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Exercise as adjunctive therapy for systemic lupus erythematosus (Review)

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[Intervention Review]

Exercise as adjunctive therapy for systemic lupus erythematosus

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ABSTRACT

Background

Systemic lupus erythematosus (SLE) is a rare, chronic autoimmune inflammatory disease with a prevalence varying from 4.3 to 150 people in 100,000, or approximately five million people worldwide. Systemic manifestations frequently include internal organ involvement, a characteristic malar rash on the face, pain in joints and muscles, and profound fatigue. Exercise is purported to be beneficial for people with SLE. For this review, we focused on studies that examined all types of structured exercise as an adjunctive therapy in the management of SLE.

Objectives

To evaluate the benefits and harms of structured exercise as adjunctive therapy for adults with SLE compared with usual pharmacological care, usual pharmacological care plus placebo and usual pharmacological care plus non-pharmacological care.

Search methods

We used standard, extensive Cochrane search methods. The latest search date was 30 March 2022.

Selection criteria

We included randomised controlled trials (RCTs) of exercise as an adjunct to usual pharmacological treatment in SLE compared with placebo, usual pharmacological care alone and another non-pharmacological treatment. Major outcomes were fatigue, functional capacity, disease activity, quality of life, pain, serious adverse events, and withdrawals due to any reason, including any adverse events.

Data collection and analysis

We used standard Cochrane methods. Our major outcomes were 1. fatigue, 2. functional capacity, 3. disease activity, 4. quality of life, 5. pain, 6. serious adverse events, and 7. withdrawals due to any reason. Our minor outcomes were 8. responder rate, 9. aerobic fitness, 10. depression, and 11. anxiety. We used GRADE to assess certainty of evidence. The primary comparison was exercise compared with placebo.

Main results

We included 13 studies (540 participants) in this review. Studies compared exercise as an adjunct to usual pharmacological care (antimalarials, immunosuppressants, and oral glucocorticoids) with usual pharmacological care plus placebo (one study); usual pharmacological care (six studies); and another non-pharmacological treatment such as relaxation therapy (seven studies). Most studies

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had selection bias, and all studies had performance and detection bias. We downgraded the evidence for all comparisons because of a high risk of bias and imprecision.

Exercise plus usual pharmacological care versus placebo plus usual pharmacological care

Evidence from a single small study (17 participants) that compared whole body vibration exercise to whole body placebo vibration exercise (vibrations switched off) indicated that exercise may have little to no effect on fatigue, functional capacity, and pain (low-certainty evidence). We are uncertain whether exercise results in fewer or more withdrawals (very low-certainty evidence). The study did not report disease activity, quality of life, and serious adverse events.

The study measured fatigue using the self-reported Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-Fatigue), scale 0 to 52; lower score means less fatigue. People who did not exercise rated their fatigue at 38 points and those who did exercise rated their fatigue at 33 points (mean difference (MD) 5 points lower, 95% confidence interval (CI) 13.29 lower to 3.29 higher).

The study measured functional capacity using the self-reported 36-item Short Form health questionnaire (SF-36) Physical Function domain, scale 0 to 100; higher score means better function. People who did not exercise rated their functional capacity at 70 points and those who did exercise rated their functional capacity at 67.5 points (MD 2.5 points lower, 95% CI 23.78 lower to 18.78 higher).

The study measured pain using the SF-36 Pain domain, scale 0 to 100; lower scores mean less pain. People who did not exercise rated their pain at 43 points and those who did exercise rated their pain at 34 points (MD 9 points lower, 95% CI 28.88 lower to 10.88 higher).

More participants from the exercise group (3/11, 27%) withdrew from the study than the placebo group (1/10, 10%) (risk ratio (RR) 2.73, 95% CI 0.34 to 22.16).

Exercise plus usual pharmacological care versus usual pharmacological care alone

The addition of exercise to usual pharmacological care may have little to no effect on fatigue, functional capacity, and disease activity (low-certainty evidence). We are uncertain whether the addition of exercise improves pain (very low-certainty evidence), or results in fewer or more withdrawals (very low-certainty evidence). Serious adverse events and quality of life were not reported.

Exercise plus usual care versus another non-pharmacological intervention such as receiving information about the disease or relaxation therapy

Compared with education or relaxation therapy, exercise may reduce fatigue slightly (low-certainty evidence), may improve functional capacity (low-certainty evidence), probably results in little to no difference in disease activity (moderate-certainty evidence), and may result in little to no difference in pain (low-certainty evidence). We are uncertain whether exercise results in fewer or more withdrawals (very low-certainty evidence). Quality of life and serious adverse events were not reported.

Authors' conclusions

Due to low- to very low-certainty evidence, we are not confident on the benefits of exercise on fatigue, functional capacity, disease activity, and pain, compared with placebo, usual care, or advice and relaxation therapy. Harms data were not well reported.

PLAIN LANGUAGE SUMMARY

What are the benefits and risks of exercise for people with systemic lupus erythematosus?

Key messages

Exercise in addition to 'usual care' may have little benefit on fatigue, functional capacity, and pain in people with systemic lupus erythematosus (SLE).

No studies reported side effects during exercise. However, we have low confidence in the overall evidence.

What is systemic lupus erythematosus?

SLE (or 'lupus') is a disease in which the body's immune (defence) system mistakenly attacks healthy tissue in many parts of the body. It is a long-term disease (one that lasts longer than six weeks and is usually life-long). Often, SLE causes pain in joints and muscles, and extreme tiredness. Symptoms can improve temporarily, or worsen suddenly (flares).

How is systemic lupus erythematosus treated?

Management or usual care in SLE may include, but is not limited to, treatment with medicines such as disease-modifying antirheumatic drugs (DMARDs) or non-steroidal anti-inflammatory drugs (NSAIDs). It may also include treatments that are not medicines such as sun avoidance, supplementation (i.e. vitamin D), education about the disease and other illnesses (i.e. hypertension), and physical activity or exercise. Regular exercise training could serve as an adjunct treatment for people with SLE.

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What did we want to find out?

We wanted to find out if exercise in addition to usual care improved fatigue, functional capacity (ability to perform normal everyday tasks), quality of life, pain, and disease activity, and caused no harm.

What did we do?

We searched for studies that investigated structured exercise programmes such as aerobic exercise, resistance, stretching or combinations of these (including a specific dosage of exercise, e.g. frequency, intensity, time, type) in addition to usual care compared with placebo (pretend medicine), usual care alone, or another non-medicine intervention (e.g. relaxation therapy) in people with SLE.

We compared and summarised the results of the studies and rated our confidence in the evidence, based on factors such as study methods and sizes.

What did we find?

We found 13 studies that involved 540 participants with SLE that included a structured exercise programme that lasted up to 12 weeks in duration. Usual care included DMARDs and glucocorticoids.

The main results of the review are:

1. Whole body vibration exercise plus usual care may result in little to no effect on fatigue, functional capacity, and pain when compared to whole body placebo vibration exercise (vibration switched off) plus usual care (1 study, 17 participants).

The study measured fatigue using the Functional Assessment of Chronic Illness Therapy – Fatigue domain (FACIT-Fatigue) (0 to 52 scale, where 0 means no fatigue) and, at 12 weeks, fatigue improved by 5 points in the exercise group compared to the group that did not exercise:

– People who exercised rated their fatigue at 33 points.

– People who did not exercise rated their fatigue at 38 points.

The study measured functional capacity using the Functional Capacity domain in the 36-item Short Form health questionnaire (SF-36) (0 to 100 scale, where 100 means best function) and, at 12 weeks, function worsened by 2.5 points in the exercise group compared to the group that did not exercise:

– People who exercised rated their functional capacity at 67.5 points.

– People who did not exercise rated their functional capacity at 70 points.

The study measured pain on the Pain domain of the SF-36 (0 to 100 scale, where 0 means no pain) and, at 12 weeks, pain improved by 9 points in the exercise group compared to the group that did not exercise:

– People who exercised rated their pain at 34 points.

– People who did not exercise rated their pain at 43 points.

More people from the exercise group (27%) withdrew from the study compared those in the placebo group (10%).

The study did not measure disease activity or quality of life.

2. Exercise plus usual care may result in little to no effect on fatigue, functional capacity, and disease activity when compared to usual care alone. And we are uncertain whether exercise improves pain when compared to usual care alone.

3. Exercise plus usual care may reduce fatigue, improve functional capacity, and probably results in little to no difference in disease activity, and may result in little to no difference in pain when compared to another non-medicine intervention plus usual care.

No studies reported any serious side effects that were related to the exercise programme during or following the intervention.

What are the limitations of the evidence?

We have little confidence in the evidence because the number of studies was very small, and it is possible that people in the studies were aware of which treatment they were getting.

Most studies assessed the effectiveness of exercise for a short duration (12 weeks or less) and it is unclear if people would adhere to exercise over time. More rigorous studies of structured exercise over a period of time longer than 12 weeks are needed to improve our confidence in the benefits and safety of exercise in people with SLE.

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How up to date is this evidence?

The evidence is up to date to 30 March 2022.

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SUMMARY OF FINDINGS

Summary of findings 1. Summary of findings table - Exercise plus usual pharmacological care compared to placebo plus usual pharmacological care for systemic lupus erythematosus

Exercise plus usual pharmacological care compared to placebo plus usual pharmacological care for systemic lupus erythematosus

Patient or population: systemic lupus erythematosus
Setting: community
Intervention: exercise plus usual pharmacological care
Comparison: placebo plus usual pharmacological care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo plus usual pharmacological care	Risk with exercise plus usual pharmacological care				
Fatigue (FACIT-Fatigue, score 0-52, lower scores indicate less fatigue) follow-up: 12 weeks	The mean fatigue (FACIT-Fatigue, score 0-52, lower scores indicate less fatigue) was **38** points	MD **5 points lower** (13.29 lower to 3.29 higher)	-	17 (1 RCT)	⊕⊕⊖⊖ Low[b,c]	Exercise may have little to no effect on fatigue.
Functional capacity (SF-36 Function Capacity domain, score 0-100, higher scores indicate better functional capacity) follow-up: 12 weeks	The mean functional capacity (SF-36 Function Capacity domain, score 0-100, higher scores indicate better functional capacity) was **70** points	MD **2.5 points lower** (23.78 lower to 18.78 higher)	-	17 (1 RCT)	⊕⊕⊖⊖ Low[b,c]	Exercise may have little to no effect on functional capacity.
Pain (SF-36 Pain domain, score 0-100, lower scores indicate less pain) follow-up: 12 weeks	The mean pain (SF-36 Pain domain, score 0-100, lower scores indicate less pain) was **43** points	MD **9 points lower** (28.88 lower to 10.88 higher)	-	17 (1 RCT)	⊕⊕⊖⊖ Low[b,c]	Exercise may have little to no effect on pain.
Disease activity - not measured	-	-	-	-	-	This outcome was measured at baseline, but it was not reported at end of intervention.
Quality of life - not measured	-	-	-	-	-	This outcome was measured, but the Mental Com-

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						ponent Summary score was not reported.
Serious adverse events - not reported	-	-	-	-	-	No serious adverse events were reported.
Withdrawals due to any reason follow-up: 12 weeks	100 per 1000	**273 per 1000** (34 to 1000)	**RR 2.73** (0.34 to 22.16)	21 (1 RCT)	⊕⊖⊖⊖ Very low[b,c]	We are uncertain whether exercise results in fewer or more withdrawals.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

See interactive version of this table: https://gdt.gradepro.org/presentations/#/isof/isof_question_revman_web_432987629440706015.

[a] Usual pharmacological care consisted of immunosuppressants and glucocorticoids.
[b] Downgraded one level due to risk of detection and potentially selection bias.
[c] Downgraded one level due to small number of participants from a single trial.

Summary of findings 2. Summary of findings table - Exercise plus usual pharmacological care compared to usual pharmacological care alone for systemic lupus erythematosus

Exercise plus usual pharmacological care compared to usual pharmacological care alone for systemic lupus erythematosus

Patient or population: systemic lupus erythematosus
Setting: community
Intervention: exercise plus usual pharmacological care
Comparison: usual pharmacological care alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with usual pharmacological care alone	Risk with exercise plus usual				

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		pharmacological care				
Fatigue (Fatigue Severity Scale, score 1-7, lower score indicates less fatigue) follow-up: 12 weeks	The mean fatigue (Fatigue Severity Scale, score 1-7, lower score indicates less fatigue) was **5.4** points	MD **0.6 points lower** (1.4 lower to 0.2 higher)	-	104 (2 RCTs)	⊕⊕⊖⊖ Low[a,b]	Exercise plus usual pharmacological care may have little to no effect on fatigue.[c]
Functional capacity (SF-36 Physical Function domain, score 0-100, higher scores indicate better functional capacity) follow-up: 12 weeks	The mean functional capacity (SF-36 Physical Function domain, score 0-100, higher scores indicate better functional capacity) was **60** points	MD **5.4 points higher** (5.97 lower to 16.75 higher)	-	96 (2 RCTs)	⊕⊕⊖⊖ Low[a,b]	Exercise plus usual pharmacological care may have little to no effect on functional capacity.
Disease activity (SLEDAI scale, scores 0-105, lower scores indicate less disease activity) follow-up: 12 weeks	The mean disease activity (SLEDAI scale, scores 0-105, lower scores indicate less disease activity) was **0.5** points	MD **0.26 points lower** (3.69 lower to 3.17 higher)	-	100 (2 RCTs)	⊕⊕⊖⊖ Low[a,b]	Exercise plus usual pharmacological care may have little to no effect on disease activity.
Quality of life - not reported	-	-	-	-	-	This outcome was measured, but the Mental Component Summary score was not reported.
Pain (SF-36 Bodily Pain domain, score 0-100, lower scores indicate less pain) follow-up: 12 weeks	The mean pain (SF-36 Bodily Pain domain, score 0-100, lower scores indicate less pain) was **38** points	MD **16 points higher** (0.18 lower to 32.18 higher)	-	31 (1 RCT)	⊕⊖⊖⊖ Very low[a,b]	We are uncertain whether exercise improves pain.
Serious adverse events - not reported	-	-	-	-	-	No serious adverse events were reported.
Withdrawals due to any reason follow-up: 12 weeks	175 per 1000	**161 per 1000** (93 to 280)	**RR 0.92** (0.53 to 1.60)	235 (6 RCTs)	⊕⊖⊖⊖ Very low[a,b]	We are uncertain whether exercise results in fewer or more withdrawals.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

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Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

See interactive version of this table: https://gdt.gradepro.org/presentations/#/isof/isof_question_revman_web_433149155812397472.

[a] Downgraded one level for risk of detection bias in unblinded trials with self-reported outcomes.
[b] Downgraded one level due to low participant numbers and the confidence intervals included a large effect and no effect.
[c] Usual pharmacological care consists of immunosuppressants, steroids and antimalarials

Summary of findings 3. Summary of findings table - Exercise plus usual pharmacological care compared to another intervention (education, joint aids, or relaxation) plus usual pharmacological care for systemic lupus erythematosus

Exercise plus usual pharmacological care compared to another intervention (education, joint aids, or relaxation) plus usual pharmacological care for systemic lupus erythematosus

Patient or population: systemic lupus erythematosus
Setting: community
Intervention: exercise plus usual pharmacological care
Comparison: another intervention (education, joint aids, or relaxation) plus usual pharmacological care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with another intervention (education, joint aids, or relaxation) plus usual pharmacological care	Risk with exercise plus usual pharmacological care				
Fatigue (Fatigue Severity Scale, scores 0-7, lower scores indicate less fatigue) follow-up: 12 weeks	The mean fatigue (Fatigue Severity Scale, scores 0-7, lower scores indicate less fatigue) was **5.3** points	MD **0.51 points lower** (0.88 lower to 0.14 lower)	-	119 (2 RCTs)	⊕⊕⊖⊖ Low[a,b]	Exercise plus usual pharmacological care may reduce fatigue slightly.
Functional capacity (SF-36 Physical Function domain, score 0-100, higher scores indicate better functional capacity) follow-up: 12 weeks	The mean functional capacity (SF-36 Physical Function domain, score 0-100, higher scores indicate better functional capacity) was **41.4** points	MD **13.2 points higher** (6.17 higher to 20.22 higher)	-	182 (3 RCTs)	⊕⊕⊖⊖ Low[a,c]	Exercise plus usual pharmacological care may increase functional capacity.

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Disease activity (SLEDAI scale, score 0-105, lower scores indicate less disease activity) follow-up: 12 weeks	The mean disease activity (SLEDAI scale, score 0-105, lower scores indicate less disease activity) was **1.2** points	MD **0.034 points higher** (0.476 lower to 0.544 higher)	-	184 (4 RCTs)	⊕⊕⊕⊖ Moderate[a]	Exercise plus usual pharmacological care probably results in little to no difference in disease activity. SMD 0.02 (95% CI -0.28 to 0.32). Baseline control group SD for converting SMD to MD was 1.7 and taken from Abrahão 2016.
Pain (VAS Pain scale, score 0-10, lower scores indicate less pain) follow-up: 12 weeks	The mean pain (VAS Pain scale, score 0-10, lower scores indicate less pain) was **4.97** points	MD **1.59 points lower** (2.46 lower to 0.71 lower)	-	121 (2 RCTs)	⊕⊕⊖⊖ Low[a,c]	Exercise plus usual pharmacological care may result in little to no difference in pain.
Withdrawals due to any reason follow-up: 12 weeks	49 per 1000	**43 per 1000** (6 to 289)	**RR 0.89** (0.13 to 5.94)	317 (7 RCTs)	⊕⊖⊖⊖ Very low[a,d]	We are uncertain whether exercise results in fewer or more withdrawals.
Serious adverse events - not reported	-	-	-	-	-	No serious adverse events were reported.
Quality of life - not reported	-	-	-	-	-	This outcome was measured, but the Mental Component Summary score was not reported.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

See interactive version of this table: https://gdt.gradepro.org/presentations/#/isof/isof_question_revman_web_433149459092821699.

[a] Downgraded one level due to risk of detection bias in unblinded trials with self-reported outcomes.
[b] Downgraded one level due to low participant numbers and the confidence intervals included a large effect and no effect.
[c] Downgraded one level due to possible imprecision. The confidence intervals included a small effect and a large effect.
[d] Downgraded two levels due to very few events.

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BACKGROUND

Description of the condition

Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease with a wide spectrum of clinical and serological manifestations caused by autoantibody production, complement activation, and immune complex deposition. The pathogenesis of SLE is characterised by the formation of autoantibodies and a breakdown in the immune milieu of the body leading to an unregulated inflammatory response and consequent internal organ and tissue damage (Fanouriakis 2019). Systemic manifestations frequently include internal organ involvement, a characteristic malar rash on the face, sicca symptoms, and profound fatigue. People with SLE experience multiple, varied symptoms and laboratory abnormalities that occur in different combinations, at different time points. SLE is heterogeneous, meaning that symptoms vary widely from one person to the next, for example, one person may develop a rash, while another may have high blood pressure, joint pain, and anaemia. Although SLE constitutes the most common form of lupus, which is the broad term to describe the disease, there are other forms of lupus which include discoid lupus erythematosus (DLE) or cutaneous lupus erythematosus (CLE), characterised by mostly cutaneous involvement (Fanouriakis 2019).

SLE is a rare disease with an incidence of approximately 1 to 10 per 100,000 person-years and a prevalence varying from 4.3 to 150 people in 100,000 (Nikpour 2014), or approximately five million people worldwide. The prevalence in Australia varies between 19.3 and 39 people in 100,000 for non-Aboriginal Australians and 52.0 to 92.8 people in 100,000 for Aboriginal Australians (Bossingham 2003; Segasothy 2001). There is a higher SLE incidence in Asian (especially Chinese), African, and Hispanic populations. These last two populations are especially associated with high disease activity and damage. SLE can affect both men and women of any age, with 90% being female. It predominantly affects young women and middle-aged women, between the ages of 15 and 45 years. By age, the female:male ratio is 3:1 before puberty, 10 to 15:1 during childbearing years, with a slight decrease again after menopause at 8:1 (Askanase 2012).

SLE has a severe and pervasive effect on people living with the disease, with people reporting the disease to cause debilitating fatigue; mental deterioration; pervasive pain; disrupted identity from feeling of hopelessness, guilt and punishment, or feeling as though they are a burden (Sutanto 2013). In contrast, some people have also reported the disease to have increased their resilience, empowerment, and optimism. Debilitating pain, musculoskeletal manifestations, fatigue, and renal and cutaneous problems were reported to limit people's ability to work and participate in family and social activities (Sutanto 2013).

People with SLE are at higher risk of developing comorbidities such as osteoporosis (Gu 2020) and atherosclerotic cardiovascular disease (CVD) (Manzi 1997; Schoenfeld 2013). CVD risk amongst people with SLE compared to the general population is at least doubled. While older people with SLE appear to have the highest absolute risks of CVD, young women have alarmingly high relative risks, given the rarity of CVD in the comparable general population (Schoenfeld 2013). People with SLE are also less physically active than people without SLE (Margiotta 2018), with 60% of people not meeting sufficient physical activity guidelines according to the World Health Organization (WHO) recommendations. Subsequent inactivity may add to the heightened risk of secondary complications, as well as lead to physical deconditioning and poor health-related quality of life.

Management or 'usual care' in SLE may include, but is not limited to, the following pharmacological treatments; conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) such as hydroxychloroquine, prednisolone or glucocorticoids, mycophenolate mofetil, methotrexate, azathioprine, cyclophosphamide, or a combination of these; biological disease-modifying antirheumatic drugs (bDMARDs) such as rituximab or belimumab; non-steroidal anti-inflammatory drugs (NSAIDs) such as naproxen or celecoxib (Fanouriakis 2019). It may also include non-pharmacological measures such as sun avoidance; supplementation (i.e. vitamin D); education about the disease or comorbidities (i.e. hypertension), or both; and physical activity or exercise (Fanouriakis 2019). Regular exercise training could serve as an adjunct treatment for people with SLE to reduce the risk of developing secondary complications, help manage symptoms related to the disease, and improve key clinical outcomes such as quality of life and fatigue.

Description of the intervention

The treatment for SLE depends on the organs and systems involved as well as disease severity. It can include topical applications for skin problems, NSAIDs for musculoskeletal diseases, and immunosuppression. Common medications to treat the inflammatory response associated with subsequent widespread organ involvement include corticosteroids, immune suppressants, hydroxychloroquine, and biological agents (Ali 2018).

Exercise is generally used as an adjunct to pharmacological management of SLE (Yorganci 2020). For this review, we focused on studies that examined all types of structured exercise as an adjunctive therapy in the management of SLE. Evidence suggests that exercise interventions are safe, with no change in disease activity or adverse events, and effective in managing key clinical outcomes such as fatigue (Del Pino-Sedeno 2016; O'Dwyer 2017; Wu 2017; Yuen 2014). According to the American College of Sports Medicine (ACSM), exercise is defined as a type of physical activity consisting of planned, structured, and repetitive bodily movement done to improve or maintain (or both) one or more components of physical fitness (Pescatello 2014).

