -0.11$ ,  $p$ -value 0.00). Although the effects on mental health, fatigue and physical function were in the expected direction, they were not statistically significant ( $p > 0.05$ ). The present data indicate that psychological interventions are promising treatments for patients with SLE. The findings were based on only six randomized controlled trials (RCTs), some of which were relatively small, so more methodologically rigorous large-scale randomized controlled trials are required to confirm these preliminary estimates of effectiveness. *Lupus* (2012) **21**, 1077–1087.

**Key words:** Meta-analysis; psychological intervention; systemic lupus erythematosus (SLE); systematic review

## Introduction

Systemic lupus erythematosus (SLE), prototype of the autoimmune diseases, is an affliction that can produce a broad spectrum of clinical manifestations and diverse immunological disorders involving almost all organ systems.<sup>1,2</sup> There is currently no cure for SLE, and this condition can be life threatening when major organs are affected. Recently, we have seen a dramatic decrease in mortality from all causes among patients with SLE that can be partially attributed to treatment advances that delay the progression of the disease and minimize organ damage. However, for many SLE

patients, the disease continues to have a profound impact on their daily life.<sup>3</sup> They not only inevitably experience a range of somatic symptoms like pain and fatigue,<sup>4,5</sup> but also deal with existential, emotional, social and psychological difficulties such as reduced stress threshold, anxiety, depression and changes in social roles brought on by their disease.<sup>6–8</sup> All of these have been linked to reductions in work productivity and the worsening of lupus symptoms.<sup>9–12</sup> Nonetheless, patients may be reluctant to add further analgesics, opioids and antidepressants to the numerous agents necessary for basic management of SLE. Therefore, non-pharmacologic methods may be advantageous.

In recent years, there has been a growing use and acceptance of psychotherapy for people with a variety of problems, some primarily medical,<sup>13,14</sup> others psychological<sup>15,16</sup> and others social.<sup>17,18</sup> Results from this emerging literature indicate that participants in such programs have enhanced

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knowledge regarding their disease, have improved psychological and physical health and have made appropriate behavioural modifications. Currently psychological interventions are being studied as potentially beneficial interventions for patients with rheumatic disease.<sup>19–21</sup> A meta-analysis conducted by Astin *et al.* showed that psychological interventions in rheumatoid arthritis provide significant improvement in relief of pain, functional disability and psychological morbidity, over and above that of the usual medical interventions.<sup>22</sup> Glombiewski *et al.* similarly confirmed the positive impact of psychological interventions on pain, sleep problems, depression, functional status and catastrophizing in patients with fibromyalgia.<sup>23</sup> However, to date, it is not well known whether psychological intervention is effective for patients with SLE because the published studies for providing SLE patients with psychological interventions indicate considerable variability in the findings. Therefore, we think it is necessary to carry out a quantitative review to summarize the evidence that specifically examines the effects of psychological interventions on physical health, psychological health and disease activity in patients with SLE, in order to provide the best clinical evidence for overall treatment.

## Methods

### *Literature search*

We searched PubMed, Cochrane Library, Web of Science, EBSCOhost, Chinese Biomedical Literature Database and the Chinese Digital Journals Full-text Database from their inception to June 2011 with no language restrictions. We based the search on the following strategy: (psychotherapy OR psychology OR psychological OR psychoeducation OR behaviour therapy OR cognitive therapy OR cognitive behavioural therapy OR relaxation OR hypnosis OR imagery OR psychosocial OR socioenvironmental) AND (systemic lupus erythematosus OR lupus OR SLE). The search method incorporated National Library of Medicine Medical Subject Heading terms with a text words search. We also identified related systematic reviews and meta-analyses from these databases and checked their reference lists, as well as those of randomized controlled trials (RCTs) included in the review. To reduce publication bias, we included unpublished trials retrieved from the System for Information on Grey Literature (SIGLE) database.

### *Inclusion criteria*

To be included in our review, studies were required to meet the following criteria.

1. Type of study was RCT.
2. Participants included adults aged over 18 years with a clinical diagnosis of SLE according to the American College of Rheumatology (ACR) criteria.<sup>24</sup>
3. The type of intervention was psychological interventions versus a control condition (treatment as usual, wait list or placebo); we defined psychological interventions as interventions in which verbal communication between a therapist and a client was the core element, or in which a psychological treatment was written down in book format or a computer program that the client worked through more or less independently, but with some kind of personal support from a therapist (by telephone, E-mail, or otherwise).
4. The outcome variables had to include at least one of the following variables: psychological health, physical health or disease activity.

### *Selection of studies*

Two authors according to inclusion criteria independently performed study selection. Any disagreements were resolved by discussion or by seeking an independent third opinion.