The three main types of exercise include aerobic, resistance, and range of movement. Aerobic exercise relies primarily on the cardiovascular system and represents a broad range of physical activities such as walking, jogging, cycling, and dancing (Pescatello 2014). Resistance exercise can be provided via specifically designed equipment such as resistance bands, hand weights, and machines, or achieved via functional means such as stair climbing, rising from a chair, and lifting groceries to induce muscular contraction, which builds the strength, anaerobic endurance, and size of skeletal muscles (Pescatello 2014). Range of motion exercise refers to activity aimed to improve movement of a specific joint, for example, yoga, tai chi, or stretching (Pescatello 2014). Exercise intensity may be high (70% to less than 90% of heart rate maximum (HR_{max}) or a rating of perceived exertion (RPE) value of 5/10 to 7/10), moderate

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(55% to less than 70% HR_{max} or an RPE value of 3/10 to 4/10), or light (40% to less than 55% HR_{max} OR an RPE value of 1/10 to 2/10).

The exercise intervention may be supervised by allied health practitioners, medical health practitioners, or other exercise professionals, and can be individually supervised or supervised in a group setting, or it can be completely unsupervised and performed independently. Unsupervised exercise is usually reported as home-based exercise, but can also include exercising in a park or in a gym without supervision. While people with SLE are advised to avoid sun exposure, which may limit their interest or raise concern about exercise, it is important to know that not all exercise is performed outdoors. The exercise environment may be water-based (indoors or outdoors), land-based (indoors or outdoors), in a gym or clinic, outdoors at a park or along a walking or bike track, or in ones' home (Pescatello 2014).

How the intervention might work

Regular exercise training may lead to anti-inflammatory benefits in chronic diseases with systemic low-grade inflammation (i.e. type 2 diabetes) by reducing inflammatory markers (Perandini 2012), and is regarded as a valuable self-care intervention for this population. Given the potential role of inflammation in the aetiology and clinical symptoms of SLE, including pain, redness, and swelling, if exercise training is able to alleviate the inflammatory process, it could be a helpful intervention in treating the symptoms related to inflammation in SLE (Perandini 2012). Exercise is beneficial in reducing fatigue (Del Pino-Sedeno 2016; Neill 2006; Wu 2017; Yuen 2014), improving symptoms of depression (Da Hora 2019; Kelley 2015), and improving quality of life (Da Hora 2019; Sieczkowskaa 2020). The benefits of exercise are similar in other rheumatic, inflammatory conditions with improvements in quality of life (Sieczkowskaa 2020), reduced inflammation (Metsios 2020; Perandini 2012), and reduced joint damage and symptoms (Sveaas 2017). Importantly, it is suggested that exercise does not deleteriously affect disease activity (O'Dwyer 2017), and positively influences fatigue (O'Dwyer 2017; Wu 2017; Yuen 2014), which is a significant concern for most people with SLE. As such, exercise could serve as an adjunct non-pharmaceutical therapy for people with SLE to assist in the management of disease-related symptoms such as fatigue and pain, as well as preventing comorbidities such as osteoporosis and CVD.

Why it is important to do this review

To date, there are currently three systematic reviews that assess the safety and effectiveness of exercise in adults with SLE, two of which were published in 2017 and one in 2021 (O'Dwyer 2017; Wu 2017; Lu 2021).

The first review found exercise improved depression and fatigue and not alter disease activity in adults with SLE compared to control groups (O'Dwyer 2017). Meta-analyses of seven studies found that disease activity was unchanged following exercise interventions (mean difference (MD) 0.01, 95% confidence interval (CI) −0.54 to 0.56), fatigue decreased in the exercise intervention group compared to controls (MD −0.52, 95% CI −0.91 to −0.13), and depression scores decreased in the exercise groups compared to the controls (standardised mean difference (SMD) −0.40 standard deviations (SD), 95% CI −0.71 to −0.09) (Abrahão 2016; Boström 2016; Carvalho 2005; Dos Reis-Neto 2013; Miossi 2012; Robb-Nicholson 1989; Tench 2003). Most of these studies were at risk of selection and reporting bias.

The second review found that a 12-week supervised aerobic exercise programme reduced fatigue for people with SLE with mild disease activity (Wu 2017). Meta-analysis of three trials showed that aerobic exercise training decreased fatigue severity compared to controls (MD −0.52, 95% CI −0.91 to −0.13), and had a positive effect on the 36-item Short Form (SF-36) Vitality subscale (MD 14.98, 95% CI 7.45 to 22.52) (Carvalho 2005; Ramsey-Goldman 2000; Tench 2003). However, the quality of evidence assessed using PEDro was downgraded to fair (Tench 2003) or poor (Ramsey-Goldman 2000).

The third review found that exercise improved some aspects of quality of life in people with SLE (Lu 2021). Meta-analysis of five RCTs showed a positive effect of exercise on the physical health and function aspect (SF-36 Physical Function and LupusQOL Physical Health) of health-related quality of life amongst participants with SLE (Hedges' g 0.468, 95% CI 0.206 to 0.730; $P < 0.001$). Heterogeneity between studies was low ($I^2 = 19.2\%$; $P = 0.292$) (Abrahão 2016; Bostrom 2016; Keramiotou 2020; Lopes-Souza 2021; Tench 2003).

These three reviews found that exercise is effective in managing concerning symptoms of SLE including fatigue, depression, and some aspects of qualify of life. However, more studies with more participants are needed to strengthen these results, and the optimal exercise protocol is yet to be determined. Therefore, it is important to perform this systematic review to capture any additional trials, update the existing evidence, and identify the safety and effectiveness of exercise in adults with SLE. We conducted the review according to the guidelines recommended by the Cochrane Musculoskeletal Editorial Board (Ghogomu 2014).

OBJECTIVES

To evaluate the benefits and harms of structured exercise as adjunctive therapy for adults with SLE compared with usual pharmacological care, usual pharmacological care plus placebo and usual pharmacological care plus non-pharmacological care.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) and quasi-RCTs. We included parallel and cross-over trials, and cluster-RCTs, using either non-intervention or active controls. There were no language restrictions. We included abstracts and studies with unpublished data.

Types of participants

We included trials of adults (aged 18 years or greater), diagnosed with SLE according to the study author's report; American College of Rheumatology (ACR) criteria or European League Against Rheumatism (EULAR) criteria (or both), with systemic disease involving at least two body sites or organ systems. We excluded trials of participants with SLE and another diagnosed condition in different groups (i.e. group one = people with SLE, group 2 = people with rheumatoid arthritis) if the effect of the intervention could

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not be determined on the participants with SLE alone. We included intervention trials without regard to race, sex, or disease duration of participants.

Types of interventions

Structured exercise

Adjunct to usual care, an intervention consisting of structured exercise performed at any duration, frequency, intensity, and of any type was included. The type of exercise intervention included either an individual type of exercise or a combination of various types (e.g. resistance training alone or resistance training combined with aerobic training). Exercise interventions were structured, recurring, and prescriptions included specific dosage information (i.e. frequency, intensity, timing, type). Aerobic exercise could include, but was not limited to, walking (treadmill or free), cycling (stationary or free), swimming, or aerobics classes. Range of movement exercise could include Pilates; yoga; tai chi; or active, ballistic, and static stretching. Other forms of exercise such as sports, games, and recreational activities such as dancing, lawn bowls, and Wii fit could be included. Exercise environments could include water- or, land-based exercise, indoor or outdoor settings, home-based or community led, supervised or unsupervised, face-to-face or telehealth.

Usual pharmacological care

Usual pharmacological care could include, but was not limited to, the following standard pharmacological drug treatments; antimalarials such as hydroxychloroquine, NSAIDs, glucocorticoids such as prednisone, immunosuppressives such as mycophenolate, and biologicals such as belimumab or rituximab. Other non-pharmacological measures may also have included sun avoidance, commonly prescribed supplementation (i.e. vitamin D), and education about the disease or managing comorbidities such as hypertension, for example (Fanouriakis 2019).

Comparisons

We included any RCT that evaluated the effect of exercise as an adjunct therapy to usual care, compared to:

1. usual pharmacological care plus placebo;
2. usual pharmacological care alone;
3. usual pharmacological care plus another intervention that was non-pharmacological (e.g. relaxation, counselling, education, support group).

We excluded studies if the exercise intervention was not structured (i.e. the exercise intervention did not have a dosage for frequency, intensity, or duration of exercise) or if the exercise intervention was an acute or single bout of exercise (i.e. one individual session of exercise or one exercise test).

Types of outcome measures

Studies were not excluded on the basis of outcome reporting.

Major outcomes

1. **Fatigue:** mean or mean change in fatigue assessed by Fatigue Severity Scale (FSS), Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) (FACIT group; Lai 2011), or other relevant fatigue scales such as Profile Of Moods State (POMS).
2. **Functional capacity:** mean or mean change in functional capacity measured by the Physical Component Score (PCS) of the 36-item Short-Form (SF-36), or Physical Function subscale of the SF-36, or other physical function or disability scales.
3. **Disease activity:** mean or mean change in SLE scores on validated disease activity indices such as the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), Systemic Lupus Erythematosus Disease Activity Index SELENA Modification (SELENA-SLEDAI), modified SELENA-SLEDAI Flare Index (SFI) (Petri 1999; Petri 2005); British Isles Lupus Assessment Group index (BILAG) (Hay 1993; Isenberg 2000); or other similar validated indices.
4. **Quality of life:** mean or mean change in quality of life assessed by the Mental Component Score (MCS) of the SF-36, or similar assessments such as Lupus Quality Of Life (LupusQOL) (Doward 2009; McElhone 2007).
5. **Pain:** mean or mean change in pain measured by the Visual Analogue Scale (VAS) for pain, the numerical rating scale (NRS) for pain, or the Bodily Pain subscale of the SF-36.
6. **Serious adverse events (SAEs):** including number of SAEs, or number of people with one or more SAE.
7. **Withdrawals due to any reason**

Minor outcomes

1. **Composite responder rate**, as defined with the Systemic lupus erythematosus Responder Index (SRI), where a responder is defined as a person with
   a. a 4-point or greater reduction in SELENA-SLEDAI score;
   b. no new BILAG A or no more than one new BILAG B domain score; and
   c. no deterioration from baseline in the physician's global assessment by 0.3 points or greater (Furie 2009).
2. **Aerobic capacity:** mean or mean change in aerobic capacity assessed by predicted or absolute value of maximum rate of oxygen consumption (VO_{2max}).
3. **Depression:** mean or mean change in depression assessed by Beck-Depression Index (BDI) or other relevant depression scales such as Hospital Anxiety and Depression Scale (HADS).
4. **Anxiety:** mean or mean change in anxiety assessed using HADS or other relevant anxiety scales.

We analysed all exercise interventions in the pooled primary analysis. For efficacy outcomes, we extracted data from the end of intervention time point. We defined the end of intervention as the time when the structured exercise intervention had completed. We extracted adverse event outcomes at the last time point (i.e. proportion who had an event by the end of the trial).

Search methods for identification of studies

Electronic searches

We searched Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE Ovid, Embase Ovid, CINAHL (EBSCO), SPORTDiscus (EBSCO), and Web of Science. We also conducted a search of ClinicalTrials.gov (www.clinicaltrials.gov) and the WHO trials portal (www.who.int/ictrp/en/). We searched all databases from their inception to 30 March 2022, and we imposed no restriction on language of publication.

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See Appendix 1; Appendix 2; Appendix 3; Appendix 4; Appendix 5; and Appendix 6 for the search strategies.

Searching other resources

We did not contact organisations to obtain additional references.

Data collection and analysis

Selection of studies

Two review authors (SF, EN) independently screened titles and abstracts for inclusion of all the potentially relevant studies we identified as a result of the search, and coded them as 'retrieved' (eligible or potentially eligible/unclear) or 'did not retrieve'. We retrieved the full-text study reports/publications and two review authors (SF, EN) independently screened the full texts and identified studies for inclusion, and identified and recorded reasons for exclusion of the ineligible studies. We resolved any disagreements through discussion with a third review author (MC). We identified and excluded duplicates. We recorded the selection process in sufficient detail to complete a PRISMA flow diagram (Figure 1; PRISMA Group 2009; prisma-statement.org/PRISMAStatement/Default.aspx).

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Figure 1.

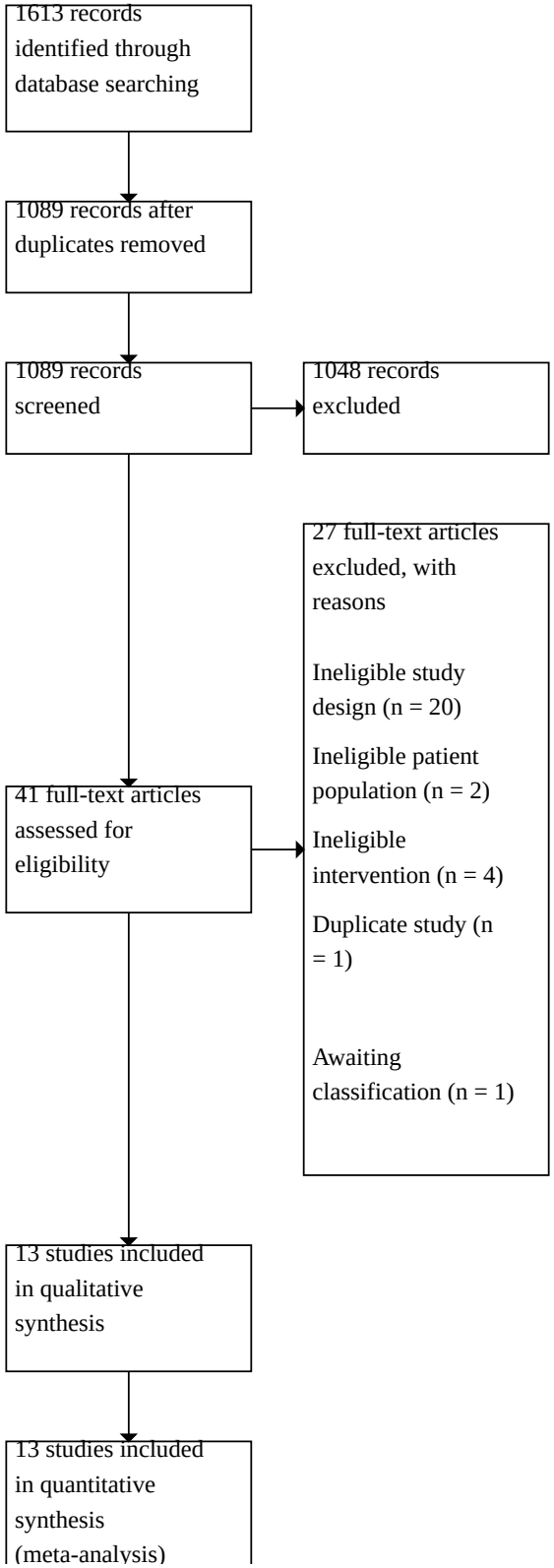

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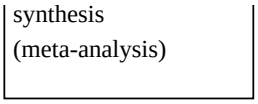
Figure 1. (Continued)



Data extraction and management

Two review authors (SF, EN) extracted the following study characteristics from included studies.

1. Methods: study design, total duration of study, number of study centres and location, study setting, withdrawals, and date of study.
2. Participants: number, mean age, age range, sex, disease duration, severity of condition, diagnostic criteria, important SLE baseline data, medication, inclusion criteria, and exclusion criteria.
3. Interventions: intervention; comparison; concomitant medications; and specific components of the intervention including type, frequency, intensity, and duration of the exercise intervention, and whether the exercise intervention was supervised. This was assessed using the Consensus on Exercise Reporting Template (CERT): Explanation and Elaboration Statement (bjsm.bmj.com/content/50/23/1428Slade 2016).
4. Outcomes: major and minor outcomes specified and collected, and time points reported.
5. Characteristics of the design of the trial as outlined in the Assessment of risk of bias in included studies section.
6. Notes: funding for trial, and notable declarations of interest of trial authors.

Two review authors (SF, MC) independently extracted outcome data from included studies. We extracted the number of events and number of participants per treatment group for dichotomous outcomes, and means, SDs, and number of participants per treatment group for continuous outcomes. We noted in the Characteristics of included studies table if outcome data were not reported in a usable way and when data were transformed or estimated from a graph. We resolved disagreements by consensus or by involving a third review author (SO). One review author (SF) transferred data into RevMan Web. We double-checked that data were entered correctly by comparing the data presented in the systematic review with the study reports.

If more than one measure for an outcome was reported, we extracted only the one reported by most of the included trials (i.e. FSS for fatigue). In the event of multiple outcome reporting, if both final values and change from baseline values were reported for the same outcome, we extracted the final values, as reported in the publication. Similarly, if data were analysed based on an intention-to-treat (ITT) sample and another sample (e.g. per-protocol, as-treated), we extracted the ITT sample for both outcomes assessing benefits and outcomes assessing harms. If data for more than one time point were provided, we used the 'end of structured exercise intervention' time point for the meta-analysis.

Assessment of risk of bias in included studies

Two review authors (SF, MC) independently assessed risk of bias using the RoB 1 tool for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Chapter 8; Higgins 2011). We resolved any disagreements by discussion or by involving other review authors (SO, DG). We assessed the risk of bias according to the following domains.

1. Random sequence generation.
2. Allocation concealment.
3. Blinding of participants and personnel.
4. Blinding of outcome assessment.
5. Incomplete outcome data.
6. Selective outcome reporting.
7. Other bias (potential threats to validity such as unit of analysis issues, inappropriate or unequal application of co-intervention across treatment groups).

We graded each potential source of bias as high, low, or unclear risk, and provided a quote from the study report together with a justification for our judgement in the risk of bias table. We summarised the risk of bias judgements across different studies for each of the domains listed. We considered blinding separately for different key outcomes where necessary (e.g. for unblinded outcome assessment, risk of bias for objective outcome measures which may be different from a participant-reported scale). In addition, we considered the impact of missing data by key outcomes.

Where information on risk of bias related to unpublished data or correspondence with a trialist, we noted this in the risk of bias table.

When considering treatment effects, we considered the risk of bias for the studies that contributed to that outcome.

We presented the figures generated by the RoB 1 tool to provide summary assessments of the risk of bias.

Assessment of bias in conducting the systematic review

We conducted the review according to the published protocol (Frade 2021), and reported any deviations from it in the Differences between protocol and review section.

Measures of treatment effect

We analysed dichotomous data as RRs when the outcome was a rare event (approximately less than 10%), with 95% CIs. We analysed continuous data as MD (if studies use the same scale) or SMD (if studies use different scales) with 95% CIs. We entered data presented as a scale with a consistent direction of effect across studies.

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When studies used different scales to measure the same conceptual outcome (e.g. disability), we calculated SMDs instead, with corresponding 95% CIs. We back-translated SMDs to a typical scale (e.g. 0 to 10 for pain) by multiplying the SMD by a typical among-person SD (e.g. the SD of the control group at baseline from the most representative trial) as recommended in *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2020a).

We assumed a minimal clinically important difference (MCID) of 1.5 points in a 10-point Likert scale for pain; and 10 points on a 100-point Likert scale for function or disability into the calculator. Using a cross-sectional approach (Goligher 2008) derived 5.9 points as the MCID for the FACIT-Fatigue scale in people with SLE. The MCID for the FSS has been reported as a decrease of 1 point on the 7-point scale (Nordin 2016). The MCID for LupusQOL is estimated using an anchor-based approach as mean changes in LupusQOL domains when minimal change (deterioration = −3 or −2 points; improvement = 2 or 3 points) (McElhone 2016). SF-36 score can be expressed in two subscores according to the domains they explore: a PCS and an MCS. We considered 3.74 for PCS and 1.7 for MCS as minimal important differences (Leung 2011). For measures with no previously reported clinically important threshold, we used the SMD interpretation where values greater than 0.8 were considered clinically significant (large effect). A change of 4 points on the SLEDAI scale is considered the MCID; however, this has not yet been well established (Brunner 2010).

For dichotomous outcomes, we calculated the absolute percent change from the difference in the risks between the intervention and control groups using GRADEpro GDT and expressed as a percentage (GRADEpro GDT).

For continuous outcomes, we calculated the absolute percent change by dividing the MD by the scale of the measure.

Unit of analysis issues

Where a single trial reported multiple trial arms, we included only the relevant arms. If two comparisons (e.g. exercise programme 1 and exercise programme 2 versus placebo) were combined in the same meta-analysis, we combined the two exercise groups into one intervention to avoid double-counting. We listed all treatment arms in the Characteristics of included studies table, even if they were not used in the review.

We analysed non-standard designs (i.e. cluster-RCTs and crossover RCTs) using methods appropriate to the design as suggested in Sections 23.1.4, 23.1.5, and 23.2.5 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2020b).

Dealing with missing data

We contacted investigators or study sponsors to verify key study characteristics and obtain missing numerical outcome data where possible (e.g. when data were not available for all participants). Where this was not possible, and the missing data were thought to introduce serious bias, we explored the impact of including such studies in the overall assessment of results using a sensitivity analysis. We described any assumptions and imputations to handle missing data and explored the effect of imputation using sensitivity analyses.

For dichotomous outcomes (e.g. number of withdrawals due to adverse events), we calculated the withdrawal rate using the number of participants randomised in the group as the denominator.

For continuous outcomes (e.g. mean change in pain score), we calculated the MD or SMD based on the number of participants analysed at that time point. If the number of participants analysed was not presented for each time point, we used the number of randomised participants in each group at baseline.

Where possible, we computed missing SDs from other statistics such as standard errors, CIs, or P values, according to the methods recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Chapter 10; Deeks 2020). If SDs could not be calculated, we imputed them (e.g. from other studies in the meta-analysis) (Deeks 2020).

Assessment of heterogeneity

We assessed clinical and methodological diversity in terms of participants, interventions, outcomes, and study characteristics for the included studies to determine whether a meta-analysis was appropriate. This was conducted by observing these data from the data extraction tables. We assessed statistical heterogeneity by visual inspection of the forest plot to assess obvious differences in results between the studies, and using the I^2 and Chi^2 statistical tests.

As recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Chapter 10; Deeks 2020), the interpretation of an I^2 value of 0% to 40% might 'not be important'; 30% to 60% may represent 'moderate' heterogeneity; 50% to 90% may represent 'substantial' heterogeneity; and 75% to 100% represents 'considerable' heterogeneity. We kept in mind that the importance of the I^2 statistic depends on: magnitude and direction of effects and strength of evidence for heterogeneity.

The Chi^2 test was interpreted where a $P \leq 0.10$ indicated evidence of statistical heterogeneity.

If we identified substantial heterogeneity, we reported it and investigated possible causes by following the recommendations in the *Cochrane Handbook for Systematic Reviews of Interventions* (Chapter 10; Deeks 2020).

Assessment of reporting biases

We created and examined a funnel plot to explore possible small-study biases. In interpreting funnel plots, we examined the different possible reasons for funnel plot asymmetry as outlined in Chapter 13 of the *Cochrane Handbook for Systematic Reviews of Interventions* and related this to the results of the review (Page 2020). If we were able to pool more than 10 trials, we undertook formal statistical tests to investigate funnel plot asymmetry, and followed the recommendations in the *Cochrane Handbook for Systematic Reviews of Interventions* (Chapter 13; Page 2020).

To assess outcome reporting bias, we checked trial protocols against published reports. For studies published after 1 July 2005, we screened the Clinical Trial Register at the International Clinical Trials Registry Platform of the WHO (apps.who.int/trialssearch) for the a priori trial protocol. We evaluated whether selective reporting of outcomes was present.

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Data synthesis

We undertook meta-analyses only where this was meaningful (i.e. if the treatments, participants, and the underlying clinical question were similar enough for pooling to make sense). We anticipated that the following comparisons would be used.

1. Exercise plus usual pharmacological care versus placebo
2. Exercise plus usual pharmacological care versus usual pharmacological care
3. Exercise plus usual pharmacological care versus another intervention (e.g. education about exercise, counselling about exercise, relaxation exercises).

We used a random-effects model. We analysed all types of exercise interventions in the pooled primary analysis.

Subgroup analysis and investigation of heterogeneity

If there were sufficient data, we would have conducted subgroup analyses for fatigue according to components of exercise. We had restricted subgroup analyses to the primary time point. We anticipate that the following exercise components may be useful.

1. Types of exercise (aerobic, resistance, relaxing/range of motion)
2. Exercise setting (supervised or unsupervised/home-based exercise)

The reason for including components of an exercise programme in the subgroup analyses is to be able to identify an optimal exercise for improving fatigue in people with SLE, which has been implicated for future research in previous reviews (O'Dwyer 2017; Wu 2017). This information will be critical for informing both practitioners and patients regarding the most appropriate exercise prescription. Pooled evidence from three studies showed that aerobic exercise training significantly decreased fatigue severity compared to relaxing exercise (Carvalho 2005; Ramsey-Goldman 2000; Tench 2003), and supervised exercise reduced fatigue symptoms to a significantly greater extent than home-based exercise (Wu 2017).

We would have used the formal test for subgroup interactions in Review Manager Web (RevMan Web 2022), and use caution in the interpretation of subgroup analyses as advised in Section 9.6 of the *Cochrane Handbook for Systematic Reviews of Interventions* (McKenzie 2021). We would compare the magnitude of the effects between the subgroups by assessing the overlap of the CIs of the summary estimate. Non-overlap of the CIs indicates statistical significance.

Sensitivity analysis

We planned to carry out the following sensitivity analyses to investigate the robustness of the treatment effect on fatigue.

1. Impact of including studies with high or unclear risk of selection, detection, and attrition biases
2. Impact of including studies with imputed data

Summary of findings and assessment of the certainty of the evidence

At least two review authors (SF, MC) assessed the certainty of the supporting evidence behind each estimate of treatment effect using the GRADE approach for the major outcomes: fatigue, functional capacity, disease activity, quality of life, pain, serious adverse events, and withdrawals due to any reason. We used methods and recommendations described in *Cochrane Handbook for Systematic Reviews of Interventions* (Chapter 14; Schünemann 2020a). We used the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the certainty of a body of evidence as it relates to the studies that contributed data to the meta-analyses for the prespecified outcomes, and reported the certainty of evidence as high, moderate, low, or very low.

We used GRADEpro GDT software to prepare and display the summary of findings tables. We justified all decisions to downgrade the certainty of evidence for each outcome using footnotes, and we made comments to aid the reader's understanding of the review where necessary. We provided the number needed to treat for an additional beneficial outcome (NNTB) or harmful outcome (NNTH) and absolute percent change in the 'Comments' column of the summary of findings table.

We preselected the following important outcomes for inclusion in the summary of findings tables.

1. Mean or mean change in fatigue assessed by FSS, FACIT-F, or other relevant fatigue scales such as POMS.
2. Mean or mean change in functional capacity measured by the PCS of the SF-36, or physical function subscale of the SF-36, or other physical function or disability scales.
3. Mean or mean change in SLE scores on validated disease activity indices such as the SLEDAI, SELENA-SLEDAI, modified SELENA-SLEDAI SFI; BILAG; or other similar validated indices.
4. Mean or mean change in quality of life assessed by the MCS of the SF-36, or similar assessments such as LupusQOL.
5. Mean or mean change in pain measured by VAS for pain, NRS for pain, or the bodily pain subscale of the SF-36.
6. SAEs, number of SAEs, or number of participants with one or more SAE.
7. Withdrawals due to any reason

We produced three summary of findings tables for the following comparisons.

1. Exercise plus usual pharmacological care versus placebo plus usual pharmacological care.
2. Exercise plus usual pharmacological care versus usual pharmacological care.
3. Exercise plus usual pharmacological care versus another intervention (e.g. education about exercise, counselling about exercise, relaxation exercises) plus usual pharmacological care.

For efficacy outcomes, we extracted data at the end of intervention time point. We extracted adverse event outcomes at the last time point (i.e. proportion who had an event by the end of the trial).

Interpreting results and reaching conclusions

We followed the guidelines in *Cochrane Handbook for Systematic Reviews of Interventions* (Chapter 15; Schünemann 2022b), for interpreting results, and were aware of distinguishing a lack of evidence of effect from a lack of effect. We based our conclusions only on findings from the quantitative or narrative synthesis, according to Synthesis Without Meta-analysis (SWiM) reporting guideline of included studies for this review (Campbell 2020). Our

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implications for research suggested priorities for future research and outlined what the remaining uncertainties are in the area.

RESULTS

Description of studies

Details of the included studies are listed in Table 1 and the Characteristics of included studies table.

Results of the search

The search was conducted up to 30 March 2022. It yielded 1613 records across six databases (CENTRAL, MEDLINE, Embase, CINAHL, SPORTDiscus, and Web of Science). After removal of duplicates, 1089 records remained. Of these, we retrieved 41 for full-text screening on the basis of title and abstract. We deemed 13 RCTs eligible for inclusion (Abrahão 2016; Avaux 2016; Benatti 2015; Benatti 2018; Bostrom 2016; Daltroy 1995; Dos Reis-Neto 2013; Hashemi 2022; Kao 2021; Keramiotou 2020; Lopes-Souza 2021; Miossi 2012; Tench 2003). We excluded 27 articles, one trial is awaiting classification (Boedecker 2020), and there are no ongoing studies. See Figure 1 for the PRISMA flow diagram of search results (Page 2021).

Included studies

Study design and setting

Studies were conducted in Brazil (7/13, 53%), Europe (3/13, 23%), the US (1/13, 8%), the UK (1/13, 8%), and Iran (1/13, 8%), Six studies were two-arm parallel RCTs (Benatti 2018; Bostrom 2016; Daltroy 1995; Hashemi 2022; Keramiotou 2020; Lopes-Souza 2021), two studies were two-arm parallel quasi-RCTS (Dos Reis-Neto 2013; Kao 2021), four studies were three-arm parallel RCTs (Abrahão 2016; Benatti 2015; Miossi 2012; Tench 2003), and one study was a three-arm parallel quasi-RCT (Avaux 2016).

Participants

There were a total of 540 participants with SLE who commenced the intervention, and 463 participants who completed the intervention (86%). There were 77 participants who dropped out of the studies (reasons reported in the Characteristics of included studies table). Across included trials the mean age of participants ranged from 21.5 to 53 years, and mean duration of disease from 2.5 to 21 years. Most studies diagnosed SLE using the ACR criteria for SLE. It is unclear whether included participants had comorbidities as this was not clearly reported in the included studies. Participants were on various pharmacological treatments including csDMARDs such as hydroxychloroquine, prednisolone or glucocorticoids, mycophenolate mofetil, methotrexate, azathioprine, and cyclophosphamide; bDMARDs such as rituximab or belimumab; and NSAIDs such as naproxen or celecoxib. See Table 1.

Interventions and comparators

Control group interventions

All 13 studies compared a type of exercise, or a combination of types of exercise, plus usual care, to a control group that received either one of the following.

1. Placebo plus usual care[a] (Lopes-Souza 2021).
    a. In this study, the exercise intervention included whole body vibration exercise where participants were asked to stand on a vibrating platform, and the placebo intervention also stood on a vibration platform, except the vibration was turned off.
2. Usual care alone[a] (Avaux 2016; Benatti 2015; Benatti 2018; Bostrom 2016; Hashemi 2022; Tench 2003).
3. Another non-pharmacological intervention plus usual care[a] (Abrahão 2016; Daltroy 1995; Dos Reis-Neto 2013; Kao 2021; Keramiotou 2020; Miossi 2012; Tench 2003). Other non-pharmacological interventions included:
    a. participants received information about the disease, and were informed that they would receive the intervention after the study was finished, and they would be invited to participate in the intervention that proved the most effective (Abrahão 2016);
    b. participants were contacted by the research team once per week. They were also asked to fill out questionnaires, and were encouraged to maintain their current level of activity (Daltroy 1995);
    c. participants received information about the disease. They received clear instruction not to start any exercise for the next 16 weeks (Dos Reis-Neto 2013);
    d. participants received information about the disease. They were asked to maintain their usual lifestyle (Kao 2021);
    e. participants had four sessions of training in alternative methods of performing daily activities, use of aids, joint protection, and energy conservation (Keramiotou 2020);
    f. participants received information about their disease. They were advised to remain physically inactive (Miossi 2012);
    g. participants listened to a relaxation audio tape in a quiet, warm, and darkened room for 30 minutes, three times per week. Participants were seen by an exercise professional every two weeks for a supervised relaxation session (Tench 2003).

[a]Usual care included pharmacological treatments: csDMARDs such as hydroxychloroquine, prednisolone or glucocorticoids, mycophenolate mofetil, methotrexate, azathioprine, and cyclophosphamide; bDMARDs such as rituximab or belimumab; and NSAIDs such as naproxen or celecoxib.

Exercise interventions

All 13 studies included a structured exercise programme as part of their intervention. The summary of interventions can be found in Table 2, and summarised below.

1. **Type of exercise:** four studies included aerobic exercise (Benatti 2018; Daltroy 1995; Dos Reis-Neto 2013; Tench 2003), seven studies included a combination of aerobic and resistance exercise (Abrahão 2016; Avaux 2016; Benatti 2015; Bostrom 2016; Hashemi 2022; Kao 2021; Miossi 2012), one study included a combination of resistance exercise and stretching (Keramiotou 2020), and one study included whole body vibration exercise, which is a subgroup of resistance training, better classified as muscle activation/neuromuscular training complementary to resistance training (Lopes-Souza 2021).
2. **Intensity of exercise:** one study was low intensity (Lopes-Souza 2021), seven studies were moderate intensity (Abrahão 2016; Avaux 2016; Daltroy 1995; Hashemi 2022; Kao 2021; Keramiotou 2020), one study was high intensity (Bostrom 2016), and four

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studies did not clearly report the intensity (Benatti 2015; Benatti 2018; Dos Reis-Neto 2013; Miossi 2012).

3. **Frequency of exercise:** participants undertook two exercise sessions per week in five studies (Benatti 2015; Benatti 2018; Bostrom 2016; Lopes-Souza 2021; Miossi 2012), three sessions per week in five studies (Abrahão 2016; Daltroy 1995; Dos Reis-Neto 2013; Hashemi 2022; Tench 2003), five sessions per week in one study (Kao 2021), daily in one study (Keramiotou 2020), and a total of three hours over the entire week, with no clarity on the number of sessions per week in one study (Avaux 2016).
4. **Duration of the exercise intervention:** the exercise intervention had a duration of 12 weeks in 11 studies (Abrahão 2016; Avaux 2016; Benatti 2015; Benatti 2018; Bostrom 2016; Daltroy 1995; Kao 2021; Keramiotou 2020; Lopes-Souza 2021; Miossi 2012; Tench 2003), with a 24-week follow-up in three studies (Daltroy 1995; Keramiotou 2020; Lopes-Souza 2021), and a 24-week plus 52-week follow-up in one study (Bostrom 2016). The exercise intervention had a duration of 16 weeks in one study (Dos Reis-Neto 2013), and eight weeks in one study (Hashemi 2022).

Outcomes

See Table 3 and Table 4 for further details on the major and minor outcomes in the included studies.

Exercise plus usual pharmacological care versus placebo plus usual pharmacological care

Major outcomes

One trial compared a structured exercise intervention to a placebo control (Lopes-Souza 2021). The certainty of evidence was low for fatigue, functional capacity, and pain, and very low for withdrawals due to any reason. We extracted data from the end of the intervention (i.e. 12 weeks). The major outcomes are reported in summary of findings Table 1.

Fatigue

Lopes-Souza 2021 measured overall fatigue (mean or mean change) using the FACIT-F, which we used in our analyses. It had a scale with 13 items scored from 0 to 4. Overall scores ranged from 0 to 52, with a lower final score indicating greater fatigue. However, for consistency with other analyses of fatigue, we reversed the scale so that a lower score indicates less fatigue.

Functional capacity

Lopes-Souza 2021 measured overall functional capacity (mean or mean change) using the SF-36 Functional Capacity/Physical Function domain, which we used in our analyses. Scores ranged from 0 to 100, with higher scores indicating better functional capacity.

Disease activity

Lopes-Souza 2021 did not report disease activity.

Quality of life

Lopes-Souza 2021 partially reported quality of life using the SF-36 Quality of Life questionnaire; however, authors did not report the MCS and PCS scores, and, therefore, this was not used in our analyses.

Pain

Lopes-Souza 2021 measured pain using the SF-36 Quality of Life questionnaire, Pain domain, which we used in our analyses. Scores ranged from 0 to 100, with higher scores indicating less pain. However, for consistency with other pain scales (i.e. VAS), we reversed the scale so that a lower score indicated less pain.

Serious adverse events

Lopes-Souza 2021 reported no SAEs.

Withdrawals due to any reason

Lopes-Souza 2021 reported three participant dropouts from the exercise group (one participant withdrew before the six-week analysis due to low back pain, and two withdrew before the 12-week analysis due to personal reasons) and one participant withdrew from the control group before the six-week analysis due to personal reasons.

Minor outcomes

Composite responder rate

Lopes-Souza 2021 did not report composite responder rate.

Aerobic fitness

Lopes-Souza 2021 did not report aerobic fitness.

Depression

Lopes-Souza 2021 did not report depression.

Anxiety

Lopes-Souza 2021 did not report anxiety.

Exercise plus usual pharmacological care versus usual pharmacological care alone

Six trials compared exercise plus usual pharmacological care versus usual pharmacological care alone (Avaux 2016; Benatti 2015; Benatti 2018; Bostrom 2016; Hashemi 2022; Tench 2003).

Major outcomes

Fatigue

Two trials measured and reported overall fatigue (mean or mean change) using the Krupp FSS, with scores ranging from 1 to 7, lower scores indicating less fatigue, which we used in our analyses (Avaux 2016; Tench 2003). Tench 2003 also measured overall fatigue using the Chalder Fatigue Scale (CFS) and VAS for fatigue; however we extracted data from the FSS only. Four trials did not measure or report (or both) fatigue (Benatti 2015; Benatti 2018; Bostrom 2016; Hashemi 2022).

Functional capacity

Two trials measured overall functional capacity (mean or mean change) using the SF-36 Physical Function domain, which we used in our analyses (Bostrom 2016; Tench 2003). Scores ranged from 0 to 100, with higher scores indicating better functional capacity. Four trials did not measure or report (or both) functional capacity (Avaux 2016; Benatti 2015; Benatti 2018; Hashemi 2022).

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Disease activity

One trial measured disease activity using the SLEDAI, which we used in our analyses (Bostrom 2016). Scores ranged from 0 to 105, with lower scores indicating less disease activity. Tench 2003 measured disease activity using the SLAM measuring system, which we used in our analyses. Scores ranged from 0 to 83, with lower scores indicating less disease activity. Four trials did not measure or report (or both) change in disease activity before and after the intervention (Avaux 2016; Benatti 2015; Benatti 2018; Hashemi 2022).

Quality of life

Two trials partially reported quality of life using the SF-36 Quality of Life questionnaire; however, authors did not report the MCS and PCS scores, and, therefore, could not be used in our analyses (Bostrom 2016; Tench 2003). Four trials did not measure or report (or both) quality of life (Avaux 2016; Benatti 2015; Benatti 2018; Hashemi 2022).

Pain

Bostrom 2016 measured and recorded pain using the SF-36 Quality of Life questionnaire, Pain domain, which we used in our analyses. Scores ranged from 0 to 100, with higher scores indicating less pain. For consistency with other pain scales (i.e. VAS), we reversed the score so that a lower score indicated less pain. Tench 2003 measured pain using the SF-36 Quality of Life questionnaire; however, authors did not report the Pain domain, and, therefore, this was not used in our analyses. Four trials did not measure or report (or both) pain (Avaux 2016; Benatti 2015; Benatti 2018; Hashemi 2022).

Withdrawals due to any reason

Avaux 2016 had three participants withdraw from the intervention; two due to personal reasons, and one due to a disease flare; however, it is unclear which group they were part of, and they were not included in our analyses. Benatti 2018 had eight participants withdraw from the intervention for the following reasons: four participants withdrew from the control group (one was pregnant, three for personal reasons) and four participants withdrew from the exercise group (one fractured a limb outside of training sessions, three for person reasons). Another two participants withdrew due to a disease flare (one from each group). Bostrom 2016 had three participants withdraw from the control group (one had depression/cognitive impairment, one had untreated dementia, one had suspected relapse of breast cancer). Tench 2003 had 14 participants withdraw due to any reason: four participants withdrew from the exercise group, five participants withdrew from the active control group (relaxation) and five participants withdrew from the usual care control group. Note that six participants dropped out of treatment and eight participants completed the study but did not wish to repeat the walking test to exhaustion at the end of the intervention. Two trials had no withdrawals from the intervention due to any reason that were reported (Benatti 2015; Hashemi 2022).

Serious adverse events

None of the six trials reported any SAEs (Avaux 2016; Benatti 2015; Benatti 2018; Bostrom 2016; Hashemi 2022; Tench 2003).

Minor outcomes

Composite responder rate

None of the six studies reported composite responder rate (Avaux 2016; Benatti 2015; Benatti 2018; Bostrom 2016; Hashemi 2022; Tench 2003).

Aerobic fitness

Bostrom 2016 recorded aerobic capacity using the maximum oxygen consumption (VO_{2max} in litres/minute), with higher scores indicating better aerobic capacity. Tench 2003 recorded aerobic capacity using peak oxygen consumption (VO_{2peak} in millilitres/kilogram/minute), with higher scores indicating better aerobic capacity. Four trials did not measure or report (or both) aerobic capacity (Avaux 2016; Benatti 2015; Benatti 2018; Hashemi 2022).

Depression

Tench 2003 recorded depression using the HADS – Depression subscale. Scores ranged from 0 to 21, with lower scores indicating a better outcome. Five trials did not measure or report (or both) depression (Avaux 2016; Benatti 2015; Benatti 2018; Bostrom 2016; Hashemi 2022).

Anxiety

Tench 2003 recorded anxiety using the HADS – Anxiety subscale. Scores ranged from 0 to 21, with lower scores indicating a better outcome. Five trials did not measure or report (or both) anxiety (Avaux 2016; Benatti 2015; Benatti 2018; Bostrom 2016; Hashemi 2022).

Exercise plus usual pharmacological care versus another non-pharmacological intervention plus usual pharmacological care

Seven studies compared exercise plus usual pharmacological care versus another non-pharmacological intervention plus usual pharmacological care (Abrahão 2016; Daltroy 1995; Dos Reis-Neto 2013; Kao 2021; Keramiotou 2020; Miossi 2012; Tench 2003).

Major outcomes

Fatigue

Daltroy 1995 measured fatigue using the MAC questionnaire and POMS Fatigue questionnaires; however, these were not included in our analyses because the results for the participants with SLE were not available separately from those of the participants with rheumatoid arthritis. Keramiotou 2020 measured overall fatigue using the LupusQOL – Fatigue questionnaire, which we used in our analyses. Scores ranged from 0 to 100, with higher scores indicating less fatigue. For consistency with other fatigue scales (i.e. FSS), we reversed the scale so that a lower score indicated less fatigue. Tench 2003 measured fatigue using the Krupp FSS, which we used in our analyses. Scores ranged from 1 to 7, with lower scores indicating less fatigue. Tench 2003 used the CFS, VAS Fatigue, and the SF-36 Quality of Life questionnaire, Vitality domain; however, these were not used in our analyses. Four trials did not measure or report (or both) overall fatigue (Abrahão 2016; Dos Reis-Neto 2013; Kao 2021; Miossi 2012).

Functional capacity

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Two trials measured functional capacity using the SF-36 Quality of Life questionnaire, Physical Function domain, which we used in our analyses (Abrahão 2016; Tench 2003). Scores ranged from 0 to 100, with higher scores indicating better functional capacity. Keramiotou 2020 measured functional capacity using the LupusQOL questionnaire Physical Health domain, which we used in our analyses. Scores ranged from 0 to 100, with higher scores indicating better functional capacity. Keramiotou 2020 also assessed functional capacity using the Health Assessment Questionnaire (HAQ); however, this was not used in our analyses. Four trials did not measure or report (or both) functional capacity (Daltroy 1995; Dos Reis-Neto 2013; Kao 2021; Miossi 2012).

Disease activity

Three trials measured disease activity using the SLEDAI, which we used in our analyses (Abrahão 2016; Dos Reis-Neto 2013; Miossi 2012). Scores ranged from 0 to 105, with lower scores indicating less disease activity. Tench 2003 measured disease activity using the SLAM measuring system, which we used in our analyses. Scores ranged from 0 to 83, with lower scores indicating less disease activity. Two trials measured fatigue using the SLEDAI; however, authors do not report the mean and SD, and, therefore, we were unable to use these in our analyses (Kao 2021; Keramiotou 2020). Two trials did not measure or report (or both) change in disease activity before and after the intervention (Daltroy 1995; Miossi 2012).

Quality of life

Two trials partially reported quality of life using the SF-36 Quality of Life questionnaire; however, authors did not report the MCS and PCS scores, and, therefore, these were not used in our analyses (Abrahão 2016; Tench 2003). Keramiotou 2020 partially reported quality of life using the LupusQOL questionnaire; however, they reported only Physical Health and Fatigue domains, and, therefore, were not used in our analyses. Four trials did not measure or report (or both) quality of life (Daltroy 1995; Dos Reis-Neto 2013; Kao 2021; Miossi 2012).

Pain

Abrahão 2016 measured pain using the SF-36 Quality of Life Pain questionnaire, which we used in our analyses. Scores ranged from 0 to 100, with higher scores indicating less pain. For consistency with other scales (i.e. VAS), we reversed the scale so that lower scores indicated less pain. Tench 2003 also used the SF-36 Quality of Life questionnaire to measure quality of life; however, authors did not report the Pain domain, and, therefore, this was not used in our analyses. Keramiotou 2020 measured pain using the VAS Pain, which we used in our analyses. Scores ranged from 0 to 10, with lower scores indicating less pain. Four trials did not report quality of life (Daltroy 1995; Dos Reis-Neto 2013; Kao 2021; Miossi 2012).

Withdrawals due to any reason

Abrahão 2016 had two participants withdraw from the control group for an unknown reason. Keramiotou 2020 had two participants from the exercise group withdraw; however, the reasons were not reported. Tench 2003 had 14 participants withdraw from the study: four participants withdrew from the exercise group, five participants withdrew from the active control group (relaxation), and five participants withdrew from the usual care control group. Note that six participants dropped out of treatment and eight participants completed the study but did not wish to repeat the walking test to exhaustion at the end of the intervention. Four trials did not clearly report withdrawals due to any reason (Daltroy 1995; Dos Reis-Neto 2013; Kao 2021; Miossi 2012).