### *Data extraction*

Two authors used a standard data extraction checklist to independently extract the data from each study, including study characteristics (e.g. first author's name, year of publication, country where the study was conducted), characteristics of study subjects (e.g. number of participants, age, gender distribution), intervention details (type of intervention, duration and frequency, patient involvement), outcome measures and methodological quality of included studies. Quantitative data were extracted to calculate effect sizes. Data on effect size that could not be obtained directly were recalculated where possible. Because multiple measurement tools were used in some trials, we selected one measure considered most appropriate for each of the three outcome domains. To guide the choice of outcome measure, we applied two rules. First, if an outcome measure was established and occurred frequently among studies it was selected over more novel instruments. Second, given a choice between self-reported and

physician-rated tools, physician-rated tools were chosen on the basis of inferred increased reliability.

### *Methodological quality assessment*

Two authors evaluated the methodological quality of the included studies for major potential sources of bias using criteria developed by Jadad *et al.*,<sup>25</sup> which is a five-point scale including a description of randomization, double-blind structure and withdrawals/dropouts. In addition, we assessed the comparability of the baseline and allocation concealment of the studies according to the criteria recommended in the Cochrane Library Handbook 5.0.1. Any disagreements were resolved through discussion or by contacting the study author to seek detailed information.

### *Data synthesis*

Review Manager Software (RevMan 5.1) was used for meta-analysis. Heterogeneity among the studies was explored using the Cochran's  $\chi^2$  test and the  $I^2$  test (Heterogeneity was investigated by evaluating whether confidence intervals around the individual effect sizes of pooled studies overlapped sufficiently). We used a fixed effects model to pool the results together unless significant heterogeneity was observed ( $p < 0.1$  and  $I^2 > 50\%$ ), which needed a random effects model. All of the variables in the included studies were continuous data, so we used the mean difference (MD) or standard mean difference (SMD) with 95% confidence interval (CI) to analyse the effect size of the studies. We describe the results from the original studies if data could not be extracted to calculate the total effect.

## **Results**

### *Study selection*

A total of 467 references were identified in our screening. Among these, 94 duplicates were excluded by Endnote software, and 344 citations were excluded after initial screening because they were not RCTs or the subjects and interventions were not related to our topic. Twenty-nine full-text articles were maintained for further screening. Of these 29 studies, 23 were excluded for the following reasons: duplicate ( $n = 3$ ), non-RCTs ( $n = 4$ ), the subjects involved were not SLE patients ( $n = 4$ ), the interventions were not eligible ( $n = 8$ ) or the outcomes of interest were not assessed ( $n = 4$ ). Finally, six RCTs<sup>26–31</sup> were included in our systematic review (Figure 1).

References cited in published original and review papers were examined until no further studies were found.

### *Characteristics of included studies*

The characteristics of studies included in the systematic review are presented in Table 1.

Of the included studies, two<sup>27,28</sup> were performed in America, two<sup>29,30</sup> in China, one<sup>26</sup> in Canada and one<sup>31</sup> in Spain. The combined sample size across the six included studies<sup>26–31</sup> was 537 participants. All participants had a clinical diagnosis of SLE according to ACR criteria.<sup>24</sup> The psychological interventions included two studies<sup>28,31</sup> of omnibus cognitive behavioural treatment (CBT), two<sup>26,29</sup> of supportive therapy, one<sup>30</sup> of multiple psychological interventions and one<sup>27</sup> of psychoeducational intervention. Although these studies used various forms of psychological interventions, training mainly involved some combinations of patient education, relaxation, stress management or the teaching of cognitive coping skills. One study<sup>28</sup> also included biofeedback as one of the treatment components. The intervention programs ranged from 12 days to six months. The formats of these interventions were conducted individually and in groups.