Serious adverse events

Seven trials reported no SAEs (Abrahão 2016; Daltroy 1995; Dos Reis-Neto 2013; Kao 2021; Keramiotou 2020; Miossi 2012; Tench 2003).

Minor outcomes

Composite responder rate

None of the seven trials measured or reported (or both) composite responder rate (Abrahão 2016; Daltroy 1995; Dos Reis-Neto 2013; Kao 2021; Keramiotou 2020; Miossi 2012; Tench 2003).

Aerobic fitness

Daltroy 1995 measured aerobic capacity using a 12-minute walking test; however, this was not used in our analyses. Two trials measured aerobic capacity using VO_{2peak} (in millilitres/kilogram/minute), which we used in our analyses (Dos Reis-Neto 2013; Tench 2003). Higher scores indicated better aerobic capacity. Four trials did not measure or report (or both) aerobic capacity (Abrahão 2016; Kao 2021; Keramiotou 2020; Miossi 2012).

Depression

Abrahão 2016 measured depression using the BDI, which we used in our analyses. Scores ranged from 0 to 63, with lower scores indicating a better outcome. Daltroy 1995 measured depression using the Center for Epidemiologic Studies Depression Scale (CES-D) and was not used in our analyses because we were unable to differentiate the participants with SLEW from those with rheumatoid arthritis. Scores ranged from 0 to 60, with lower scores indicating a better outcome. Tench 2003 measured depression using the HADS – Depression subscale and was not used in our analyses. Scores ranged from 0 to 21, with lower scores indicating a better outcome. Four trials did not measure or report (or both) depression (Dos Reis-Neto 2013; Kao 2021; Keramiotou 2020; Miossi 2012).

Anxiety

Tench 2003 measured anxiety using the HADS – Anxiety subscale. Scores ranged from 0 to 21, with lower scores indicating a better outcome. Six trials did not measure anxiety (Abrahão 2016; Daltroy 1995; Dos Reis-Neto 2013; Kao 2021; Keramiotou 2020; Miossi 2012).

Excluded studies

We excluded 27 studies for the following reasons.

1. **Ineligible intervention:** exercise was either acute (one single bout of exercise) or did not meet our inclusion criteria of an exercise intervention being structured, recurring, and including specific dosage information (i.e. frequency, intensity, timing, type).

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2. **Ineligible participant population:** intervention group included participants with SLE, however, control group participants were healthy controls.
3. **Ineligible study design:** studies were not randomised, or did not include a control group, and did not meet the inclusion criterion of an RCT.
4. **Duplicate study:** this was the abstract to one of our included studies (Abrahão 2016).

The list of all 27 excluded studies, with reason, can be found in the Characteristics of excluded studies table.

Risk of bias in included studies

The overall risk of bias assessment of the included studies is presented in Figure 2 and Figure 3.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

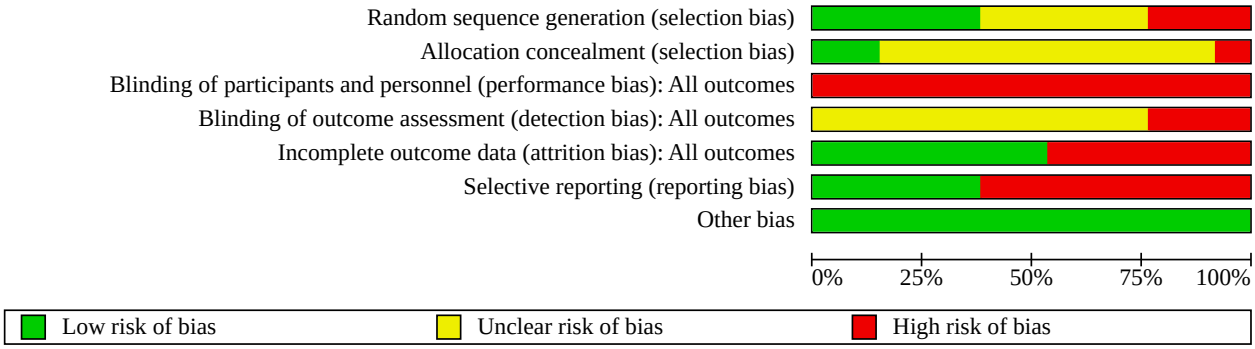

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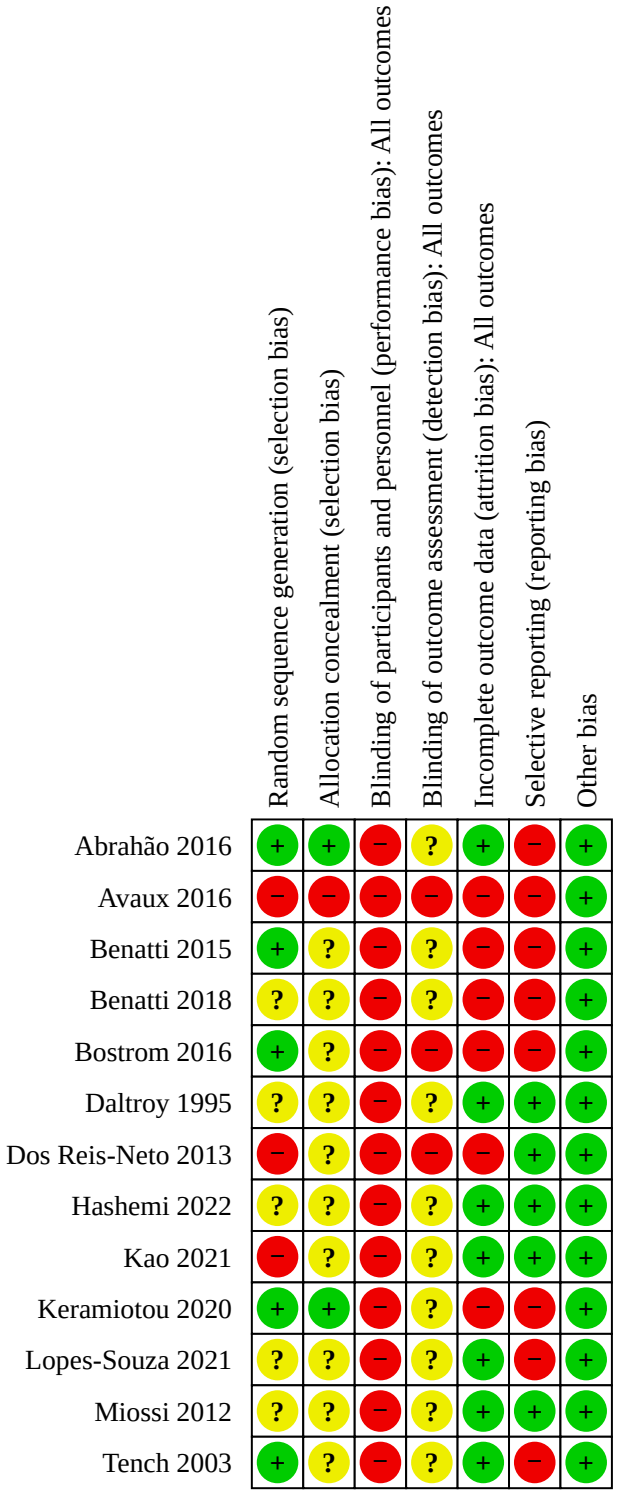
Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



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Allocation

Random sequence

We judged five studies at low risk of bias because they used and reported an appropriate method of randomisation (Abrahão 2016; Benatti 2015; Bostrom 2016; Keramiotou 2020; Tench 2003).

We assessed five studies at unclear risk of bias because the methods used to generate allocation sequence were not described, or were unclear (Benatti 2018; Daltroy 1995; Hashemi 2022; Lopes-Souza 2021; Miossi 2012).

We judged three studies at high risk of bias because their methods of randomisation were not truly random (i.e. quasi-randomised), despite authors reporting the study to be randomised (Avaux 2016; Dos Reis-Neto 2013; Kao 2021).

Allocation concealment

We judged two studies at low risk of bias, since they provided adequate information on the method of allocation concealment (Abrahão 2016; Keramiotou 2020).

For 10 studies, the method used to conceal allocation sequence was unclear, or not described (Benatti 2015; Benatti 2018; Bostrom 2016; Daltroy 1995; Dos Reis-Neto 2013; Hashemi 2022; Kao 2021; Lopes-Souza 2021; Miossi 2012; Tench 2003).

We judged one study at high risk of bias because the selection of participants based on their geographical location was deemed as selection bias (Avaux 2016).

Blinding

Participant blinding

We judged all studies at high risk of bias. Blinding participants and care providers is difficult because of the nature of the intervention. Most of the included studies did not report information on blinding, or a masking procedure for treatment allocation or delivery. No studies reported using a blinding procedure (sham or attentional comparator, or blinding of study hypothesis).

Outcome assessor

We judged all studies at high (Avaux 2016; Bostrom 2016; Dos Reis-Neto 2013) or unclear risk of bias (Abrahão 2016; Benatti 2015; Benatti 2018; Daltroy 1995; Hashemi 2022; Kao 2021; Keramiotou 2020; Lopes-Souza 2021; Miossi 2012; Tench 2003). Most included studies used subjective outcomes (self-reporting). Because participants were not blind to the treatment allocation (i.e. inability to bind an exercise trial), we considered the outcomes assessors to be unblinded.

Incomplete outcome data

We judged seven studies at low risk of attrition bias (Abrahão 2016; Daltroy 1995; Hashemi 2022; Kao 2021; Lopes-Souza 2021; Miossi 2012; Tench 2003).

We judged six studies at high risk of attrition bias because of withdrawals throughout the intervention with no clear reporting of ITT analyses (Avaux 2016; Benatti 2015; Benatti 2018; Bostrom 2016; Dos Reis-Neto 2013; Keramiotou 2020).

Selective reporting

We judged five studies at low risk of reporting bias, because all outcomes reported were prespecified in their methods (Daltroy 1995; Dos Reis-Neto 2013; Hashemi 2022; Kao 2021; Miossi 2012).

We judged seven studies at a high risk of bias because we found outcomes listed in their methods and not reported in the results (e.g. the MCS of the SF-36) (Abrahão 2016; Avaux 2016; Benatti 2015; Benatti 2018; Bostrom 2016; Keramiotou 2020; Lopes-Souza 2021; Tench 2003).

Other potential sources of bias

We judged all studies at low risk of other bias because we identified no other potential sources of bias.

Effects of interventions

See: **Summary of findings 1** Summary of findings table - Exercise plus usual pharmacological care compared to placebo plus usual pharmacological care for systemic lupus erythematosus; **Summary of findings 2** Summary of findings table - Exercise plus usual pharmacological care compared to usual pharmacological care alone for systemic lupus erythematosus; **Summary of findings 3** Summary of findings table - Exercise plus usual pharmacological care compared to another intervention (education, joint aids, or relaxation) plus usual pharmacological care for systemic lupus erythematosus

Exercise plus usual pharmacological care versus placebo plus usual pharmacological care

One study compared exercise plus usual care versus placebo plus usual care (Lopes-Souza 2021).

Major outcomes

See: Summary of findings 1.

Fatigue (FACIT-Fatigue, 0 to 52 scale, lower score indicates less fatigue severity, MCID 5.9 points)

One study (17 participants) found that exercise may result in little to no effect on fatigue. The mean fatigue score for the placebo plus usual care group was 38 points, and the mean fatigue score for the exercise plus usual care group was 33 points (MD −5.00 points, 95% CI −3.29 lower to 13.29; Analysis 1.1). There was no clinically meaningful benefit. Because of study limitations, we downgraded the evidence two levels for high risk of bias and imprecision; we rated the certainty of evidence as low.

Functional capacity (SF-36 Physical Function, 0 to 100 scale, higher scores indicate better function, MCID 10 points)

One study (17 participants) found that exercise may have little to no effect on functional capacity. The mean functional capacity score for the placebo plus usual care group was 70 points, and the mean functional capacity score for the exercise plus usual care group 67.5 points (MD −2.50 points, 95% CI −23.78 to 18.78; Analysis 1.2). There was no important clinically meaningful benefit. Because of study limitations, we downgraded the evidence two levels for high risk of bias and imprecision; we rated the certainty of evidence as low.

Disease activity

The study did not report disease activity.

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Quality of life

The study did not report quality of life.

Pain (SF-36 Pain, 0 to 100 scale, lower scores indicate less pain, MCID 10 points)

One study (17 participants) found that exercise may have little to no effect on pain. The mean pain score was 43 points for the placebo plus usual care group, and the mean pain score was 34 points for the exercise plus usual care group (MD −9.00 points, 95% CI −28.88 to 10.88; Analysis 2.4). There was no important clinically meaningful benefit. Because of study limitations, we downgraded the evidence two levels for high risk of bias and imprecision; we rated the certainty of evidence as low.

Serious adverse events

No SAEs reported.

Withdrawals due to any reason

We are uncertain whether exercise results in fewer or more withdrawals (RR 2.73, 95% CI 0.34 to 22.16; 1 study; Analysis 1.4). The study reported three dropouts from the exercise group; one participant withdrew before the six-week analysis due to low back pain ("not related directly with the intervention"), and two withdrew before the 12-week analysis for personal reasons, and one participant withdrew from the control group before the six-week analysis for personal reasons.

Minor outcomes

Composite responder rate

The study did not measure or report composite responder rate.

Aerobic fitness

The study did not measure or report aerobic fitness.

Depression

The study did not measure or report depression.

Anxiety

The study did not measure or report anxiety.

Exercise plus usual pharmacological care versus usual pharmacological care alone

Six studies compared exercise plus usual care versus usual care alone (Avaux 2016; Benatti 2015; Benatti 2018; Bostrom 2016; Hashemi 2022; Tench 2003).

Major outcomes

See: Summary of findings 2.

Fatigue (FSS, scale 1 to 7, lower score indicates less fatigue, MCID 1 point)

Two studies (104 participants) found that exercise plus usual care may have little to no effect on mean fatigue. The mean fatigue score in the usual care alone group was 5.4 points, and the mean fatigue score for the exercise plus usual care group was 4.8 points (MD −0.59 points, 95% CI −1.40 to 0.22; Analysis 2.1; Avaux 2016; Tench 2003). Statistical heterogeneity was not important (I^2 = 0%). There was no clinically meaningful benefit. Because of study limitations, we downgraded the evidence two levels for high risk of bias and imprecision; we rated the certainty of evidence as low.

Functional capacity (SF-36 Physical Function, scale 0 to 100, higher score indicates better function, MCID 10 points)

Two studies (96 participants) found that exercise plus usual care may have little to no effect on functional capacity. The mean physical function score in the usual care alone group was 60 points, and the mean physical function score for the exercise plus usual care group was 65.4 points (MD 5.39 points, 95% CI −5.97 to 16.75; Analysis 2.2; Bostrom 2016; Tench 2003). Statistical heterogeneity was not important (I^2 = 0%). There was no clinically meaningful benefit. Because of study limitations, we downgraded the evidence two levels for high risk of bias and imprecision; we rated the certainty of evidence as low.

Disease activity (SLEDAI, scale 0 to 105, lower score indicates less disease activity, MCID 4 points)

Two studies (100 participants) found that exercise plus usual care may have little to no effect on disease activity. The mean disease activity score in the usual care alone group was 0.5 points, and the mean disease activity score for the exercise plus usual care group was 0.43 points (MD −0.07 points, 95% CI −2.8 to 2.66; Analysis 2.3; Bostrom 2016; Tench 2003). Statistical heterogeneity was significant (I^2 = 88%). There was no clinically meaningful benefit. Because of study limitations, we downgraded the evidence two levels for high risk of bias and imprecision. We rated the certainty of evidence as low.

We back-translated the SMD by multiplying the SMD by the SD of the control group at baseline from the most representative trial (Tench 2003).

Note one of the two studies used SLAM to measure disease activity (Tench 2003).

Quality of life

No studies reported quality of life.

Pain (SF-36 Bodily Pain, scale 0 to 100, lower scores indicate less pain, MCID 10 points)

One study (31 participants) reported pain. We are uncertain whether exercise improves pain. The mean pain score in the usual care alone group was 38 points, and the mean pain score for the exercise plus usual care group was 52 points (MD 16.00 points, 95% −CI 0.18 to 32.18; Analysis 2.4; Bostrom 2016). There was no important clinically meaningful benefit. Because of study limitations, we downgraded the evidence three levels for high risk of bias and imprecision (low participant numbers and the CIs included a large effect and no effect). We rated the certainty of evidence as very low.

Serious adverse events

No SAEs were reported.

Withdrawals due to any reason

We are uncertain whether exercise results in fewer or more withdrawals (RR 0.92, 95% CI 0.53 to 1.60; Analysis 2.5). Avaux 2016 reported three withdrawals from the study; two for personal reasons, and one due to a disease flare; however, it is unclear which group they were part of, and, therefore, they were not included

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in our analyses. Benatti 2018 had eight participants withdraw from the intervention; four participants withdrew from the control group (one was pregnant, three for personal reasons) and four participants withdrew from the exercise group (one fractured limb outside of training sessions, three for person reasons). Another two participants withdrew due to a disease flare (one from each group). Bostrom 2016 had three participants withdraw from the control group (one had depression/cognitive impairment, one had untreated dementia, one had suspected relapse of breast cancer). Tench 2003 had 14 participants withdraw due to any reason. Four participants withdrew from the exercise group, five participants withdrew from the active control group (relaxation), and five participants withdrew from the usual care control group. Note that six participants dropped out of treatment and eight participants completed the study but did not wish to repeat the walking test to exhaustion at the end of the intervention. Two trials had no withdrawals from the intervention due to any reason that were reported (Benatti 2015; Hashemi 2022).

Minor outcomes

Composite responder rate

No studies measured or reported (or both) composite responder rate.

Aerobic capacity (peak VO_2, higher scores indicate better aerobic capacity)

Three studies (109 participants) found that exercise plus usual pharmacological care may improve aerobic capacity score when compared to usual pharmacological care alone; however, the improvement was not clinically important (MD 1.27 points, 95% CI −0.59 to 3.12; Analysis 2.6; Benatti 2018; Bostrom 2016; Tench 2003).

Depression (BDI, scale 0 to 63, lower scores indicate less depression)

One study (65 participants) found that exercise plus usual pharmacological care may improve depression score when compared to usual pharmacological care alone; however, the improvement was not clinically important (MD −0.29 points, 95% CI −0.78 to 0.20; Analysis 2.7; Tench 2003).

Anxiety (HADS, scale 0 to 21, lower scores indicate less anxiety)

One study (65 participants) found that exercise plus usual pharmacological care may improve anxiety score when compared to usual pharmacological care alone; however, the improvement was not clinically important (MD −0.80 points, 95% CI −3.02 to 1.42; Analysis 2.8; Tench 2003).

Exercise plus usual pharmacological care versus another non-pharmacological intervention plus usual pharmacological care

Seven studies compared exercise plus usual care versus another non-pharmacological intervention plus usual care (Abrahão 2016; Daltroy 1995; Dos Reis-Neto 2013; Kao 2021; Keramiotou 2020; Miossi 2012; Tench 2003).

Major outcomes

See: Summary of findings 3.

Fatigue (FSS, scale 1 to 7, lower scores indicate less fatigue severity, MCID 1 point)

Two studies (119 participants) found that exercise plus usual care may reduce fatigue. The mean fatigue score in the non-pharmacological interventions (joint aids and information about their disease, education, and relaxation therapy) plus usual care was 5.3 points, and the mean fatigue score for the exercise plus usual care group was 4.79 points (MD −0.51 points, 95% CI −0.88 to −0.14; Analysis 3.1; Keramiotou 2020; Tench 2003). Statistical heterogeneity was not important (I^2 = 0%). There was no clinically meaningful benefit. Because of study limitations, we downgraded the evidence two levels for high risk of bias and imprecision; we rated the certainty of evidence as low.

We back-translated the SMD by multiplying the SMD by the SD of the control group at baseline from the most representative trial (Tench 2003).

Note one of the two studies used LupusQOL Fatigue to measure fatigue (Tench 2003).

Functional capacity (SF-36 Physical Function, scale 0 to 100, higher scores indicate better functional capacity, MCID 10 points)

Three studies (182 participants) found that exercise plus usual care may increase functional capacity. The mean functional capacity score in the other non-pharmacological interventions (joint aids and information about their disease, education, and relaxation therapy) plus usual care was 41.4 points, and the mean functional capacity score for the exercise plus usual care group was 54.6 points (MD 13.20 points, 95% CI 6.17 to 20.22; Analysis 3.2; Abrahão 2016; Keramiotou 2020; Tench 2003). There was a clinically meaningful benefit. Because of study limitations, we downgraded the evidence two levels for high risk of bias and imprecision. We rated the certainty of evidence as low.

Note that one of the three studies used LupusQOL to assess functional capacity (scale 0 to 100, higher scores indicate better functional capacity) (Keramiotou 2020).

We back-translated the SMD by multiplying the SMD by the SD of the control group at baseline from the most representative trial (Abrahão 2016).

Disease activity (SLEDAI, scale 0 to 52, lower scores indicate lower disease activity, MCID 4 points)

Four studies (184 participants) founds that exercise plus usual care probably results in little to no difference in disease activity. The mean disease activity score in the other non-pharmacological interventions (joint aids and information about their disease, education, and relaxation therapy) plus usual care was 1.2 points, and the mean disease activity score for the exercise plus usual care group was 1.22 points (SMD 0.02 points, 95% CI −0.28 to 0.32; MD 0.034 points, 95% CI −0.476 to 0.544; Analysis 3.3; Abrahão 2016; Dos Reis-Neto 2013; Miossi 2012; Tench 2003). Baseline control group SD for converting SMD to MD was 1.7 and taken from Abrahão 2016. Statistical heterogeneity was not significant (I^2 = 1%). There was no clinically meaningful benefit. Because of study limitations, we downgraded the evidence one level for high risk of bias We rated the certainty of evidence as moderate.

Note that one of the four studies used SLAM to measure disease activity (scale 0 to 83, lower scores indicate less disease activity) (Tench 2003).

We back-translated the SMD by multiplying the SMD by the SD of the control group at baseline from the most representative trial (Abrahão 2016).

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Quality of life

This outcome was measured; however, the MCS score of the SF-36 Quality of Life questionnaire was not reported and, therefore was unable to be included in the analysis.

Pain (VAS, scale 0 to 10, lower scores indicate less pain, MCID 1.5 points)

Two studies (121 participants) found that exercise plus usual care may result in little to no difference in pain. The mean pain score in the other non-pharmacological interventions (joint aids and information about their disease, education, and relaxation therapy) plus usual care was 4.97 points, and the mean pain score for the exercise plus usual care group was −0.29 points (MD −1.59 points, 95% CI −2.46 to −0.71; Analysis 3.4; Abrahão 2016; Keramiotou 2020). Statistical heterogeneity was significant (I^2 = 74%). Because of study limitations, we downgraded the evidence two levels for high risk of bias and imprecision. We rated the certainty of evidence as low.

Note that one of the two studies used the SF-36 Bodily Pain domain to measure pain (scale 0 to 100, lower score indicates less pain) (Abrahão 2016).

We back-translated the SMD by multiplying the SMD by the SD of the control group at baseline from the most representative trial (Abrahão 2016).