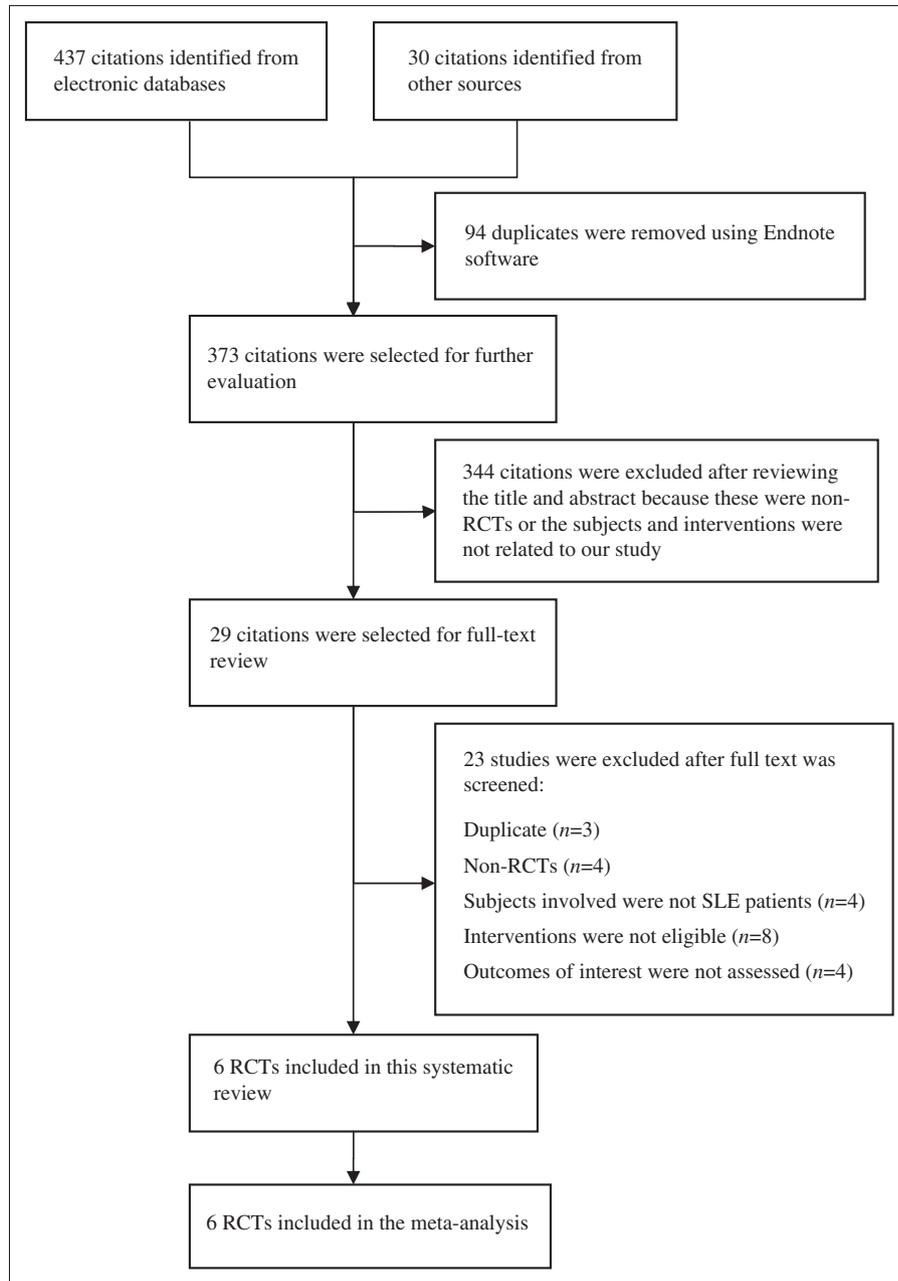
### *Methodological quality of included studies*

Table 2 shows the quality assessment of the studies in this systematic review.

Two studies<sup>26,28</sup> were assigned a Jadad score of  $\geq 4$ , whereas four studies<sup>27,29–31</sup> received a score of 2. All of six included studies were stated to be randomized, but only three<sup>28–30</sup> specified the method of randomization (e.g. table of random numbers, computer generated). Only one study<sup>30</sup> depicted the allocation concealment, and the others didn't make reference to whether any process of concealment of allocation was used. Because practitioners frequently cannot be blinded to the treatment condition in behavioural trials, we looked at whether the assessor or evaluator was blinded. In two trials<sup>26,28</sup>, the assessor was described as blinded to group assignment. Four studies<sup>26–28,31</sup> reported withdrawals, and intention to treat (ITT) was performed in three<sup>26–28</sup> of them. The remainders were either not using ITT analysis or were unclear in the reported paper.

### *Meta-analysis*

We only included RCTs in which psychological intervention was compared with no intervention control condition. We described the results from



**Figure 1** Flow diagram of included and excluded studies.  
 RCT: randomized controlled trials; SLE: systemic lupus erythematosus.

these original studies in which data could not be extracted to calculate the total effect. Statistical heterogeneity was examined for each outcome. A negative direction for MD or SMD of bad outcomes indicates that the intervention condition had more improvement on outcomes than the control condition, and vice versa. Table 3 provides a summary of the results of the overall meta-analysis for each of the outcomes postintervention.

### *Psychological health*

#### *Anxiety*

Three studies<sup>29–31</sup> reported anxiety involving 223 patients. Heterogeneity analyses revealed substantial heterogeneity across studies ( $p = 0.01$ ,  $I^2 = 78\%$ ), and therefore a random effects model was used. In pooled analysis, patients receiving psychological interventions showed less anxiety than those patients receiving no interventions (SMD  $-0.95$ , 95% CI  $-1.57$ ,  $-0.34$ ,  $p = 0.00$ ).

**Table 1** Characteristics of the studies included in the review

First author, year	Setting	Sample size (n)		Age (y), mean ± SD		Intervention		Control	Frequency and duration	Outcomes	Instruments
		Exp	Control	Exp	Control	Exp	Control				
Dobkin <sup>26</sup> 2002	Canada	64	69	42.0 ± 11.2	43.0 ± 10.4	Supportive-expressive therapy combining interpersonal social existential therapy with group support and specific coping-skills training.	Standard medical care	Standard medical care	90-minute/ session, three months	Stress, physical function, mental health, disease activity	The revised version of the Hasses scale, SF-36, SLAM-R
Karlson <sup>27</sup> 2004	America	64	58	42.7 ± 22.8	40.8 ± 11.1	A theory-based psychoeducational intervention including problem-solving technique and the management of lupus.	An attention placebo including a 45-minute video presentation about lupus and monthly telephone calls.	Usual medical care	A one-hour session at the first month followed by monthly telephone counselling, six months	Fatigue, physical function, mental health, disease activity	A scale designed specifically for lupus patients, SF-36, SLAQ
Greco <sup>28</sup> 2004	America	32	27	48.2 ± 9.1	47.0 ± 10.5	Biofeedback-assisted cognitive-behavioural treatment: biofeedback, relaxation techniques and cognitive-behavioural pain and stress management training.	Usual medical care	Usual medical care	Three months	Pain, fatigue, depression, stress, physical function, disease activity	AIMS2-pain, The nine-item fatigue severity scale, CES-D, STRESS, SF-36, SLEDAI, SLAM
Wu <sup>29</sup> 2005	China	42	42	Unreported		Supportive psychotherapy.	Usual medical care	Usual medical care	30-minute/ session, daily, 12 days	Anxiety, depression	SAS, SDS
Chen <sup>30</sup> 2008	China	49	45		18-65, mean 34.5	Multiple psychological interventions composed of counselling, cognitive behavioural therapy, and supportive therapy.	Usual medical care	Usual medical care	One month	Anxiety, depression, disease activity	HAMA, HAMD, SLEDAI
Navarrete-Navarrete <sup>31</sup> 2010	Spain	21	24	43.77 ± 9.88	40.41 ± 10.67	Cognitive behavioural therapy: stress management program composed of cognitive restructuring, relaxation techniques, coping strategies and training in social skill.	Standard medical care	Standard medical care	Two-hour/ session, weekly, 10 weeks	Pain, anxiety, depression, stress, mental health, disease activity	STAI-T, BDI, STRESS, SRLE, SF-36, SLEDAI

Exp: experimental group; Control: control group; SD: standard difference; SF-36: Short Form 36-item Health Survey; SLAM-R: the Systemic Lupus Activity Measure, Revised; SLAQ: the Systemic Lupus Activity Questionnaire; AIMS2-pain: the Revised Arthritis Impact Measurement Scales-pain subscale; CES-D: the Center for Epidemiological Studies Depression scale; STRESS: Cohen's Perceived Stress Scale; SLEDAI: the Systemic Lupus Erythematosus Disease Activity Index; SAS: Self-Rating Anxiety scale; SDS: Self-Rating Depression scale; HAMA: Hamilton Anxiety scale; HAMD: Hamilton Depression scale; STAI-T: Spielberger's State-Trait Anxiety Inventory-Trait; BDI: Beck Depression Inventory; SRLE: the Survey of Recent Life Experience.

**Table 2** Methodological quality of included studies

First author, year	Sequence generation	Allocation concealment	Blinding	Withdrawals (n) (Exp/Control)	Intention to treat	Baseline comparability	Score (/5)
Dobkin <sup>26</sup> 2002	Unclear	Unclear	Outcome assessor	6/3	Yes	Yes	4
Karlson <sup>27</sup> 2004	Unclear	Unclear	No	28	Yes	Yes	2
Greco <sup>28</sup> 2004	Software-generated	Unclear	Outcome assessor	5/1	Yes	Yes	5
Wu <sup>29</sup> 2005	Random numbers table	Unclear	No	Unmentioned	Unmentioned	Yes	2
Chen <sup>30</sup> 2008	Random numbers table	Opaque envelope	No	Unmentioned	Unmentioned	Yes	2
Navarrete-Navarrete <sup>31</sup> 2010	Unclear	Unclear	No	3/0	No	Yes	2

Exp: experimental group; Control: control group.

### Depression

Four studies<sup>28-31</sup> involving 282 patients contributed to this outcome. The random effects model was applied because of significant heterogeneity ( $p < 0.0001$ ,  $I^2 = 86\%$ ). The result of meta-analysis showed a statistically significant difference between two groups in favour of psychological interventions (SMD  $-1.14$ , 95% CI  $-1.84$ ,  $-0.44$ ,  $p = 0.00$ ).