Serious adverse events

No SAEs were reported.

Withdrawals due to any reason

We are uncertain whether exercise results in fewer or more withdrawals (RR 0.89, 95% CI 0.13 to 5.94; Analysis 2.5). Abrahão 2016 reported two participant withdrawals from the control group for an unknown reason. Keramiotou 2020 reported two participant withdrawals from the exercise group; however, the reasons were not reported. Tench 2003 reported 14 participant withdrawals from the intervention; four participants withdrew from the exercise group, five participants withdrew from the active control group (relaxation), and five participants withdrew from the usual care group. Note that six participants dropped out of treatment and eight participants completed the study but did not wish to repeat the walking test to exhaustion at the end of the intervention. Four trials did not clearly report withdrawals due to any reason (Daltroy 1995; Dos Reis-Neto 2013; Kao 2021; Miossi 2012).

Minor outcomes

Composite responder rate

No studies measured or reported (or both) composite responder rate.

Aerobic fitness (peak VO_2, higher scores indicate better aerobic capacity)

Two studies (99 participants) found an improvement in aerobic capacity score with exercise plus usual care compared to another non-pharmacological intervention (joint aids and information about their disease, education, and relaxation therapy) (MD 1.19 points, 95% CI −1.64 to 4.02; Analysis 3.6; Dos Reis-Neto 2013; Tench 2003). There was no clinically meaningful benefit.

Depression (BDI, scale 0 to 63, lower scores indicate less depression)

One study (61 participants) found that exercise plus usual pharmacological care may improve depression score when compared to another non-pharmacological intervention (joint aids and information about their disease, education, or relaxation therapy); however, the improvement was not clinically important (MD −1.40 points, 95% CI −4.61 to 1.81; Analysis 3.7; Abrahão 2016).

Anxiety (HADS, scale 0 to 21, lower scores indicate less anxiety)

One study (61 participants) found that exercise plus usual pharmacological care may improve anxiety score when compared to another non-pharmacological intervention (joint aids and information about their disease, education, or relaxation therapy); however, the improvement was not clinically important (MD −1.10 points, 95% CI −3.61 to 1.41; Analysis 3.8; Tench 2003).

Subgroup and sensitivity analyses

Given the small number of studies, we did not conduct subgroup analysis to explore the possible effect of type of exercise (resistance versus cardiorespiratory) on estimated effect size. Neither did we conduct a sensitivity analysis, because we judged all studies at unclear or high risk of bias for most items.

Assessment of publication bias

We had planned to assess publication bias by visual inspection of funnel plots, but we did not generate funnel plots because of the limited number of studies (fewer than 10), and the risk of an underpowered test. We were unable to determine the existence of publication bias.

DISCUSSION

Summary of main results

The main purpose of this review was to evaluate the effectiveness of structured exercise as an adjunctive therapy to usual pharmacological care for people with SLE. Overall, 13 RCTs (540 participants) met the inclusion criteria. The structured exercise programmes amongst the 13 included studies varied; see Table 2, therefore the results of this review are not specific to one type or dosage of exercise. All studies compared a type of exercise, or a combination of types of exercise, plus usual pharmacological care, to a control group that received one of the following; placebo plus usual pharmacological care (Lopes-Souza 2021); usual pharmacological care alone (Avaux 2016; Benatti 2015; Benatti 2018; Bostrom 2016; Hashemi 2022; Tench 2003); or another non-pharmacological intervention (education about the disease/exercise, relaxation therapy, etc.) plus usual pharmacological care (Abrahão 2016; Daltroy 1995; Dos Reis-Neto 2013; Kao 2021; Keramiotou 2020; Miossi 2012; Tench 2003).

We found low-certainty evidence indicating that structured exercise plus usual pharmacological care compared to placebo plus usual pharmacological care may result in little to no effect on fatigue, functional capacity, and pain, measured after the completion of the intervention. And we are uncertain whether exercise results in fewer or more withdrawals (very low-certainty evidence).

We found low-certainty evidence that structured exercise plus usual pharmacological care compared with usual pharmacological care alone may result in little to no effect on fatigue, functional

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capacity, and disease activity, measured after the completion of the intervention. And we are uncertain whether exercise improves pain (very low-certainty evidence) or results in fewer or more withdrawals (very low-certainty evidence).

We found low- to moderate-certainty evidence that structured exercise plus usual pharmacological care compared to another non-pharmacological intervention (relaxation, education, support aids) plus usual pharmacological care may reduce fatigue (low-certainty evidence), may improve functional capacity (low-certainty evidence), probably results in little to no difference in disease activity (moderate-certainty evidence), and may result in little to no difference in pain (low-certainty evidence), measured after the completion of the intervention. We are uncertain whether exercise results in fewer or more withdrawals (very low-certainty evidence).

We have no clear evidence that structured exercise can induce more adverse events. No studies clearly reported an adverse event as an outcome, or elaborated further on the reasons for a withdrawal and whether this led to further complications, hospitalisation, or death. We were unable to draw any conclusions.

Overall completeness and applicability of evidence

The evidence provided by this review is limited to the 13 included RCTs that assessed the effectiveness of exercise plus usual pharmacological care versus a control group (placebo plus usual pharmacological care, usual pharmacological care alone, another non-pharmacological intervention plus usual pharmacological care). One RCT that is potentially eligible for this review is awaiting classification because their results have not yet been reported in full (Boedecker 2020).

All studies compared exercise in addition to their usual pharmacological care to no additional exercise; however, there was heterogeneity between exercise interventions with no dose control between the studies. The included studies investigated several different types and combinations of exercise components. Aerobic exercise, in particular walking, was the most frequent exercise type. However, the components were incompletely described in most trials. For example, the material used, who provided the intervention, how it was supervised, and where the exercise was delivered were often missing. The exercise dosage, and level of supervision, could not be explored with indirect statistical techniques, such as meta-regression. Thus, we did not investigate heterogeneity by the type of exercise, or supervision because we were unable to isolate these components from the included studies.

Twelve studies assessed outcome measures at the end of the intervention only (i.e. 12 weeks), which may not have accounted for the long-term effect of exercise, and its feasibility (Abrahão 2016; Avaux 2016; Benatti 2015; Benatti 2018; Daltroy 1995; Dos Reis-Neto 2013; Hashemi 2022; Kao 2021; Keramiotou 2020; Lopes-Souza 2021; Miossi 2012; Tench 2003). Importantly, because SLE may progress or vary over time, it is necessary to assess outcome measurements at more time points, and over a longer period of time (greater than 12 months) to verify the relationship between treatment effect and outcomes (i.e. fatigue).

Most exercise programmes were delivered in conjunction with drug therapy (standard NSAIDs, DMARDs, or biological agents). The benefits of exercise interventions, depending on the type of drug therapy received, could not be determined. Therefore, we do not know if some drugs in addition to exercise have better or worse outcomes for people with SLE. Also, no study specifically evaluated the efficacy of exercise with biological medication versus standard NSAID or DMARD therapy.

An important consideration is that most participants in the studies had minimal disease activity (SLEDAI score less than 4) at baseline, and, therefore, the overall results could not be applicable to all people with SLE. Also, considering that people with SLE can experience varying symptoms and degree of symptoms over time, the change in outcomes from baseline to the end of intervention need to be read with caution (i.e. the change in outcome reporting might be more a reflection of how they were feeling on that day of testing, rather than a change in feelings before and after the intervention).

Other outcomes needed to understand more about the risk/benefit ratio of exercise, which have been included in this review, is participant-reported fatigue, quality of life, pain, depression, and anxiety. Importantly, these outcomes should be evaluated using standardised outcome tools that are validated in SLE (e.g. FACIT) (Lai 2011), as well as dynamic muscle strength and aerobic fitness, which could be observed to link the relationship between disease-related outcomes and exercise. With respect to the instruments used to measure health-related quality of life, the SF-36 was the most frequently used tool in the included studies. Although the use of the SF-36 allows for comparison of quality of life in various diseases, it lacks characteristic details that are specific in SLE, such as body image and intimate relationships (McElhone 2010). SLE-specific instruments, such as the 34-item LupusQOL developed by McElhone and colleagues in 2007 (McElhone 2007) and the 40-item SLEQOL developed by Leong and colleagues in 2005 (Leong 2005), might be able to offer enhanced responsiveness to changes in health-related quality of life than the SF-36. Future studies may want to use these instruments either alone or in combination with a generic measure to ensure that both disease-specific and wider aspects of quality of life are assessed.

Inherent with exercise trials, it is difficult to blind participants to the intervention. Therefore, bias introduced by a placebo effect can potentially overestimate the efficacy of an intervention, particularly in the evaluation of subjective outcomes. As such, future trial designs could instead be double blinded and compare different modes (aerobic, resistance, range of motion), intensities (low, moderate, and high according to RPE or percentage of maximum heart rate), time of exercise (i.e. 10-minute or 60-minutes bouts), or a combination of these to increase our understanding of exercise guidelines in SLE. In addition, to minimise detection bias, consistent blinding of outcomes assessors is recommended, since participants cannot be blinded to the intervention.

There was heterogeneity between outcome measures amongst studies and outcomes that were included in dose-matched studies. There was also methodological limitations, risk of bias, and an overall limited number of participants in the studies. The evidence derived from the included studies does not allow strong conclusions to be drawn about which specific components of exercise are best in terms of dose of exercise, and level of supervision. There needs to be 1. more studies completed assessing the effects of exercise in people with varying levels of disease activity; 2. more participants in the trials; 3. homogeneous

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outcomes that are more sensitive to change in SLE (i.e. FACIT-Fatigue, LupusQOL, SLEDAI, etc.); 4. trials that compare various doses of exercise (i.e. aerobic versus resistance training on fatigue, disease activity etc.); and 5. longitudinal study designs that focus on change in disease-related outcomes as well as exercise adherence, physical activity levels, and sustainability of outcomes over a longer period of time.

Quality of the evidence

We had concerns about the risk of bias for all studies included: eight (62%) studies had either high or unclear allocation concealment; all failed to blind participants or outcome assessors; six (46%) had incomplete outcome data; and seven (54%) had a high risk of selective reporting. Given the number of studies included in the review, we cannot rule out the existence of a small-study effect, explaining the magnitude of the positive results we found.

We considered statistically significant group differences between exercise plus usual pharmacological care versus a control group (placebo plus usual pharmacological care, usual pharmacological care alone, or another non-pharmacological intervention such as relaxation therapy, support aids, or education about the disease plus usual pharmacological care). For each comparison, the number of studies (fewer than 10), and small samples (many studies were small, with fewer than 100 participants) might have contributed to a low-power analysis. Low power is associated with bias (Button 2013). Most studies we included were at high or unclear risk of bias, which suggests that the estimated effects might be overestimated, and reduces the likelihood that they reflect a true effect. We cannot provide conclusions with a high level of confidence. The magnitude of the estimated effects may change with larger studies.

We only presented the findings of trials that reported the major outcomes of interest in Summary of findings 1; Summary of findings 2; Summary of findings 3; and used the GRADE approach to assess the certainty of the evidence examined for each outcome (Schünemann 2020a). Most of the evidence was downgraded to low or very low certainty, based on two factors: risk of bias and imprecision with small trials and large CIs.

Potential biases in the review process

We made all attempts to reduce the bias involved in the review process by including the best available evidence. All studies included were RCTs or quasi-RCTs. However, by restricting the inclusion criteria to RCTs only, we may have limited the number of included trials and potentially missed useful additional evidence. We conducted an extensive search of the literature in all relevant databases and identified all relevant trials meeting the reviews' eligibility criteria. None of the review authors have been involved in the conduct of the included trials. A minimum of two review authors independently selected studies, extracted data, assessed the risk of bias, and graded the certainty of evidence in all studies. Even though we searched as extensively as possible, we may have missed eligible studies, such as studies reported only in dissertations or conference proceedings. For missing data, we systematically sought information from study authors. However, most of our attempts to contact study authors were unsuccessful, and most data came from published sources.

This review has some limitations. We could not determine whether participants who received usual pharmacological care also completed their own exercise independent of the trials exercise intervention, because the included studies poorly described the content of usual pharmacological care interventions. In some studies, we could not determine what constituted usual care. Participants in the usual pharmacological care groups could have practised exercises, or could have been on more drugs than outlined in the study, which could explain why there was a smaller effect size or no effect when comparing exercise to a control group. A possible explanation could also be the result of performance bias, due to lack of blinding, inherent in exercise interventions and when using subjective participant-reported outcome measures (PROMs). Another limitation was the heterogeneous use of outcome measures amongst the included studies, making it difficult to meta-analyse the data.

We found wide variations amongst the trials, likely related to different exercise components. Despite the prespecification stated in our protocol, we could not perform subgroup analyses to explore heterogeneity for factors such as exercise supervision or modalities of exercises. We had to decide what type of 'exercise' should be included; we excluded single bouts of exercise (i.e. one exercise session or exercise test), or unstructured exercise (i.e. no clear dosage prescription). The cutoff might be contentious, particularly with unstructured exercise, and discussion regarding whether to include structured and unstructured exercise into another review should be considered. Last, the number of included studies and participants in this review was too small.

Agreements and disagreements with other studies or reviews

Three different systematic reviews have examined the effects of exercise in people with SLE (Lu 2021; O'Dwyer 2017; Wu 2017). None included all the RCTs we identified, all of which compared the effects of exercise to placebo, usual care alone, or another non-pharmacological intervention.

O'Dwyer 2017 performed a systematic review and included 11 studies (Abrahão 2016; Avaux 2016; Benatti 2015; Bogdanovic 2015; Bostrom 2016; Carvalho 2005; Dos Reis-Neto 2013; Miossi 2012; Ramsey-Goldman 2000; Robb-Nicholson 1989; Tench 2003), consisting of six RCTs and five quasi-RCTs. Five studies compared an exercise intervention to a control group (usual care, or unchanged physical activity status) (Bostrom 2016; Carvalho 2005; Dos Reis-Neto 2013; Miossi 2012; Robb-Nicholson 1989), and two studies compared an aerobic exercise programme to a range of movement/muscle strength programme (Bogdanovic 2015; Ramsey-Goldman 2000). The systematic review included seven studies in the meta-analyses (Abrahão 2016; Boström 2016; Carvalho 2005; Dos Reis-Neto 2013; Miossi 2012; Robb-Nicholson 1989; Tench 2003). Meta-analyses were deemed appropriate for four outcomes: disease activity, fatigue, aerobic capacity, and depression. Results showed that disease activity was not changed following exercise interventions (MD 0.01, 95% CI −0.54 to 0.56), fatigue decreased in the exercise intervention group compared to controls (MD −0.52, 95% CI −0.91 to −0.13), and depression scores lowered in the exercise groups compared to the controls (SMD −0.40 SD, 95% CI −0.71 to −0.09). Most of these studies were at risk of selection and reporting bias.

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Wu 2017 performed a systematic review and included three studies (Carvalho 2005; Ramsey-Goldman 2000; Tench 2003), consisting of two RCTs and one quasi-experimental study. Aerobic exercise, three times a week and of moderate intensity, was a common component of the three studies. Two studies were conducted in a supervised setting and one study was based at home. One study had a duration of eight weeks and two studies had a duration of 12 weeks. All three studies were included in the meta-analyses and showed that compared to controls aerobic exercise training decreased fatigue severity (MD −0.52, 95% CI −0.91 to −0.13), and showed a positive effect on the SF-36 Vitality subscale (MD 14.98, 95% CI 7.45 to 22.52). However, the quality of evidence assessed using PEDro was downgraded to fair (Tench 2003) or poor (Ramsey-Goldman 2000).

Lu 2021 performed a systematic review on the effects of exercise on health-related quality of life and included nine studies, consisting of five RCTs (Abrahão 2016; Bostrom 2016; Keramiotou 2020; Lopes-Souza 2021; Tench 2003), and four non-RCTs (random allocation or control group were not available). Not all studies used the SF-36 Health-related Quality of Life measure or all of its subscales, therefore, nine separate meta-analyses were conducted, including: one analysis on all five studies regardless of the health-related quality of life measure; another analysis on four studies that used the SF-36 Physical Function domain; and seven analyses on studies that used the remaining seven domains of the SF-36. The results of the meta-analysis of the five RCTs showed a positive effect of exercise on the physical health and function aspect (SF-36 Physical Function and LupusQOL Physical Health) of health-related quality of life amongst participants with SLE (Hedges' g: 0.468, 95% CI 0.206 to 0.730; P < 0.001). Heterogeneity between studies was low (I^2 = 19.2%; P = 0.292).

Our findings are largely consistent with the findings of the above systematic reviews in terms of exercise effectiveness. The differences with our review are that we have included an updated trial (Hashemi 2022), and we have only included RCTs, whereas the other reviews also included other study designs. In addition, we included three separate analyses to evaluate the effectiveness of exercise as 'adjunctive therapy' in SLE (exercise plus usual pharmacological care versus 1. placebo plus usual pharmacological care, 2. usual pharmacological care alone, and 3. another non-pharmacological intervention plus usual pharmacological care). This review adds to the existing knowledge of exercise in SLE by emphasising that exercise can be used as an adjunctive therapy to the usual pharmacological care for SLE. The reason this is important is that most people with SLE will be taking or practising one or more pharmaceutical or non-pharmaceutical interventions (or both), thus exercise should be considered as adjunctive to this; it would be difficult to know the true effect of exercise alone on people with SLE. Furthermore, this review revealed the lack of homogeneous study designs, outcome tools used, and lack of detail in exercise prescription amongst trials, and has shown the need for more rigorous studies in SLE and exercise to be considered.

AUTHORS' CONCLUSIONS

Implications for practice

We found low-certainty evidence indicating that structured exercise plus usual care compared to placebo plus usual care may result in little to no effect on fatigue, functional capacity, and pain, measured after the completion of the intervention. We are uncertain whether exercise results in fewer or more withdrawals (very low-certainty evidence).

We found low-certainty evidence that structured exercise plus usual care compared with usual care alone may result in little to no effect on fatigue, functional capacity, and disease activity, measured after the completion of the intervention. We are uncertain whether exercise improves pain (very low-certainty evidence) or results in fewer or more withdrawals (very low-certainty evidence).

We found moderate- to low-certainty evidence that structured exercise plus usual care compared to another non-pharmacological intervention (relaxation, education, support aids) plus usual care may reduce fatigue (low-certainty evidence), may improve functional capacity (low-certainty evidence), probably results in little to no difference in disease activity (moderate-certainty evidence), and may result in little to no difference in pain (low-certainty evidence), measured after the completion of the intervention. We are uncertain whether exercise results in fewer or more withdrawals (very low-certainty evidence).

We are uncertain of the potential for harm from structured exercise, because of the limited number of studies reporting adverse events. We are unable to distinguish the best dosage of exercise, including frequency, intensity, type, or its mode of delivery.

Considering there is low-certainty evidence on the benefits and harms of exercise, clinicians should ensure that exercise is tailored to the individual, prescribed according to the individuals' physical abilities and limitations, and monitored by an exercise professional (e.g. exercise physiologist, physical therapist, physiotherapist). People with systemic lupus erythematosus (SLE) should seek advice from their healthcare team when starting any new exercise programme, choose exercise that they enjoy, that is individually appropriate to their physical ability, and avoid exercising in the sun when the ultraviolet index is high (greater than 3).

Implications for research

The evidence for the major outcomes was moderate, low, or very low certainty, so new studies could change the estimate effects. This review has raised new questions to answer and implications for further research.

The long-term effects of structured exercise for people with SLE, and whether they are clinically relevant are unclear. Longitudinal studies of exercise in SLE that report harms data (adverse events and withdrawals, with reason) on more people with SLE, followed for a longer duration (i.e. exercise performed for more than three months) are needed to improve our understanding of the benefit/risk ratio of exercise. Furthermore, well-designed trials are needed to elucidate the benefits/harms of exercise in SLE, focusing on important outcomes such as disease activity using standardise outcome tools such as the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)-2K, damage indices such as Systemic Lupus International Collaborating Clinics Damage Indices (SLICC-DI), and specifically looking at changes in serological markers including anti-double stranded DNA (anti-dsDNA), complement levels C3 and C4, as well as inflammatory markers erythrocyte sedimentation rate, C-reactive protein, and interleukin-6. Adverse events were rarely measured or reported (or both) in the included trials. Whether structured exercise as an adjunct therapy to usual care

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produces harmful effects is difficult to determine. Studies should systematically investigate and report adverse events.

Future trials of exercise in SLE should provide an accurate description of the content, dose, application, and adherence to the exercise interventions. The Consensus on Exercise Reporting Template, or the CONSORT Template for Intervention Description and Replication should be used in future trials of exercise to improve the description of exercise programmes and facilitate its application and findings in clinical practical. Furthermore, new trials of exercise in SLE could be well-designed and double blinded to effectively compare different modes (aerobic, resistance, range of motion), intensities (low, moderate, and high according to rating of perceived exertion or percentage of maximum heart rate), time of exercise (i.e. 10-minute or 60-minutes bouts), or a combination of these. We also recommend that future trials include more diverse participants (disease activity, age, sex, race/ethnicity, functional capacity), and results be further analysed by subgroups. In particular, we recommend that participants with higher disease activity (SLEDAI greater than 4) be included in future exercise trials. Further research should aim to determine the efficacy of exercise interventions in people with SLE receiving different therapies (non-steroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs, biological agents, and no treatment).

Last, standardised efficacy outcomes in exercise trials for people with SLE are needed. For example, all studies using the 36-item Short Form questionnaire to assess quality of life should report the Mental Component Summary and Physical Component Summary scores. All trials should report disease activity using a standardised and validated tool such as SLEDAI to report changes in disease activity before and following an intervention, to add further information regarding the potential harms or benefits of exercise. Furthermore, all trials should measure and report fatigue, functional capacity, and other exercise capacity measures such as aerobic capacity and strength to determine the effectiveness of the exercise intervention.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Abrahão 2016

Study characteristics	
Methods	**Study design:** single-centre, parallel-group, 3-arm RCT **Setting:** Rheumatology Services at the Interlagos Specialty Outpatient Clinic, Santo Amaro University (UNISA), São Paulo, Brazil

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Abrahão 2016 *(Continued)*

Time trial period: study process occurred between March 2011 and March 2012

Interventions: cardiovascular exercise plus usual care vs resistance exercise plus usual care vs control group plus usual care

Sample size calculation: sample size calculated based on primary outcome considering a clinically significant difference with moderate treatment effect of 40%. Considering a significance level of 5% and power of 90%, they estimated 20 participants in each group.

Analysis: data presented take into consideration that 2 participants dropped out of study, thus ITT analyses performed to adjust the analysis of the intervention effects.