### Stress

Two studies<sup>28,31</sup> involving 104 participants were included in this comparison. The fixed effects model was applied because no significant heterogeneity was found ( $p = 0.96$ ,  $I^2 = 0\%$ ). A statistically significant difference was observed (SMD  $-0.63$ , 95% CI  $-1.02$ ,  $-0.23$ ,  $p = 0.00$ ), which indicated that psychological interventions reduced the stress perceived by SLE patients, as compared to the control condition.

### Mental health

Two studies<sup>27,31</sup> with 137 participants assessed the mental health of SLE patients before and after the intervention. The fixed effects model was used because the heterogeneity was not evident among these studies ( $p = 0.15$ ,  $I^2 = 51\%$ ). There was no statistically significant difference in the change of mental health between the two groups (MD 4.15, 95% CI  $-3.86$ , 12.15,  $p = 0.31$ ).

### Physiological health

#### Pain

Two studies<sup>28,31</sup> reported pain involving 104 patients. Because the evaluation instruments used in the two trials were significantly different, we omitted the pooled estimate and just performed a narrative synthesis.

In Greco et al.'s study,<sup>28</sup> the Revised Arthritis Impact Measurement Scale-Pain Subscale (AIMS2-Pain) was used to assess the severity of pain, with higher scores indicating greater severity. The result showed those undergoing CBT experienced a greater reduction in pain compared with the group of patients who received usual care. In the study by Navarrete-Navarrete et al.,<sup>31</sup> they used a short form 36-item health survey (SF-36) to evaluate physical pain, with higher scores indicating lesser pain. A significant difference between the two groups was observed in favour of the psychological intervention group.

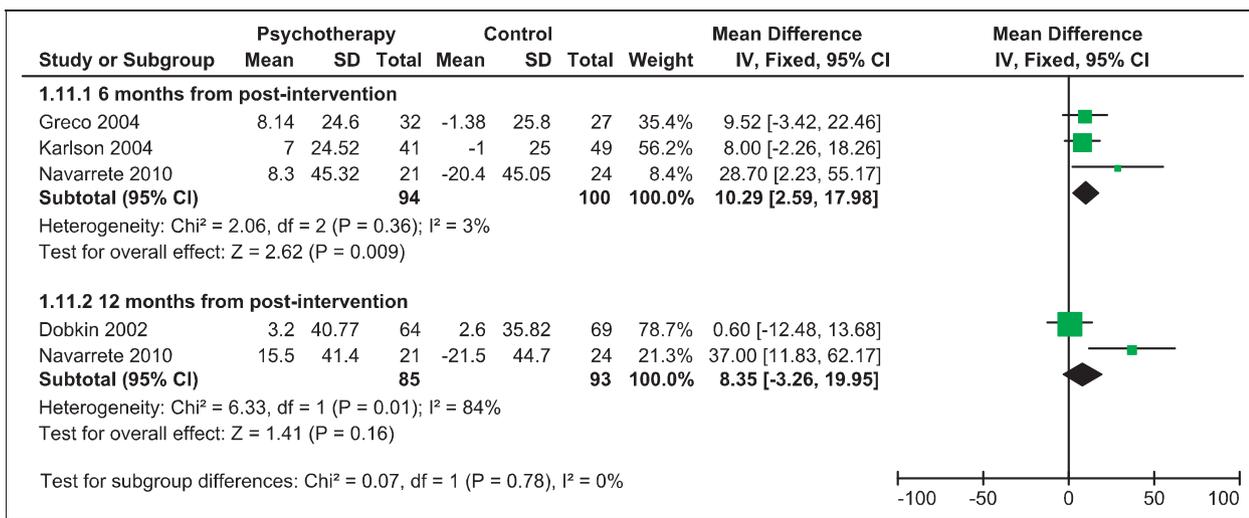
#### Fatigue

Two studies<sup>27,28</sup> involving 151 patients were entered into the analysis of effects of intervention

**Table 3** Meta-analysis of outcome measures at postintervention

Outcomes	No. of studies	Sample size (Exp/Control)	Heterogeneity test		Model sselections	MD or SMD	95% CI	p
			p	I <sup>2</sup> (%)				
Anxiety	3 <sup>29-31</sup>	112/111	0.01	78	Random	-0.95	(-1.57, -0.34)	0.00
Depression	4 <sup>28-31</sup>	144/138	<0.0001	86	Random	-1.14	(-1.84, -0.44)	0.00
Stress	2 <sup>28,31</sup>	53/51	0.96	0	Fixed	-0.63	(-1.02, -0.23)	0.00
Mental health	2 <sup>27,31</sup>	67/70	0.15	51	Fixed	4.15	(-3.86, 12.15)	0.31
Fatigue	2 <sup>27,28</sup>	78/73	0.52	0	Fixed	-0.17	(-0.49, 0.15)	0.30
Physical function	3 <sup>27,28,31</sup>	99/97	0.61	0	Fixed	7.65	(0.16, 15.13)	0.05
Disease activity	4 <sup>27,28,30,31</sup>	148/142	0.30	19	Fixed	-0.34	(-0.57, -0.11)	0.00

Exp: experimental group; Control: control group; MD: mean difference; SMD: standard mean difference; CI: confidence interval.



**Figure 2** Effect sizes of psychological interventions on physical function in SLE patients compared to control conditions at follow-up.

SLE: systemic lupus erythematosus; SD: standard difference; CI: confidence interval; df = degree of freedom.

on fatigue. There was no heterogeneity between the trials ( $p = 0.52$ ,  $I^2 = 0\%$ ), so we used the fixed effect model to pool an estimate. Pooled analysis from these studies indicated that there was no significant difference between the two groups (MD  $-0.17$ , 95% CI  $-0.49, 0.15$ ,  $p = 0.30$ ).

*Physical function*

Three studies<sup>27,28,31</sup> involving 196 patients reported a change of physiological function before and after the intervention. The fixed effects model was used because the heterogeneity test showed an  $I^2$  of 0% among the studies. The pooled data showed that the change of physical function was not significantly different between the groups (MD 7.65, 95% CI 0.16, 15.13,  $p = 0.05$ ).

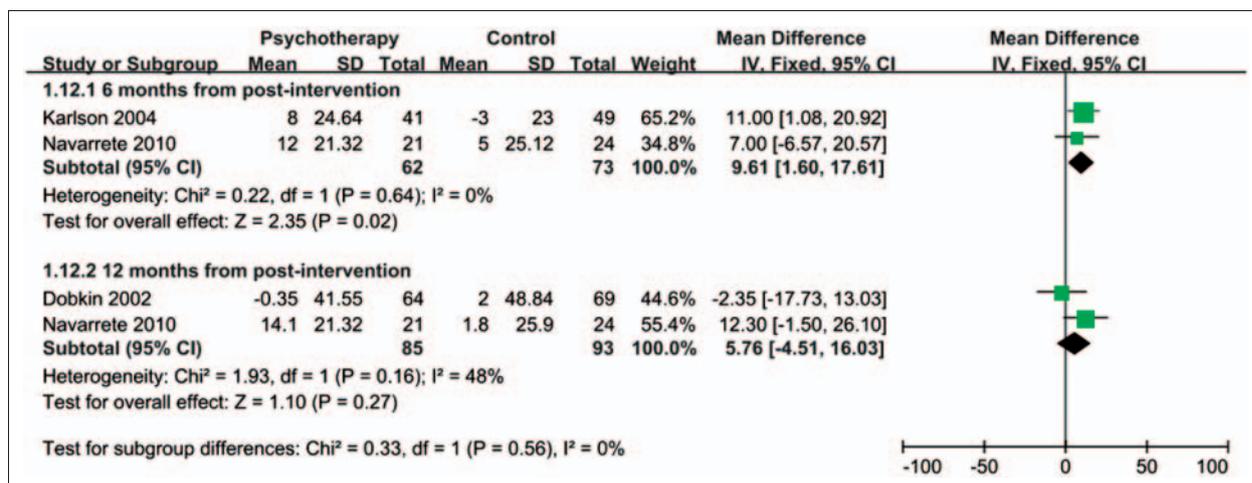
*Disease activity*

Four studies<sup>27,28,30,31</sup> involving 290 patients reported a change of disease activity before and

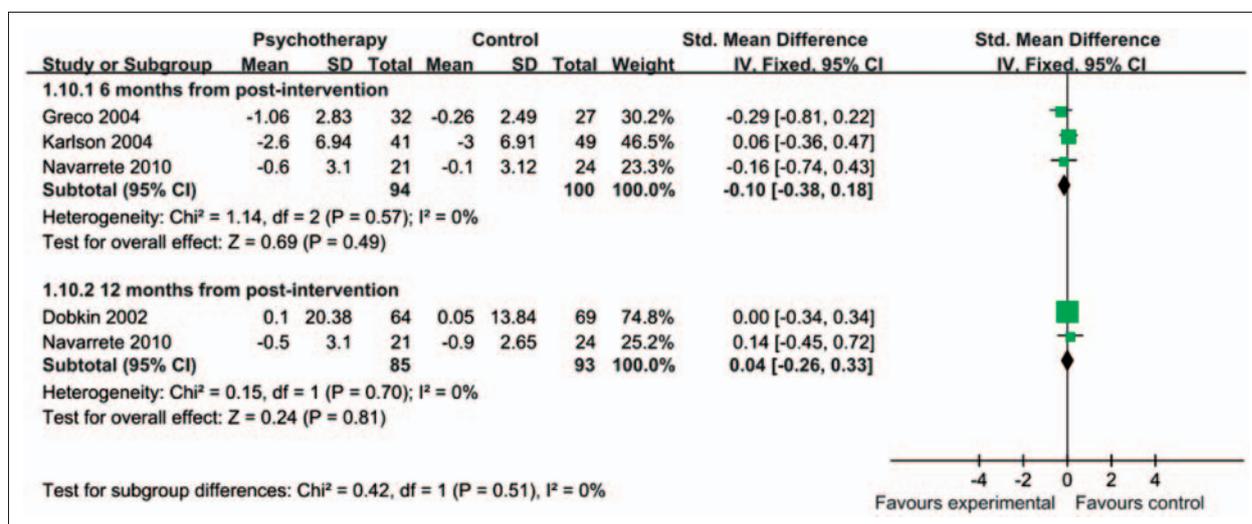
after the intervention. The fixed effects model was used because the heterogeneity was small among these studies ( $p = 0.30$ ,  $I^2 = 19\%$ ). The results of meta-analysis revealed that psychological intervention had a positive effect on the disease activity in comparison to the control conditions. This effect was statistically significant (SMD  $-0.34$ , 95% CI  $-0.57, -0.11$ ,  $p = 0.00$ ).