Participants

Number of participants

1. Screened: 92 (29 were not eligible and did not meet inclusion criteria)
2. Randomised: 63 (21 in cardiovascular exercise group, 21 in resistance exercise group, 21 in the control group)
3. Included in analyses: 61 participants included in the 3-month analysis (2 participants from the control group abandoned the study without reason)

Inclusion criteria

1. Aged ≥ 18 years
2. Diagnosis of SLE according to ACR criteria

Exclusion criteria

1. Absolute or relative contraindications to physical exercise according to ACSM guidelines
2. Not being available for 2 consecutive weeks during 12-week study period
3. Participation in regular physical activity in past 6 months

Baseline characteristics

Total participants (n = 63) comprised 61 women and 2 men, mean age 42.9 (SD 14.4) years, with mean BMI 28.7 (SD 10.6) kg/m^2, and mean disease duration 3.8 (SD 3.3) years

Cardiovascular exercise group (n = 21)

1. Mean age: 43.8 (SD 14.6) years
2. Mean BMI: 27.5 (SD 10.4) kg/m^2
3. Mean disease duration: 4.9 (SD 4.3) years
4. Mean SLEDAI disease activity: 1.8 (SD 0.6) points
5. Mean BDI: 20.6 (SD 5.3) points
6. Mean 12-min walk test: 1019.7 (SD 224.9) m
7. Mean SF-36
   a. Physical Role Functioning: 33.3 (SD 34.5)
   b. Physical Functioning: 38.7 (SD 27.9)
   c. Vitality: 30.3 (SD 18.8)
   d. Emotional Role Functioning: 27.1 (SD 28.1)
   e. Social Role Functioning: 34.2 (SD 23.9)
   f. Mental Health: 25.6 (SD 21.2)
   g. Bodily Pain: 24.2 (SD 23.9)
   h. General Health Perception: 37.5 (SD 26.3)
   i. Change in Health Status: 3.3 (SD 0.8)

Resistance training exercise group (n = 21)

1. Mean age: 39.1 (SD 14.4) years
2. Mean BMI: 27.8 (SD 11.6) kg/m^2

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Abrahão 2016 *(Continued)*

3. Mean disease duration: 3.5 (SD 3.3) years
4. Mean SLEDAI disease activity: 1.4 (SD 0.6) points
5. Mean BDI: 19.4 (SD 5.0) points
6. Mean 12-min walk test: 911.2 (SD 171.8) m
7. Mean SF-36
   a. Physical Role Functioning: 17.3 (SD 16.5)
   b. Physical Functioning: 33.3 (SD 14.4)
   c. Vitality: 28.3 (SD 17.1)
   d. Emotional Role Functioning: 18.8 (SD 20.7)
   e. Social Role Functioning: 21.8 (SD 16.4)
   f. Mental Health: 29.0 (SD 15.7)
   g. Bodily Pain: 24.2 (SD 15.3)
   h. General Health Perception: 22.4 (SD 12.5)
   i. Change in Health Status: 3.2 (SD 0.8)

Control group (n = 21)

1. Mean age: 46.1 (SD 14.1) years
2. Mean BMI: 30.9 (SD 10.1) kg/m^2
3. Mean disease duration: 3.08 (SD 1.7) years
4. Mean SLEDAI disease activity: 2.3 (SD 1.7) points
5. Mean BDI: 19.1 (SD 5.6) points
6. Mean 12-min walk test: 936.5 (SD 169.1) m
7. Mean SF-36
   a. Physical Role Functioning: 24.9 (SD 27.2)
   b. Physical Functioning: 41.9 (SD 21.7)
   c. Vitality: 29.4 (SD 16.3)
   d. Emotional Role Functioning: 24.7 (SD 17.9)
   e. Social Role Functioning: 28.9 (SD 23.9)
   f. Mental Health: 23.6 (SD 13.7)
   g. Bodily Pain: 22.0 (SD 15.5)
   h. General Health Perception: 32.4 (SD 26.3)
   i. Change in Health Status: 3.4 (SD 0.7)

Pretreatment group differences: the 3 groups were homogeneous for age, disease duration, weight, and height at baseline.

Interventions	**Exercise: cardiovascular training group plus usual care** 1. **Frequency of exercise sessions:** 3 times/week 2. **Intensity of exercise:** moderate intensity (65–75% of maximum HR according to the ACSM guidelines). Exercise intensity determined by HR reserve (HRR), which was calculated by HRR = MHR – RHR. MHR determined using: MHR = 205 − (0.42 × age). 3. **Time of exercise session:** 50 min per session 4. **Type of exercise:** cardiovascular exercise walking and bicycle ergometry interventions (Model CLB 10 Classic, Caloi, Sao Paulo, Brazil). Each training session consisted of a 10-min warm-up followed by 30 min of exercise at target HR and a 10-min cool-down. 5. **Duration of intervention:** 12 weeks 6. **Supervision/setting:** trained professional in Rheumatology Services at Interlagos Specialty Outpatient Clinic **Exercise: resistance training group plus usual care** 1. **Frequency of exercise sessions:** 3 times/week

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2. **Intensity of exercise:** moderate intensity (65–75% of 1 repetition maximum (1 RM) according to the ACSM guidelines). To establish the training intensity for each participant, their 1 RM for each exercise was determined. Training intensity changed over time as the participants progressed.
3. **Time of exercise session:** 50 min per session
4. **Type of exercise:** resistance training exercise. Each session consisted of 8 exercises, including holds (crucifix) with free weights, extension-machine exercises, rowing exercise with an elastic band, knee flexion with ankle weights, 2-arm biceps curls, adduction exercises with an elastic band, French curls, and abdominal exercises. Training involved small and large muscle group exercises. Participants performed 3 sets of 15 repetitions with rest intervals of 1 min between sets.
5. **Duration of intervention:** 12 weeks
6. **Supervision/setting:** trained professional in the Rheumatology Services at Interlagos Specialty Outpatient Clinic

Control group (another non-pharmacological intervention plus usual care)

Participants in control group received usual care and information about the disease, but no exercise intervention. These participants were informed that they would receive the intervention after the study was finished, and they would be invited to participate in the intervention that proved the most effective.

Outcomes

All outcomes measured at baseline and at 3 months.

1. **Health-related quality of life:** measured using the SF-36. Measure is grouped into 8 domains: Physical Functioning, Physical Role Functioning, Bodily Pain, General Health Perceptions, Vitality, Social Role Functioning, Emotional Role Functioning, and Mental Health. Scores on each subscale ranged from 0 to 100, with 0 = worst health status and 100 = best health status. Change in health status after intervention from baseline was also assessed.
2. **Severity of depression:** measured using BDI. This is a 21-item, multiple-choice inventory. Individual scale items are scored on a 4-point continuum (0 = least, 3 = most), with a total summed score range of 0–63. Lower scores indicate a better outcome.
3. **Disease activity:** measured using SLEDAI. This gives a score range of 0–101, higher score = higher overall disease activity.
4. **Aerobic capacity:** measured using the 12-min walk test. The more distance covered in 12 min = the better the outcome.

Notes

Country: Brazil

Funding: no funding source reported

Trial registration: ClinicalTrials.gov as NCT01016665

Serious adverse events: none reported

Other adverse events: none reported

Total adverse events: none reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Reported as an RCT and clearly reported randomisation process. Quote: "Allocation sequence was generated using a computer-generated randomisation chart".
Allocation concealment (selection bias)	Low risk	Allocation sequence clearly reported. Quote: "…was concealed in opaque sealed envelopes that were opened just before the intervention was started".

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Abrahão 2016 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Patients in the control group received usual care and information about the disease, but no exercise intervention. These patients were informed that they would receive the intervention after the study was finished". Comment: it is evident that participants were not blinded to the study groups; judged at high risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Assessor reported: unclear risk The personnel conducting the assessor reported outcome for aerobic capacity was not clearly identified, and, therefore, it is unclear whether assessors were blinded to the study design and groups. Authors did report that the same rheumatologist clinically evaluated participants during the course of the intervention, who was blinded to the hypothesis; however, it is unclear if they were blinded to the groups. Participant reported: high risk Assessors (i.e. participants) were not blinded to the self-reported outcome measures (i.e. fatigue); judged at high risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 participants dropped out of study for unknown reasons, and ITT was performed to analyse intervention effects.
Selective reporting (reporting bias)	High risk	Authors assessed QoL using the SF-36 questionnaire; however, did not report the Mental Component Summary score or the Physical Component Summary score, or both.
Other bias	Low risk	No other biases.

Avaux 2016

Study characteristics	
Methods	**Study design:** quasi-randomised 3-arm parallel RCT **Setting:** supervised training group trained in the hospital-based revalidation centre under the supervision of a multidisciplinary team, while the home training group exercised at home on their own. **Time trial period:** process occurred between June 2012 and January 2013 **Interventions:** home training group plus usual care vs supervised training group plus usual care vs plus usual care (control group) **Sample size calculation:** pilot and exploratory study, therefore, study author did not perform statistical power analyses. **Analysis:** results were compared by paired t-tests or Wilcoxon signed rank tests, as appropriate.
Participants	**Number of participants** 1. Screened: 45 2. Randomised: 42 (18 in home training group, 15 in supervised training group, and 9 in control group). 3 did not meet the inclusion criteria at baseline (screening failures: FSS too low in 1, and major physical disability in 2). 3. Included in 3-month analyses: 39 (17 in home training group, 14 in supervised training group, 8 in control group). 3 participants left the protocol during the first 3 months due to disease flare (n = 1), or personal reasons (n = 2). However, it is unclear which reason was associated to which group.

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Avaux 2016 *(Continued)*

4. Included in 9-month analyses: 29 (13 in home training group, 10 in supervised training group, and 6 in control group). 10 participants declined evaluation at 9 months.

Inclusion criteria

1. Diagnosis of SLE according to ACR criteria
2. Presence of fatigue, as defined by a Krupp's FSS ≥ 3.7
3. Followed at their lupus clinic

Exclusion criteria

1. If fatigue was due to anaemia, iron deficiency, hypothyroidism, or any other organic cause, as assessed by the same senior clinician
2. If they had extreme physical disability compromising exercise

Baseline characteristics

Total participants comprised 40 women and 2 men

Home training group (n = 18)

1. Gender (F/M): 16/2
2. Mean age: 37 (SD 7) years
3. Mean disease duration: 12 (SD 7) years
4. Mean SLEDAI disease activity: 2.33 (SD 3.78) points
5. Mean SLICC/ACR-DI: 0.6 (SD 0.9) points
6. Mean FSS: 5.8 (SD 0.7) points
7. Mean $PWC_{75\%}$/kg: 1.1 (SD 0.4)
8. Mean Borg scale: 4.6 (SD 3.5)

Supervised training group (n = 15)

1. Gender (F/M): 15/0
2. Mean age: 43 (SD 7) years
3. Mean disease duration: 16 (SD 10) years
4. Mean SLEDAI disease activity: 3.60 (SD 3.87) points
5. Mean SLICC/ACR-DI: 0.5 (SD 0.7) points
6. Mean FSS: 5.8 (SD 0.7) points
7. Mean $PWC_{75\%}$/kg: 1.0 (SD 0.3)
8. Mean Borg scale: 5.7 (SD 5.1)

Control group (n = 9)

1. Gender (F/M): 9/0
2. Mean age: 46 (SD 11) years
3. Mean disease duration: 16 (SD 10) years
4. Mean SLEDAI disease activity: 1.78 (SD 2.72) points
5. Mean SLICC/ACR-DI: 0.4 (SD 0.7) points
6. Mean FSS: 5.3 (SD 1.2) points
7. Mean $PWC_{75\%}$/kg: 1.0 (SD 0.3)
8. Mean Borg scale: 5.7 (SD 5.1)

Pretreatment group differences: baseline characteristics of the 3 groups did not differ.

Interventions	**Exercise: home training group plus usual care** 1. **Frequency of exercise sessions:** not specified. Participants were asked to perform 3 hours of exercise per week.

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Avaux 2016 *(Continued)*

2. **Intensity of exercise:** moderate intensity (60–80% of theoretical MHR). The modified Borg scale was used to determine participant's perception of exertion at $PWC_{75\%}$.
3. **Time of exercise session:** not specified. Participants were asked to perform 3 hours of exercise per week.
4. **Type of exercise:** endurance exercise (walking or bicycle) and strengthening exercises (elastic band or weights for upper and lower limbs), performed at home on their own.
5. **Duration of intervention:** 12 weeks
6. **Setting:** unsupervised and performed at home.

Exercise: supervised training group plus usual care

1. **Frequency of exercise sessions:** not specified. Participants were asked to perform 3 hours of exercise per week.
2. **Intensity of exercise:** moderate intensity (60–80% of theoretical MHR). The modified Borg scale was used to determine participant's perception of exertion at $PWC_{75\%}$.
3. **Time of exercise session:** not specified. Participants were asked to perform 3 hours of exercise per week.
4. **Type of exercise:** endurance exercise (walking or bicycle) and strengthening exercises (elastic band or weights for upper and lower limbs), performed in hospital-based revalidation centre under supervision of multidisciplinary team.
5. **Duration of intervention:** 12 weeks
6. **Supervision/setting:** supervised by multidisciplinary team in hospital-based revalidation centre.

At the start of programme, the home and supervised groups participated in a multidisciplinary information session about the benefits of exercise in SLE, during which practical information was also delivered. Participants in the home and supervised groups were asked to record their number of training hours.

Control group (usual care alone)

Participants in the control group did not participate in the information session and were asked not to change their level of physical activity.

Outcomes

All outcomes measured at baseline, 3 months, and 9 months.

1. **Change in fatigue:** measured using Krupp's FSS. FSS is a 9-item questionnaire, scored on a 7-point Likert scale with 1 = strongly disagree, and 7 = strongly agree. Minimum raw score is 9 and maximum score is 63. However, the mean of all scores can also be taken with a minimum score of 1 and a maximum score of 7. Higher score = greater fatigue severity. A change score of 1.9 points is considered a clinically important change.
2. **Cardiorespiratory endurance:** assessed as physical working capacity (expressed in Watts/kilogram bodyweight) measured at 75% of the predicted MHR ($PWC_{75\%}$/kg). This index was calculated during a multistage submaximal bicycle test, starting at 30 W and increased by 30 W every 2 min, until participant's HR reached ≥ 75% of predicted value. The modified BORG scale was used to determined participant's perception of exertion at $PWC_{75\%}$*(data not shown in this study).*
3. **Compliance:** measured by training hours recorded by participants. They subdivided participants into 2 groups, those who performed > 50% of prescribed exercises (compliant group n = 15) and those who performed less (non-compliant group n = 15), irrespective of their initial assignment to the home or supervised group.

Notes

Country: Belgium

Funding: grant from Association Lupus Erythémateux, via the Fonds pour la Recherche Scientifique en Rhumatologie/Fondation Roi Baudouin.

Trial registration: not reported

Serious adverse events: none reported

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Avaux 2016 *(Continued)*

Other adverse events: 1 participant withdrew following the 3-month analysis due to a disease flare. However, it is unclear which arm the participant was part of, or the extent of the disease flare.

Total adverse events: none reported

Data analysis: contacted authors to request missing data for FSS scores; however, no response received.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Although the authors reported randomisation in the methods, we considered this study to be quasi-randomised. Method of randomisation was not truly random; judged at high risk of bias. Quote: "Patients living less than 30 min away from the hospital were included in the supervised training group (STG), the others in the home training group (HTG). Those patients who declined to train (n = 4) or refused their allocation (n = 7) constituted the control group (CG)".
Allocation concealment (selection bias)	High risk	No allocation concealment was reported in the article. However, based on the randomisation process described above, there was a selection bias based on the geographical location of the participants; judged at high risk of bias.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Being an active exercise intervention, it is not possible to blind the participants and supervisors of the intervention; judged at high risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Assessor reported: unclear risk It is unclear whether the outcome assessor assessing the outcome physical working capacity was also the exercise programme supervisor, and, therefore, the blinding of outcome assessment was unclear. Participant reported: high risk Outcomes such as fatigue is a participant-reported outcome, and the participants knew which group they were in; judged at high risk of detection bias.
Incomplete outcome data (attrition bias) All outcomes	High risk	Authors did not clearly report any data for participants who withdrew from the study after baseline. We assumed that analysis was conducted per protocol, and not ITT; judged at high risk of bias.
Selective reporting (reporting bias)	High risk	Authors clearly reported that they did not show data for cardiorespiratory endurance at 3 months and 9 months, despite it being measured. Quote: "By contrast, the $PWC_{75\%}$/kg and the Borg scale did not improve over time in none of the 3 groups, nor at month 3, neither at month 9 (data not shown)".
Other bias	Low risk	No other biases.

Benatti 2015

Study characteristics

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Benatti 2015 *(Continued)*

Methods	**Study design:** single-centre, parallel-group, 3-arm RCT. Study is part of a larger clinical trial that aims to comprehensively investigate the effects of exercise training on autonomic function and cardiorespiratory parameters (data previously published), inflammatory markers, and cardio-metabolic risk factors in people with SLE (registered at ClinicalTrials.gov as NCT01515163) (Miossi 2012). **Setting:** Laboratory of Physical Conditioning for Rheumatologic Patients of the School of Medicine, University of São Paulo, Brazil **Time trial period:** not reported **Interventions:** supervised exercise training group SLE plus usual care vs non-trained SLE control group (usual care alone) vs healthy controls who performed a supervised exercise training group **Sample size calculation:** not reported **Analysis:** Kolmogorov–Smirnov's test with Lilliefor's correction revealed that only the glucose levels and total cholesterol levels showed a normal distribution. Therefore, all other dependent variables were tested by non-parametric tests. Independent samples were compared using the Mann–Whitney U test, whereas dependent samples were compared using the Wilcoxon test. Glucose and total cholesterol levels were tested by an unpaired T test for independent samples and the paired T test for dependent samples. Furthermore, Fisher's exact tests were used to compare the use of drugs at baseline between SLE trained (SLE-TR) and non-trained (SLE-NT) groups. Finally, effect sizes were calculated. The significance level was set at $P < 0.05$. All analyses were performed using Statistical Package for Social Sciences (SPSS), version 19.0 for Windows.
Participants	**Number of participants with SLE** 1. Screened and met inclusion criteria: 45 2. Randomised: 40 (20 allocated to exercise training group, and 20 allocated to the non-trained group). 5 did not agree to participate. 3. Included in 3-month analyses: 33 (17 in exercise training group and 16 in the non-trained group). 3 participants withdrew from exercise training group, and 4 participants withdrew from the non-trained group. All for personal reasons. **Number of participants (healthy controls)** 1. Screened and met inclusion criteria: 20 (2 did not agree to participate) 2. Allocated to training group: 18 (7 withdrew due to personal reasons) 3. Included in 3-month analyses: 11 **Inclusion criteria** 1. Diagnosed with SLE according to the ACR criteria 2. Aged 20–40 years 3. Physically inactive for ≥ 6 months before entering study 4. SLEDAI ≤ 4 **Exclusion criteria** 1. Cardiovascular and musculoskeletal disorders 2. Kidney and pulmonary involvements 3. Peripheral neuropathy 4. Use of tobacco 5. Treatment with statins or fibrate 6. Secondary rheumatic disease (e.g. Sjögren's syndrome, fibromyalgia, and antiphospholipid syndrome) 7. Use of antihypertensive drugs **Baseline characteristics** All 33 participants were women.

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Benatti 2015 *(Continued)*

Supervised training group (n = 17)

1. Mean age: 31.3 (SD 5.9) years
2. Mean BMI: 25.9 (SD 5.7) kg/m^2
3. Mean disease duration: 6.1 (SD 3.0) years
4. Mean SLEDAI disease activity: 0.9 (SD 1.4) points
5. Mean cumulative prednisone dose: 31.2 (SD 33.7) g
6. Mean prednisone dose: 11.5 (SD 12.8) mg
7. Number (%) drugs:
   a. Prednisone: 12 (70.6%)
   b. Azathioprine: 9 (52.9%)
   c. Chloroquine: 11 (64.7%)
   d. Methotrexate: 1 (5.9%)
   e. Mycophenolate mofetil: 5 (29.4%)
   f. Cyclophosphamide: 2 (11.8%)

Non-trained SLE controls (n = 16)

1. Mean age: 29.7 (SD 5.3) years
2. Mean BMI: 26.3 (SD 8.3) kg/m^2
3. Mean disease duration: 6.1 (4.8) years
4. Mean SLEDAI disease activity: 1.2 (SD 1.4) points
5. Mean cumulative prednisone dose: 21.8 (SD 15.6) g
6. Mean prednisone dose: 7.2 (SD 8.6) mg
7. Number (%) drugs:
   a. Prednisone: 10 (62.5%)
   b. Azathioprine: 7 (43.7%)
   c. Chloroquine: 10 (62.5%)
   d. Methotrexate: 4 (25.0%)
   e. Mycophenolate mofetil: 2 (12.5%)
   f. Cyclophosphamide: 0 (0%)

Healthy control group (n = 11)

1. Mean age: 30.9 (SD 7.2) years
2. Mean BMI: 23.9 (SD 3.1) kg/m^2

Pretreatment group differences: groups were similar regarding age, weight, height, and BMI. Supervised training and non-trained groups had similar drug regimens (P > 0.05).

Interventions

Exercise: supervised training group SLE plus usual care

1. **Frequency of exercise sessions:** 2 times/week
2. **Intensity of exercise:** HR corresponding to the interval between ventilatory anaerobic threshold and 10% below respiratory compensation point.
3. **Time of exercise session:** cardiovascular endurance exercise = 30 min and strength exercise = time not specified, per session.
4. **Type of exercise:** cardiovascular endurance exercise (treadmill walking) and strength exercises (7 exercises for major muscle groups: 4 sets of 8–12 repetitions maximum for each exercise)
5. **Duration of intervention:** 12 weeks

Non-trained SLE control group (usual care alone)

Participants remained physically inactive.

Exercise: healthy control group

1. **Frequency of exercise sessions:** 2 times/week

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Benatti 2015 *(Continued)*

2. **Intensity of exercise:** HR corresponding to the interval between ventilatory anaerobic threshold and 10% below respiratory compensation point.
3. **Time of exercise session:** cardiovascular endurance exercise = 30 min and strength exercise = time not specified, per session.
4. **Type of exercise:** cardiovascular endurance exercise (treadmill walking) and strength exercises (7 exercises for major muscle groups: 4 sets of 8–12 repetitions maximum for each exercise)
5. **Duration of intervention:** 12 weeks

Outcomes	All outcomes measured at baseline and 3 months. Specifically, blood samples were collected following a 12-hour overnight fast and 48–72 hours after the last exercise session. **Outcomes** 1. **Blood measurements and HDL composition:** total cholesterol, HDL, LDL, VLDL, triglycerides, apolipoprotein A-I, apolipoprotein A-II, apolipoprotein B, apolipoprotein E, insulin, glucose
Notes	**Country:** Brazil **Funding:** no funding source reported **Trial registration:** NCT01515163 **Serious adverse events:** none reported **Other adverse events:** none reported **Total adverse events:** none reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Reported as an RCT. Quote: "Randomly assigned (1:1) using a computer-generated randomization code to either participate in a supervised exercise training program (SLETR; n = 17) or to remain physically inactive (SLE-NT; n = 16). Gender-, BMI-, and age-matched healthy subjects (C-TR; n = 11) also performed a supervised exercise training program as a control group".
Allocation concealment (selection bias)	Unclear risk	Allocation concealment was not clearly reported, and, therefore, it was unclear whether it was included.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Being an active exercise intervention, it is not possible to blind the participants and supervisors of the intervention; judged at high risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Assessor reported: unclear risk It is unclear whether the outcome assessor was also the exercise supervisor, and, therefore, the blinding of outcome assessment was unclear.
Incomplete outcome data (attrition bias) All outcomes	High risk	3/17 from the trained group withdrew (18% withdrawals), 4/16 from the non-trained group withdrew (25% withdrawals). No evidence of ITT analyses.
Selective reporting (reporting bias)	High risk	Missing data from subanalysis.

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Benatti 2015 *(Continued)*

		Quote: "In a further sub-analysis, it was showed that the SLE patients with and without Hydroxychloroquine (HCQ) had a comparable response to exercise training in terms of changes in lipid profile (data not shown)".
Other bias	Low risk	No other biases.

Benatti 2018

Study characteristics

Methods	**Study design:** single-centre, parallel-group, 2-arm RCT **Setting:** intrahospital gymnasium, Laboratory of Physical Conditioning for Rheumatologic Patients of the School of Medicine (LACRE), University of São Paulo, Brazil **Time trial period:** not reported **Interventions:** supervised exercise training plus usual care vs usual care alone **Sample size calculation:** not reported **Analysis:** to minimise the impact of interindividual variability, all values were converted into delta scores (i.e. post−pre values) and thereafter tested by a mixed model, considering pre values from all dependent variables as covariates. Tukey post hoc was used for multiple comparisons. Baseline data were compared using Fisher's exact tests and unpaired Student's t-tests. Cohen's d was used to determine between-group effect sizes for dependent variables. The significance level was previously set at $P \leq 0.05$, with a trend towards significance being accepted at $P \leq 0.1$. All analyses were performed using SAS 9.2, SAS Institute Inc., Cary, NC, USA. Data were presented as means ± SDs. Post hoc power analyses were performed with the assistance of the G-Power software (Version 3.1.2) and demonstrated a power of 70% and 60% at an alpha level of 5% to detect significant differences in insulin sensitivity (assessed by the HOMA IR and AUCinsulin in response to the MT) between trained and non-trained participants, with effect sizes of −1.0 and −0.8.
Participants	**Number of participants** 1. Screened: 900 (708 did not meet inclusion criteria) 2. Invited to participate: 192 (129 did not agree to participate, and 34 withdrew before baseline assessments) 3. Randomised: 29 (14 allocated to the trained group, and 15 allocated to the non-trained group) 4. Included in 3-month analyses: 19 (9 in trained group and 10 in non-trained group). 5 withdrew from the trained group (1 limb fracture, 1 disease flare, 3 personal reasons), and 5 withdrew from the non-trained group (1 pregnant, 1 disease flare, 3 personal reasons) **Inclusion criteria** 1. Diagnosed with SLE according to the ACR criteria 2. Aged < 45 years 3. SLEDAI ≤ 4 **Exclusion criteria** 1. Aged > 45 years 2. BMI ≥ 35 kg/m^2 3. SLEDAI > 4 4. Prednisone dose > 10 mg/day 5. Menopause; diagnosed type 2 diabetes, cardiovascular dysfunction, rhythm and conduction disorders, musculoskeletal disturbances, current kidney and pulmonary involvements, peripheral neu-

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Benatti 2018 *(Continued)*

ropathy; tobacco use; use of statins, fibrate, insulin or insulin sensitisers; and other systemic autoimmune diseases

Baseline characteristics

All 29 participants were women.

Supervised training group (n = 14)

1. Mean age: 34.8 (SD 4.1) years
2. Mean BMI: 26.3 (SD 3.4) kg/m^2
3. Mean disease duration: 9.8 (SD 4.1) years
4. Mean SLEDAI disease activity: 0.22 (SD 0.67) points
5. Mean cumulative glucocorticoid dose: 42.1 (SD 31.8) g/kg bodyweight
6. Mean current glucocorticoid dose: 1.7 (SD 3.5) mg
7. Number (%) drugs:
   a. Glucocorticoid: 2 (22%)
   b. Hydroxychloroquine: 5 (56%)
   c. Methotrexate: 2 (SD%)
   d. Azathioprine: 5 (56%)
   e. Mycophenolate: 1 (11%)
   f. Cyclophosphamide: 0 (0%)
   g. Oral contraceptive: 6 (67%)
8. Physical inactivity level
   a. Sedentary time (% of day): 56.2 (9.6%)
   b. Total MVPA: 29.1 (SD 13.7) min/day
   c. MVPA in > 10-minute bouts: 8.6 (SD 7.7) min/day

Non-trained SLE controls (n = 15)

1. Mean age: 32.4 (SD 6.5) years
2. Mean BMI: 26.2 (SD 3.8) kg/m^2
3. Mean disease duration: 8.5 (SD 5.9) years
4. Mean SLEDAI disease activity: 0.40 (SD 1.26) points
5. Mean cumulative glucocorticoid dose: 32.4 (SD 19.1) g/kg
6. Mean current glucocorticoid dose: 2.0 (SD 4.2) mg
7. Number (%) drugs:
   a. Glucocorticoid: 2 (20%)
   b. Hydroxychloroquine: 7 (70%)
   c. Methotrexate: 2 (20%)
   d. Azathioprine: 4 (40%)
   e. Mycophenolate: 2 (20%)
   f. Cyclophosphamide: 0 (0%)
   g. Oral contraceptive: 6 (60%)
8. Physical inactivity level
   a. Sedentary time (% of day): 59.4 (8.4%)
   b. Total MVPA: 25.4 (SD 17.4) min/day
   c. MVPA in > 10-minute bouts: 6.8 (SD 8.5) min/day

Pretreatment group differences: groups were similar regarding age, BMI, body composition, physical activity levels, current clinical treatment, disease activity status, and disease duration (all P > 0.05).

Interventions	**Exercise: supervised training group plus usual care** 1. **Frequency of exercise sessions:** 2 times/week

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Benatti 2018 *(Continued)*

2. **Intensity of exercise:** HR corresponding to the interval between ventilatory anaerobic threshold and 10% below respiratory compensation point
3. **Time of exercise session:** 40–60 min (5-min warm-up, followed by 30–50 min, and a 5-min cool-down). Walking duration increased every 4 weeks, from 30 to 50 min.
4. **Type of exercise:** aerobic exercise (treadmill walking)
5. **Duration of intervention:** 12 weeks

Non-trained control group (usual care alone)

Participants were strongly instructed to maintain their usual living activities throughout the study.

Outcomes	All outcomes measured at baseline and 3 months. 1. **Body composition** (bodyweight, fat mass, lean mass, and trunk fat): measured by DEXA using Hologic densitometry equipment 2. **Skeletal muscle protein expression and GLUT4 translocation** in response to the meal test 3. **Aerobic capacity:** ventilatory anaerobic threshold, time at respiratory compensation point, time to exhaustion, VO_{2peak}, HR_{peak}: measured by a graded maximal treadmill test 4. **Blood parameters** C3, C4, ESR, creatine phosphokinase, creatinine, urea, C-reactive protein, platelets, leukocytes, erythrocytes, haematocrit: measured by blood samples 5. **Insulin sensitivity and beta cell function estimates:** measured by blood samples 6. **Dietary intake:** total energy, protein, carbohydrate, fat
Notes	**Country:** Brazil **Funding:** no funding source reported **Trial registration:** NCT01515163 **Serious adverse events:** none reported **Other adverse events:** 1 withdrew from the intervention group due to a disease flare (unclear whether this was associated with the exercise intervention) and 1 withdrew from the control group due to a disease flare. **Total adverse events:** 2

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Reported as RCT; however, the randomisation process was unclear. Quote: "Nineteen adult women with SLE were randomly assigned …"
Allocation concealment (selection bias)	Unclear risk	No allocation concealment was reported; judged at unclear risk of bias.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Being an active exercise intervention, it is not possible to blind the participants and supervisors of the intervention; judged at high risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Assessor reported: unclear risk It is unclear whether the outcome assessor was also the exercise supervisor, and, therefore, the blinding of outcome assessment is not clear.
Incomplete outcome data (attrition bias)	High risk	Quote: "Due to technical issues, four patients (one from SLE-TR [training group] and three from SLE-NT [no training group]) were not assessed for

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Benatti 2018 *(Continued)*

All outcomes		glucagon and two patients from SLE-NT were not assessed for proinsulin levels". Therefore, judged at high risk of bias.
Selective reporting (reporting bias)	High risk	Soma data not shown. Quote: "Importantly, baseline comparisons using Fisher's exact tests and unpaired T tests analyses of those who were lost to follow-up and those who retained in each group did not show any drop-out bias (data not shown)".
Other bias	Low risk	No other biases.

Bostrom 2016

Study characteristics

Methods	**Study design:** single-centre, parallel-group, 2-arm RCT **Setting:** Department of Rheumatology at Karolinska University Hospital, Solna, Stockholm, Sweden **Time trial period:** not reported **Interventions:** exercise plus usual care vs usual care alone **Sample size calculation:** not reported **Analysis:** software used to analyse data: SAD System 9.1, SAS Institute Inc., Cary, USA for Mixes- and Genmode procedures and Statistica 7.1, StaSoft, Inc. Tulsa, USA
Participants	**Number of participants** 1. Assessed for eligibility: 128 (88 declined to participate, 5 did not meet inclusion criteria) 2. Randomised: 35 (18 to intervention, 17 to control group) 3. Included at 3 months: 32 (18 in intervention group, and 14 in control group). 3 participants were excluded from control group after 2 weeks due to depression/cognitive impairment, untreated dementia, suspected relapse breast cancer. 4. Included at 6 months: 29 (16 in intervention group, and 13 in control group). 2 dropouts in intervention group; 1 was ill with concomitant systemic alveolitis, and 1 was not motivated. 1 dropout in control group due to being ill. 5. Included at 12 months: 27 (15 in intervention group, and 12 in control group). 1 dropout in intervention group due to being too ill, and 1 dropout in control group for unknown reason 6. Included in 3-month, 6-month, and 12-month analysis: 25 (12 in intervention group, and 13 in control group) **Inclusion criteria** 1. Fulfilled ≥ 4 ACR criteria for SLE 2. Women with SLE who were followed regularly at the Department of Rheumatology, Karolinska University Hospital, Solna, Sweden. 3. Aged 18–70 years 4. Stable and low-to-moderate disease activity and organ damage according to a rheumatologist's evaluation **Exclusion criteria** 1. Symptoms or signs during the preceding 6 months indicating cardiovascular disease, pulmonary embolus, pulmonary fibrosis, cerebrovascular disease, uncontrolled diabetes, dyspnoea at rest, pulmonary hypertension, angina pectoris, and myocardial infarction during the year before study entry

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Bostrom 2016 *(Continued)*

2. American Heart Association absolute contraindications for exercise testing were applied.
3. Performed regular aerobic fitness training sessions at fixed times as this would interfere with the randomised study of the physical activity programme.

Baseline characteristics

Exercise intervention group (n = 18)

1. Mean age: 52 (SD 10) years
2. Mean BMI: 26.5 (SD 5.8) kg/m^2
3. Mean disease duration: 15 (SD 9) years
4. Median SLEDAI disease activity: 1 (quartiles Q1–Q3 0–8) points
5. Median SLICC: 0 (quartiles Q1–Q3 0–1) points
6. Median prednisolone: 3.1 (quartiles Q1–Q3 0–5) mg
7. Number of participants who were/were on:
   a. beta-blockers: 3
   b. smokers: 3
   c. employed: 10
   d. sick listed (full or part-time)/other (studying/unemployed): 5/1
   e. sickness (full or part-time)/retirement pension: 9/1

Exercise intervention group baseline outcomes (n = 17)

1. Median SF-36
   a. Physical Role Functioning: 75 (quartiles Q1–Q3 25–100)
   b. Physical Functioning: 75 (quartiles Q1–Q3 55–85)
   c. Vitality: 35 (quartiles Q1–Q3 25–45)
   d. Emotional Role Functioning: 66.7 (quartiles Q1–Q3 33.3–100)
   e. Social Role Functioning: 75 (quartiles Q1–Q3 62.5–75)
   f. Mental Health: 68 (quartiles Q1–Q3 60–84)
   g. Bodily Pain: 51 (quartiles Q1–Q3 41–62)
   h. General Health Perception: 35 (quartiles Q1–Q3 25–45)

Exercise intervention group baseline outcomes (n = 12)

1. Mean VO_{2max}: 20.5 (SEM 1.3) mL/kg/min
2. Mean maximum workload: 114.9 (SEM 5.4) watts
3. Mean maximum exercise time: 9.6 (SEM 0.5) min

Control group (n = 17)

1. Mean age: 53 (SD 9) years
2. Mean BMI: 25.8 (SD 3.9) kg/m^2
3. Mean disease duration: 21 (SD 14) years
4. Median SLEDAI disease activity: 2 (quartiles Q1–Q3 0–3) points
5. Median SLICC: 0 (quartiles Q1–Q3 0–2) points
6. Median prednisolone: 1.3 (quartiles Q1–Q3 0–5) mg
7. Number of participants who were/were on:
   a. beta-blockers: 1
   b. smokers: 4
   c. employed: 7
   d. sick listed (full or part-time)/other (studying/unemployed): 1/2
   e. sickness (full or part-time)/retirement pension: 9/1

Control group baseline outcomes (n = 14)

1. Median SF-36

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Bostrom 2016 *(Continued)*

a. Physical Role Functioning: 50 (quartiles Q1–Q3 0–100)
b. Physical Functioning: 67.5 (quartiles Q1–Q3 55–75)
c. Vitality: 55 (quartiles Q1–Q3 30–65)
d. Emotional Role Functioning: 66.7 (quartiles Q1–Q3 0–100)
e. Social Role Functioning: 62.5 (quartiles Q1–Q3 50–87.5)
f. Mental Health: 66 (quartiles Q1–Q3 52–88)
g. Bodily Pain: 63 (quartiles Q1–Q3 41–74)
h. General Health Perception: 51 (quartiles Q1–Q3 30–65)

Control group baseline outcomes (n = 13)

1. Mean VO_{2max}: 20.5 (SEM 1.3) mL/kg/min
2. Mean maximum workload: 119.9 (SEM 5.7) watts
3. Mean maximum exercise time: 10.1 (SEM 0.6) min

Pretreatment group differences: no differences at baseline between participants who participated in whole study period (n = 27) and dropouts (n = 8) concerning age, disease duration and VO_{2max} (mL/kg/min). There were no significant main effects of time, main effects of group, or interactions group × time concerning bodyweight and BMI.

Interventions	**Exercise intervention group plus usual care** **Phase 1 (0–3 months)** 1. **Frequency of exercise sessions:** 2 times/week 2. **Intensity of exercise:** high (65–80% of maximum HR or a rating of 13–16 out of 20 on the Borg Rating of Perceived Exertion scale) 3. **Time of exercise session:** 60 min per session 4. **Type of exercise:** mainly aerobic exercise (about 20 min) and muscle strength and endurance exercise (about 15 min). Note: participants could alternatively choose any preferred self-managed high-intensity physical activity, as some participants lived far from the hospital. 5. **Duration of intervention:** 12 weeks (supervised as described above) Note: physical activity at low-to-moderate intensity was self-managed and consisted of any type of preferred physical activity. **Phase included:** 1-hour education session held by a rheumatologist and another by a physiotherapist to educate them on: their disease, the risk for cardiovascular disease, the treatment of the disease, and the importance of, and how to perform, physical activity and exercise. It also included education on how to use a HR monitor, how to assess intensity according to Borg Rating of Perceived Exertion scale, and how to document physical activity with modes, frequency, durations, and intensities. This phase also included supervised exercise training, 30 min of individual coaching of physical activity at 6- and 12 weeks, loan and use of HR monitor, and use of a physical activity diary. **Phase 2 (4–9 months)** During this period, the physical activity was self-managed with the help of videotapes or sound cassettes (or both) from the high-intensity aerobic group exercise programme performed during the first 3 months. As an alternative, any physical activity at high intensity could be chosen. This phase included: 30 min of individual coaching of physical activity at 6 and 9 months, use of HR monitor, and use of the physical activity diary. Participants also received 10 min of telephone support which reduced towards the end of 12 months. **Phase 3 (9–12 months)** This phase included use of the HR monitor and physical activity diary. **Control group (usual care alone)**

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	Participants were asked not to change their physical activity lifestyle during the study period and they were not given any specific information related to the study.
Outcomes	All outcomes measured at baseline; at month 0 (2–3 weeks after baseline when the intervention started); and after 3, 6, and 12 months. 1. **Aerobic capacity:** VO_{2max} in mL/kg/min, maximum watts, and maximum exercise time duration was recorded. In addition to VO_{2max}, 60% and 80% of VO_{2max} were measured. This outcome was measured using a maximal symptom-limited, bicycle ergometer exercise test (test was terminated when participant had indicated exhaustion). The higher the result, the better the outcome. 2. **Frequency of physical activity:** physical activity defined as all types of housework, gardening, walking, dancing, or regular physical activity that increase HR and exertion levels. This was measured by 2 self-reported questionnaires concerning frequency of physical activity for high intensity physical activity and low-to-moderate physical activity performed during the week (i.e. how often have you been physically active at high intensity, at least 30 minutes? "Never or irregularly, once a week, 2–3 times per week, 4–5 times per week, or 6–7 times per week"). 3. **Health-related quality of life:** measured using the SF-36. Each of the 8 domains were reported. Possible score for each of the 8 subscales is 0–100; the higher the score, the better the function. 4. **Disease activity:** measured using the modified version of SLEDAI. This gave a score range 0–101, and the higher the score, the higher the overall disease activity. 5. **Organ damage:** measured using the SLICC. Score range 0–46, where 0 indicates no damage and 46 worst damage.
Notes	**Country:** Sweden **Funding:** supported by grants from The Swedish Rheumatism Association, the Vardal Foundation, the Board of Research and Postgraduate Education and the Centre for Health Care Science, Karolinska Institutet, Sweden. **Trial registration:** not reported **Serious adverse events:** none reported **Other adverse events:** none reported **Total adverse events:** none reported **Data analysis:** we contacted study authors to request missing data for SLEDAI scores; however, we received no response.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Reported as an RCT. Quote: "The remaining 35 patients were block randomized, by a statistician not involved in the study otherwise, into an intervention group (I-group, n=18) or a control group (C-group, n=17)".
Allocation concealment (selection bias)	Unclear risk	Allocation concealment was reported. However, the method of concealment was not reported. Quote: "The result of the randomization was concealed until interventions were assigned".
Blinding of participants and personnel (performance bias) All outcomes	High risk	Being an active exercise intervention, it is not possible to blind the participants and supervisors of the intervention; judged at high risk of bias.

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Bostrom 2016 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Assessor reported: low risk Blinding of outcome assessments were reported. Quote: "The assessments throughout the study were performed by professionals who were blinded to which group the patient had been randomized to". Participant reported: high risk Assessors (i.e. participants) were not blinded to self-reported outcomes measures (i.e. fatigue); judged at high risk of bias.
Incomplete outcome data (attrition bias) All outcomes	High risk	All participants and all participant outcomes were accounted for in the statistical analysis. Quote: "All patients who had data from at least one sampling time point measurement were included in the statistical analyses. Problems caused by missing data for one or more time points do not arise when fitting models in Mixed- and Genmode procedures, provided that the missing data can be assumed missing at random".
Selective reporting (reporting bias)	High risk	Study authors assessed QoL using the SF-36; however, the Mental Component Summary score and Physical Component Summary scores were not reported. Study authors did not report mean and SD for outcomes.
Other bias	Low risk	No other biases.

Daltroy 1995

Study characteristics	
Methods	**Study design:** single-centre, parallel-group, 2-arm RCT **Setting:** home-based exercise intervention **Time trial period:** not reported **Interventions:** exercise plus usual care vs another non-pharmacological intervention plus usual care **Sample size calculation:** sample size calculations were based on the desire to detect a 15% improvement in exercise tolerance test time, using a 2-tailed t-test, with alpha set at 0.01. Based on results from their pilot study, 24 participants per group provided 80% power to detect this difference. They determined 50 participants per disease group, to maintain power within diagnosis. **Analysis:** differences between the 4 diseases-by-treatment groups at baseline were tested with F or Chi^2 tests, as appropriate. For each outcome (exercise tolerance test, endurance, fatigue, depression, helplessness), a set of relevant variables were selected, by stepwise linear regression, for use as covariates and selected for significance easting to reduce the likelihood of false positives due to multiple testing. Overall tests of the intervention effect were performed with multivariate analysis of variance. All analyses were performed with SAS on an IBM PS2 computer.
Participants	**Number of total participants (SLE and RA)** 1. Who received recruitment letters: 196 participants with RA (84 required further information) and 158 participants with SLE (77 required further information) 2. Screened: 40 participates with RA and 35 participants with SLE (2 were ineligible, and to dropped out before testing. It is unclear who had SLE or RA).

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Daltroy 1995 *(Continued)*

3. Randomised: 71 total participants (RA and SLE). 35 to treatment (n = 16 with SLE, n = 19 with RA), and 36 to control (n = 18 with SLE, n = 18 with RA)
4. Number included in 3-month analysis: 34 participants with SLE (16 in treatment group, 18 in control group)

Inclusion criteria (SLE and RA)

1. Met the ACR criteria for SLE or RA
2. Aged 18–50 years
3. Had permission from their primary physician
4. Currently, exercising < 3 times/week
5. Signed informed consent

Exclusion criteria (SLE and RA)

1. Safety considerations such as serum creatinine > 3.0 mg/dL, haematocrit < 30%, previous myocardial infarction, previous cerebral vascular accidents, severe cognitive impairment, diastolic blood pressure > 100 mmHg at rest, or severe arthritis of ≥ 3 weight-bearing joints

Baseline characteristics of participants with SLE

All 34 participants with SLE were women.

Treatment group (n = 16)

1. Mean age: 38.8 (SEM 1.2) years
2. Mean SLAM disease activity: 6.3 (SEM 1.1) points
3. Mean ESR: 19.7 (SEM 4.6) mm/h
4. Mean creatinine: 1.0 (SEM 0.07) mg/dL
5. Mean haematocrit 40.5 (SEM 0.8) mg%
6. % exercise at least occasionally: 81%
7. % high school or more: 72%
8. % smoker: 19%
9. % taking steroids: 38%
10. % taking NSAIDs: 31%
11. Mean exercise tolerance: 9.0 (SEM 0.5) min
12. Mean endurance: 14.2 (SEM 2.0) min
13. Mean MAC fatigue: 22.3 (SEM 2.6) points
14. Mean POMS Fatigue: 9.4 (SEM 1.6) points
15. Mean CES-D: 11.4 (SEM 2.5) points
16. Mean Arthritis Helplessness Index: 31.4 (SEM 1.6) points

Control group (n = 18)

1. Mean age: 31.3 (SEM 1.5) years
2. Mean SLAM disease activity: 6.7 (SEM 0.8) points
3. Mean ESR: 35.5 (SEM 6.0) mm/h
4. Mean creatinine: 0.8 (SEM 0.04) mg/dL
5. Mean haematocrit 37.9 (SEM 1.4) mg%
6. % exercise at least occasionally: 72%
7. % high school or more: 72%
8. % smoker: 22%
9. % taking steroids: 61%
10. % taking NSAIDs: 67%
11. Mean exercise tolerance: 8.0 (SEM 0.4) min
12. Mean endurance: 14.0 (SEM 2.0) min
13. Mean MAC Fatigue: 20.3 (SEM 1.8) points

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Daltroy 1995 *(Continued)*

14.Mean POMS Fatigue: 9.9 (SEM 1.2) points
15.Mean CES-D: 16.3 (SEM 2.4) points
16.Mean Arthritis Helplessness Index: 330.1 (1.3) points

Pretreatment group differences: no differences amongst the 4 treatment-by-diagnosis groups.