*Sustainability of results*

Four studies<sup>26-28,31</sup> reported follow-up data no longer than 12 months after the intervention. We sought to identify outcomes that were assessed across the majority of the trials and that would provide the basis for a meta-analytic review. Three outcomes were identified: physical function, mental health and disease activity. The results of other outcomes could not be pooled because of



**Figure 3** Effect sizes of psychological interventions on mental health in SLE patients compared to control conditions at follow-up. SLE: systemic lupus erythematosus; SD = standard difference; CI: confidence interval; df = degree of freedom.



**Figure 4** Effect sizes of psychological interventions on disease activity in SLE patients compared to control conditions at follow-up. SLE: systemic lupus erythematosus; SD = standard difference; CI: confidence interval; df = degree of freedom.

the small sample size and the limited number of studies available for analysis.

At the six-month follow-up, the intervention resulted in significant improvement in physical function (MD 10.29, 95% CI 2.59, 17.98,  $p=0.01$ ) and mental health (MD 9.61, 95% CI 1.60, 17.61,  $p=0.02$ ). No difference was observed in disease activity (SMD -0.10, 95% CI -0.38, 0.18,  $p=0.49$ ). At the 12-month follow-up, the results showed that the overall effects for physical function, mental health and disease activity were

statistically non-significant ( $p > 0.05$ ) (Figure 2, Figure 3, Figure 4).

### Sensitivity analyses

In the trial by Greco et al.,<sup>28</sup> it was not reported exactly whether the subjects had reached the age of 18. Therefore, we excluded this study to perform sensitivity analysis. We only examined the difference in effects when this study was removed from either disease activity or depression, because we

were not able to recalculate the effect sizes for other outcomes such as physical function, fatigue and stress in this analysis because of the small number of studies that examined these outcomes. After sensitivity analysis, the results were unchanged, and there were still statistically significant differences between the groups regarding disease activity (SMD  $-0.41$ , 95% CI  $-0.67$ ,  $-0.14$ ,  $p = 0.00$ ) and depression (SMD  $-1.34$ , 95% CI  $-2.15$ ,  $-0.52$ ,  $p = 0.00$ ).

In the assessment of statistical heterogeneity for mental health, the result of Cochran's  $\chi^2$  test was not consistent with the  $I^2$  statistic's result. In order to assess the robustness of conclusions about quality of data, we used a random effect model instead of a fixed effect model to recalculate effect sizes. After sensitivity analysis, no change was found in the result (MD  $5.16$ , 95% CI  $-6.74$ ,  $17.06$ ,  $p = 0.40$ ).

## Discussion

The primary goal of this systematic review was to examine the effects of psychological interventions for reducing somatic symptoms related to disease and improving psychological health in patients with SLE, as these are important clinical concerns, and outcomes of treatments for SLE patients. To examine this issue, we screened 467 studies and identified six RCTs that compared psychological interventions to usual medical care or attention controls. The combined results of these RCTs showed that a statistically significant reduction was found in anxiety, depression, stress and disease activity in the intervention group compared to the control group posttreatment. The effects on mental health, fatigue and physical function were in the expected direction, but no statistically significant differences were observed. At follow-up, the positive effects of psychological interventions on mental health and physical function were evident at a six-month follow-up evaluation, whereas no significant differences were observed regarding the disease activity index throughout the entire follow-up period.

Until we conducted the present analyses, there had been no review of the literature pertaining to psychological interventions for SLE patients. The only authors who had compared non-pharmacological interventions among SLE patients were Neill *et al.*<sup>32</sup> They found behavioural strategies, such as educational intervention, rehabilitation and counselling, produced statistically significant reductions

in fatigue for people with SLE. Nevertheless, less work has been done to measure a patient's psychological response.

In the studies we reviewed, various forms of psychological interventions were used. However, approaches are mainly based on psychotherapeutic counselling and psychoeducational interventions. These interventions focused on providing information on symptoms management and therapeutic approaches or giving greater emphasis to the coping response to illness and everyday life. They could help SLE patients understand their comorbidity better, so that the patients were able to understand the link between negative emotions and relapse, thus strengthening physical, psychological and social self-care strategies, and thereby directly reducing substance use independently of effects on depression and anxiety. Because many of these interventions were multimodal (e.g. integrating a variety of different psychological techniques), it is unclear from our review whether particular component parts or certain combinations of modalities may have been responsible for the observed treatment effects. In addition, because of the limited number of trials and insufficient data in some trials, we were unable to carry out a subgroup analysis of the type of intervention to define which subgroup of intervention had the best results for patients.

In our meta-analysis, no statistically significant effects were observed from pooling data on fatigue, physical function and mental health. However, discussion of some trends was possible. As expected, there was a tendency for a decrease in fatigue and an increase in physical function and mental health postintervention. The minimal impacts of psychological interventions on these outcomes may be explained by several factors, including the small number of studies included in the review, differing measures used across the included studies, and the limitations of available measures. We conducted a subgroup analysis of follow-up intervals. The results showed that a statistically significant difference was found for the effect of psychological intervention on physical function and mental health at the six-month follow-up, but did not exist at the 12-month follow-up.

Four of six RCTs provided a quantitative measure of disease activity. In these, a difference favouring psychological interventions was observed postintervention. However, this effect was no longer significant in the long term, with somewhat lower effects at the six-month follow-up and markedly diminished effects at 12 months. It should be highlighted that, at the individual study level, the

majority of trials we examined failed to show significant treatment effects on disease activity, and a few cases actually showed a negative treatment effect (e.g. controls showed greater improvement). One explanation for these findings is lack of statistical power.

### *Limitations*

In order to reach a high internal validity, we only included RCTs to explore the effects of psychological interventions for patients with SLE. We avoided selection bias by pre-specified inclusion criteria, a systematic search by consulting relevant reviews and independent evaluation of trial inclusion by two reviewers. Moreover, we searched unpublished studies through tracking the SIGLE database in order to reduce publication bias as far as possible. But, as is the case with all systematic reviews, several important limitations of this systematic review should be noted.

One limitation of this review was the low number of eligible studies and small sample sizes within trials. These characteristics may result from the strict inclusion criteria for psychological interventions. Given the low number of eligible studies, we didn't perform sensitivity analysis for some outcomes. In addition, the limited studies precluded meaningful subgroup analysis (e.g. according to intervention type), which is important given the heterogeneity of the study. So, there is no doubt that further trials in this field are definitely needed. Studies with a much larger number of participants should be carried out to clarify the efficacy or lack of efficacy of psychological interventions in the treatment of SLE patients.

The methodological quality of included studies in this review was not high. All six studies mentioned randomization, but only two reported the randomization method. Only one trial reported using the allocation concealment method. In these cases, selection bias may exist in these studies. In addition, the difficulty of blinding ratings of outcomes may result in these studies being prone to observation bias. Because there is some evidence that the absence of such methods may serve to inflate effect size estimates,<sup>33</sup> future trials should utilize such methods.

A wide range of outcome instruments were used in the studies. Although we expressed each study result as SMD with 95% CI with the purpose of reducing measure bias, this still means that multiple comparisons from these studies were included in the same analysis, which may have resulted in an artificial reduction of heterogeneity. In addition,

because of the small number of studies eligible for the review and different follow-up intervals in these studies, the extent to which the effects of these psychological interventions produce long-term effects is not fully answered by our meta-analytic review. Therefore, standardization of outcomes and instruments to assess them is vital for any further studies. If possible, decisions about which measures and at which durations of follow-up to assess outcomes should be made according to the methods of the existing trials.

We did not limit the language in the process of literature retrieval, but only English-language and Chinese-language trials were identified according to the inclusion criteria. This may introduce publication and language bias. Furthermore, this systematic review is limited because of the possibility of missing eligible unpublished or other language studies. With only six small trials it is difficult to use techniques such as funnel plots to examine the possibility of publication bias.

### **Conclusion**

This systematic review provides a comprehensive summary of the currently available RCTs exploring the effects of psychological interventions in patients with SLE. Our findings show the potential value of psychological interventions as adjunctive treatments in the medical management of SLE. It is effective for SLE patients to manage negative emotions and to reduce stress and disease activity. The findings were based on a small body of evidence in which methodological quality was not high. Further well-designed RCTs with larger samples are urgently needed to clarify the utility of psychological interventions for this population. In particular, further studies should seek to directly compare different psychological interventions against one another to make conclusions about the superiority of one intervention over the others.

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## Conflict of interest

None declared.

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