Interventions	**Exercise: treatment group plus usual care** 1. **Frequency of exercise sessions:** 3 times/week 2. **Time of exercise session:** 30 min per session 3. **Intensity of exercise:** moderate-to-high (60–80% of maximum HR achieved on the exercise tolerance test) 4. **Type of exercise:** aerobic exercise performed on a stationary bike that was set up in their home. 5. **Duration of intervention:** 12 weeks A physiotherapist contacted the participant once a week to update logs of exercise, report of symptoms, and perceived fatigue. Pulse oximeters were provided to help participants monitor their HRs and as a compliance-enhancing strategy. The physiotherapist instructed the participant at home when setting up the bike, and made a second visit 2–3 weeks later at an exercise session to check the participants' ability to follow the regimen correctly. **Control group (another non-pharmacological intervention plus usual care)** Participants were encouraged to maintain their current level of activity during the 12-week programme. They also filled out questionnaires and were contacted once per week as an attention control.
Outcomes	All outcomes measured at baseline and 3 months. 1. **Fatigue** a. Measured using the MAC questionnaire, which assesses energy for daily activities. The MAC scale is the sum of 4 VAS, and ranges from 0 (no fatigue/lots of energy) to 40 (extreme fatigue/no energy). Higher scores indicate worse fatigue. b. Measured using the POMS Fatigue questionnaire, which assesses mood. The POMS scale sums responses to 6 adjectives (bushed, tired, etc.) on a 5-point Likert scale, covering the last week, and has response ranging from 0 (not at all fatigued) to 30 (extremely fatigued). Higher scores indicate worse fatigue. 2. **Depression:** measured using the CES-D, a 20-item measure of the frequency of various somatic and psychological symptoms over the last month. Scores range from 0 (no depression) to 60 (extremely depressed). A score of > 16 indicates clinical depression. 3. **Helplessness:** helplessness, or the perceived lack of ability to control and cope with one's arthritis, measured by the 15-item Arthritis Helplessness Index, with scores ranging from 15 (low helplessness) to 60 (great helplessness). 4. **Exercise tolerance:** measured using a graded exercise tolerance test using a cycle ergometer, starting at 30 W and increasing by 30 W every 3 min until the participant asked to stop the test. Electrocardiogram, blood pressure, and symptoms were carefully monitored for signs of exercise intolerance. Exercise test was stopped if the participant exhibited angina, fall in blood pressure, severe shortness of breath, ≥ 3 premature ventricular contractions in sequence. The time taken to complete the test was recorded (higher the time = the better the outcome).
Notes	**Country:** US **Funding:** not reported **Trial registration:** not reported **Serious adverse events:** none reported **Other adverse events:** none reported **Total adverse events:** none reported

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Daltroy 1995 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation was reported but unclear how this process was completed; judged at unclear risk of bias.
Allocation concealment (selection bias)	Unclear risk	No allocation concealment reported; judged at unclear risk of bias.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Being an active exercise intervention, it is not possible to blind the participants and supervisors of the intervention; judged at high risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Assessor reported: unclear risk It is unclear whether the assessors were blinded from the intent of the study or knew which participants were in which group. Quote: "The testing was administered by a cardiologist and nurse in an exercise physiology laboratory". Participant reported: high risk Assessors (i.e. participants) were not blinded to study groups, and performed self-reported outcome measures (i.e. depression); judged at high risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No evidence of attrition bias.
Selective reporting (reporting bias)	Low risk	All outcome measures were reported for all participants.
Other bias	Low risk	No other bias identified.

Dos Reis-Neto 2013

Study characteristics

Methods	**Study design:** quasi-randomised 2-arm parallel controlled trial **Setting:** Rheumatology Division and Cardiology Division, Universidade Federal de São Paulo/Escola Paulista de Medicina (UNIFESP/EPM), São Paulo, Brazil **Time trial period:** unknown **Interventions:** exercise training plus usual care vs another non-pharmacological intervention plus usual care **Sample size calculation:** unknown **Analysis:** statistical analysis performed through normality tests, Student's t-test and non-parametric tests for data with non-normal distribution. $P < 0.05$ considered significant.
Participants	**Number of participants**

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Dos Reis-Neto 2013 *(Continued)*

1. Screened: 224 (99 participants not eligible and did not meet inclusion criteria, and 76 participants quit for personal reasons)
2. Allocated into 2 groups according to convenience: 44 (23 in exercise group, and 21 in control group)
3. Included in 3-month analyses: 38 (5 participants in exercise group left for personal reasons, and 1 participant from control group left for personal reasons)

Inclusion criteria

1. Aged 18–45 years
2. Diagnosis of SLE according to ACR criteria

Exclusion criteria

1. Haemoglobin < 10 mg/dL
2. Neuropsychiatric, pulmonary, articular, or vascular damage that would not allow the practice of exercise
3. Coronary disease
4. Heart failure (functional class > II)
5. Pulmonary hypertension
6. Uncontrolled hypertension
7. Creatinine ≥ 1.4 mg/dL
8. BMI ≥ 35 kg/m^2
9. Diabetes mellitus
10. Uncontrolled hypothyroidism
11. Smoking in last 12 months
12. Pregnancy
13. Menopause
14. Use of statins or regular practice of exercise in past 3 months and overlap with other autoimmune rheumatic diseases, except antiphospholipid syndrome

Baseline characteristics

All 38 participants were women, mean age 35.3 (SD 6.8) years, mean BMI 26.0 (SD 4.7) kg/m^2, and mean disease duration 78.9 (SD 65.0) months

Exercise group (n = 18)

1. Mean age: 35.3 (SD 6.8) years
2. Mean BMI: 26.9 (SD 4.7) kg/m^2
3. Mean disease duration: 79.8 (SD 65.0) months
4. White ethnicity, n: 7 (38.9%)
5. Mean SLEDAI disease activity: 2.0 (SD 2.1) points
6. Median SLICC/ACR-DIL 0 (minimum–maximum 0–1)
7. Prednisone use, n: 10 (55.6%)
8. Mean current prednisone dose: 2 (minimum–maximum value 0–40) mg
9. Antimalarial use, n: 13 (72.2%)
10. Immunosuppressive drug use, n: 8 (44.4%)
11. Antihypertensive use, n: 3 (16.7%)
12. Aspirin use, n: 2 (11.1%)
13. Contraceptive use, n: 3 (16.7%)
14. Mean systolic blood pressure: 122.1 (SD 14.4) mmHg
15. Mean diastolic blood pressure: 80.3 (SD 7.4) mmHg
16. Mean abdominal circumference: 87.2 (SD 9.9) cm
17. Mean waist:hip ratio: 0.81 (SD 0.06)
18. Mean fasting glucose: 84.6 (SD 4.9) mg/dL
19. Mean total cholesterol: 161.4 (SD 32.9) mg/dL

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Dos Reis-Neto 2013 *(Continued)*

20.Mean HDL: 50.8 (SD 16.0) mg/dL
21.Mean LDL: 88.3 (SD 22.9) mg/dL
22.Mean triglycerides: 109.9 (SD 48.3) mg/dL
23.Coronary artery disease family history, n: 4 (22.2%)
24.Hypertension, n: 4 (22.2%)
25.Dyslipidaemia, n: 4 (22.2%)

Control group (n = 20)

1. Mean age: 30.8 (SD 7.2) years
2. Mean BMI: 25.7 (SD 4.0) kg/m^2
3. Mean disease duration: 107.9 (SD 91.3) months
4. White ethnicity, n: 9 (45.0%)
5. Mean SLEDAI disease activity: 2.4 (SD 2.3) points
6. Median SLICC/ACR-DI: 0 (minimum–maximum 0–2)
7. Prednisone use, n: 13 (65.0%)
8. Mean current prednisone dose: 5 (minimum–maximum value 0–30) mg
9. Antimalarial use, n: 16 (80.0%)
10.Immunosuppressive drug use, n: 14 (70.0%)
11.Antihypertensive use, n: 7 (35.0%)
12.Aspirin use, n: 3 (15.0%)
13.Contraceptive use, n: 8 (40.0%)
14.Mean systolic blood pressure: 115.8 (SD 13.0) mmHg
15.Mean diastolic blood pressure: 74.0 (SD 9.3) mmHg
16.Mean abdominal circumference: 86.1 (SD 10.0) cm
17.Mean waist:hip ratio: 0.79 (SD 0.06)
18.Mean fasting glucose: 81.3 (SD 6.1) mg/dL
19.Mean total cholesterol: 164.1 (SD 38.0) mg/dL
20.Mean HDL: 49.4 (SD 12.3) mg/dL
21.Mean LDL: 95.1 (SD 31.9) mg/dL
22.Mean triglycerides: 97.2 (SD 35.8) mg/dL
23.Coronary artery disease family history, n: 3 (15.0%)
24.Hypertension, n: 1 (5.0%)
25.Dyslipidaemia, n: 5 (25.0%)

Pretreatment group differences: groups were homogeneous for age, ethnicity, BMI, abdominal circumference, waist:hip ratio, fasting glucose, total cholesterol, HDL, coronary artery disease family history, and dyslipidaemia at baseline.

Interventions

Exercise training group plus usual care

1. **Frequency of exercise sessions:** 3 times/week
2. **Intensity of exercise:** HR corresponding to the ventilatory 1 threshold obtained from ergospirometry and monitored by frequency meter (Poland Electro, Kempele, Finland). Intensity of walking was unclear.
3. **Time of exercise session:** 60-min sessions (10-min warm-up, 40 min of walking and 10-min cool-down)
4. **Type of exercise:** walking, outdoors in the morning
5. **Duration of intervention:** 16 weeks
6. **Supervision/setting:** in the morning at a public park, supervised by a physical educator or physician.

Control group (another non-pharmacological intervention plus usual care)

Participants received usual care and information about the disease, but no exercise intervention. Received clear instruction not to start any exercise programme for the next 16 weeks.

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Dos Reis-Neto 2013 *(Continued)*

Outcomes	Outcomes measures at baseline and postintervention (16 weeks) 1. **Endothelial function:** measured using resting diameter, hyperaemia diameter and flow-mediated dilation, ergospirometry. Non-invasive methods of measuring endothelial function include ultrasound flow-mediated dilation, salbutamol-mediated endothelial function measured by pulse wave analysis or pulse contour analysis, flow-mediated magnetic resonance imaging, laser Doppler flowmetry, and flow-mediated pulse amplitude tonometry. 2. **Ergospirometric assessment:** ergospirometry was performed at the laboratory of the Center for Studies in Psychobiology and Exercise using a Quark PFT ergospirometric testing device. (pulmonary function test) (Cosmed, Italy). Measured through the continuous analysis of carbon monoxide and methane (tracer) fractions with fast analysers. Normal value is 95% confidence interval. Test measures the amount of air the lungs can hold. Test also measures how forcefully one can empty air from the lungs. 3. **Disease Activity:** measured using the SLEDAI. This gives a score range 0–101, and the higher the score, the higher the overall disease activity.
Notes	**Country:** Brazil **Funding:** no funding source reported **Trial registration:** NCT01712529 **Serious adverse events:** unclear **Other adverse events:** unclear **Total adverse events:** unclear

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Study was quasi-RCT and the method of randomisation was not truly random; judged at high risk of bias. Quote: "Prospective study where the patients were divided into two groups according to their convenience, those who were willing to train where placed into the exercise group (EG) and those who were not available were allocated into the control group (CG)".
Allocation concealment (selection bias)	Unclear risk	No allocation concealment was reported; judged at unclear risk of bias.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Being an active exercise intervention, it is not possible to blind the participants and supervisors of the intervention; judged at high risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Assessor reported: low risk Quote: "All assessments were performed at baseline (0 weeks) and end of intervention (16 weeks), in both the EG [exercise] and CG [control] by blinded evaluators". In the exercise group, assessments were performed 72 hours after the last training session to reduce the possible effects of acute exercise. Participant reported: high risk Because the assessor (i.e. participants) were not blinded to the self-reported outcomes measures (i.e. fatigue); judged at high risk of bias.

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Dos Reis-Neto 2013 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	High risk	5/23 in exercise group withdrew (22% withdrawals). No evidence of ITT analyses.
Selective reporting (reporting bias)	Low risk	All outcome measures were clearly reported.
Other bias	Low risk	No other biases.

Hashemi 2022

Study characteristics	
Methods	**Study design:** single-centre, parallel-group, 2-arm RCT **Setting:** Hafez hospital, Shiraz University of Medical Sciences, Shiraz, Southern Iran **Trial time period:** September 2015 to March 2016 **Interventions:** combined aerobic running and anaerobic Pilates exercise training programme plus usual care vs usual care alone **Sample size calculations:** authors did not describe how the sample size was estimated. **Analysis:** continuous variables were first checked for normality, followed by assessment using parametric tests to compare the means since the data were normal. Data were compared by parametric and non-parametric a multiple comparison t-test. Data are presented as mean ± SDs of the mean of ≥ 3 independent experiments. P ≤ 0.05 were considered to be statistically significant.
Participants	**Number of participants** 1. Screened: 30 (6 participants were excluded from the study for not participating in post-test measurements: 1 from exercise group and 5 from control group) 2. Randomised: 24 (14 in exercise group and 10 in control group) 3. Included in 2-month analyses: 19 (10 in exercise group and 9 in control group). 4 from the exercise group were not included in analyses, and 1 from control group was not included in analyses. **Inclusion criteria** 1. Aged 20–29 years 2. Diagnosis of SLE according to ACR 3. SLEDAI < 4 **Exclusion criteria** 1. Showing severe illness with SLEDAI scores > 5 2. Exhibiting any other systemic or rheumatic disorders capable of limiting physical function or its assessment 3. Undertaking regular exercise training ≥ 3 times/week 4. Having significant mental problems such as severe depression 5. Severe cardiovascular disease or very poor cardiovascular fitness **Baseline characteristics** All 24 participants were women. Mean age 29.00 (SD 3.19) years in exercise group and 21.50 (SD 5.52) years in control group ***Exercise group (n = 10)***

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Hashemi 2022 *(Continued)*

1. Mean age: 29.00 (SD 3.19) years
2. Number of participants, gender male: 0
3. Number of participants, gender female: 14
4. Number of participants, marital status, single: 3
5. Number of participants, marital status, married: 12
6. Number of participants, education, diploma: 5
7. Number of participants, education, bachelor: 2
8. Number of participants, education, unemployed: 6
9. Number of participants, employment, employed: 5
10. Number of participants, employment, student: 4
11. Number of participants with pain and inflammation, yes: 7
12. Number of participants with pain and inflammation, no: 3
13. Number of participants with cutaneous findings, yes: 4
14. Number of participants with cutaneous findings, no: 3
15. Number of participants with family history, yes: 1
16. Number of participants with family history, no: 5
17. Height: 1.63 (SD 0.03) m
18. Weight: 67.70 (SD 14.82) kg
19. BMI: 25.51 (SD 5.95) kg/m^2
20. Mean disease duration: 8.30 (SD 4.62) years

Control group (n = 9)

1. Mean age: 21.50 (SD 5.52) years
2. Number of participants, gender male: 0
3. Number of participants, gender female: 10
4. Number of participants, marital status, single: 4
5. Number of participants, marital status, married: 6
6. Number of participants, education, diploma: 2
7. Number of participants, education, bachelor: 5
8. Number of participants, education, unemployed: 6
9. Number of participants, employment, employed: 4
10. Number of participants, employment, student: 0
11. Number of participants with pain and inflammation, yes: 7
12. Number of participants with pain and inflammation, no: 1
13. Number of participants with cutaneous findings, yes: 2
14. Number of participants with cutaneous findings, no: 6
15. Number of participants with family history, yes: 1
16. Number of participants with family history, no: 5
17. Height: 1.59 (SD 0.63) m
18. Weight: 60.33 (SD 9.06) kg
19. BMI: 23.71 (SD 3.31) kg/m^2
20. Mean disease duration: 7.73 (SD 3.73) years

Pretreatment group differences: groups were homogeneous for age, sex, and disease duration.

Interventions	**Exercise group** 1. **Frequency of exercise sessions:** 3 times/week 2. **Intensity of exercise:** stage 2 of session (aerobic exercise programme, including 10 min of cycling and 10 min of running, both at intensity 50–60% maximum, as predetermined in the VO_{2peak} measurements). 3. **Time of exercise session:** 60 min per session (40 min for the first week, to allow for acclimatisation, but increased thereafter).

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Hashemi 2022 *(Continued)*

4. **Type of exercise:** Pilates exercise, which is classified as low-intensity resistance exercise. Each exercise session consisted of 4 stages, including 1. 10-min warm-up, 2. aerobic exercise programme (10-min cycling and 10 min running), 3. 60-min Pilates training using bodyweight as the resistive load, and 4. 10-min cool-down. Borg scale used to assess participant's perception of physical exertion during aerobic exercises that were used in stage 2.
5. **Duration of intervention:** 8 weeks
6. **Supervision/setting:** unknown

Control group

Participants received usual care and information about the disease, but no exercise intervention.

Outcomes	Serum levels of IFN-γ, TNF-α, IL-6, IL-2, IL-4, IL-5, IL-9, IL-10, IL-13, IL-17A, IL-17F, IL-21, and IL-22, and cytokines were measured in all 24 participants by cytokine assay. Although some levels of IFN-γ decreased after 8 weeks, no differences found in the participants' levels between the intervention or control groups. The levels of TNF-α, while increasing in control group, decreased in intervention group. Although participants with SLE presented higher levels of IL-2 at baseline, the levels of IL-2 decreased after 8 weeks in both the intervention and control groups. Levels of IL-4 and IL-5 decreased in intervention group compared with control group. Levels of IL-10, IL-13, and IL-22 increased after 8 weeks. Control group showed increased levels of IL-10, IL-13, and IL-22 compared with intervention group.
Notes	**Country:** Iran **Funding:** supported by Shiraz University of Medical Sciences **Trial registration:** unknown **Serious adverse events:** none reported **Other adverse events:** none reported **Total adverse events:** none reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Authors reported that participants were randomised into groups; however they did not report randomisation methods; judged at unclear risk of bias. Quote: "The patients were randomly divided into two groups, including exercise (n = 15) and control (n = 15) groups".
Allocation concealment (selection bias)	Unclear risk	Insufficient description of the method of concealment; judged at unclear risk of bias.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Being an active exercise intervention, it is not possible to blind the participants and supervisors of the intervention; judged at high risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Assessor reported: unclear risk

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Hashemi 2022 *(Continued)*

		Blinding of participants and investigators was not clearly reported; judged at unclear risk of detection bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No evidence of attrition bias.
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting.
Other bias	Low risk	No other biases.

Kao 2021

Study characteristics	
Methods	**Study design:** quasi-randomised 2-arm parallel controlled trial **Setting:** Division of Allergy, Immunology & Rheumatology, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan 2 School of Medicine, Tzu Chi University, Hualien, Taiwan 3 Center of Physical Education, Tzu Chi University, Hualien, Taiwan 4 Sports Medicine Center, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan. **Time trial period:** unknown **Interventions:** aerobic exercise combined with resistance training plus usual care vs another non-pharmacological intervention plus usual care **Sample size calculation:** unknown **Analysis:** normally distributed parameters are presented as mean (SD) and were analysed using an unpaired t-test to compare the baseline differences between the control and combined exercise groups. Non-normally distributed values were presented as medians (IQR) and were analysed using the Mann-Whitney U test.
Participants	**Number of participants** 1. Screened: 26 (3 participants dropped out for personal reasons) 2. Randomised: 23 (12 in exercise group and 11 in control group) 3. Included in 12-week analyses: 23 participants **Inclusion criteria** 1. Aged 20–65 years 2. Diagnosis of SLE according to ACR, or SLICC criteria for the classification of SLE **Exclusion criteria** 1. Pregnant 2. Uncontrolled hypertension 3. Severe anaemia 4. Conditions that were unsuitable for exercise (e.g. chronic lung disease and active arthritis) **Baseline characteristics** All 23 participants were women. ***Exercise group (n = 12)***

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Kao 2021 *(Continued)*

1. Mean age: 38.75 (SD 12.78) years
2. Median BMI: 22.32 (IQR 19.85–23.86) kg/m^2
3. Median WBC: 4.81 (IQR 3.31–6.65) 10^3/μL
4. Mean haemoglobin: 11.82 (SD 1.54) g/dL
5. Median number of platelet: 294 (IQR 206–334) 10^3/μL
6. Median ESR: 28.5 (IQR 8.3–37.8) mm/hour
7. Mean creatinine: 0.67 (SD 0.11) mg/dL
8. Median anti-dsDNA: 19.05 (IQR 1.03–42.55) IU/mL
9. Median SLEDAI-2K: 2 (IQR 0–5.5) points
10. Mean complement 3: 95.00 (SD 26.42) mg/dL
11. Mean complement 4: 16.99 (SD 7.24) mg/dL
12. Mean fat body mass: 34.15% (SD 6.12%)

Control group (n = 11)

1. Mean age: 40.27 (SD 9.97) years
2. Median BMI: 23.5 (IQR 21.2–26.5) kg/m^2
3. Median WBC: 6.44 (IQR 3.43–7.47) 10^3/μL
4. Mean haemoglobin: 11.75 (SD 1.56) g/dL
5. Median number of platelet: 259 (IQR 237–303) 10^3/μL
6. Median ESR: 23.5 (IQR 10.5–58.8) mm/hour
7. Mean creatinine: 0.57 (SD 0.12) mg/dL
8. Median anti-dsDNA: 19.90 (IQR 0.60–35.00) IU/mL
9. Median SLEDAI-2K: 4 (IQR 2–10)
10. Mean complement 3: 95.24 (SD 15.68) mg/dL
11. Mean complement 4: 18.80 (SD 8.18) mg/dL
12. Mean fat body mass: 37.49% (SD 6.66%)

Pretreatment group differences: groups were homogeneous at baseline for body composition, disease activity, 2-km walking test, and executive function test.

Interventions	**Exercise plus usual care** 1. **Frequency of exercise sessions:** 5 days/week 2. **Intensity of exercise:** moderate intensity determined by HRR 50–50%, according to the ACSM guidelines. HRR = MHR − RHR. MHR determined using formula: MHR = 205 − (0.42 × age). 3. **Time of exercise session:** 30 min per session (3- to 5-min warm-up, 4 sets of combined exercise session for approximately 30 min in total, and final set of 3- to 5-min of relaxation and stretching). Each set of combined exercise lasting for 7 min 15 s, with a brief break between sets. 4. **Type of exercise:** aerobic exercise combined with bodyweight or 500–620 mL of dumbbell water weights for resistance training. Combined exercise sessions consisted of various styles of basic exercises, alternating workouts of legs with trunk movement, and arm exercises. 5. **Duration of intervention:** 12 weeks 6. **Supervision/setting:** home-based exercise. The research team member contacted participants periodically by telephone or text messages to ensure their compliance. Each week the participants reported their maximal HR after each exercise session by written logs. Instructed by an exercise physiologist/professional exercise instructor on the performance of aerobic exercise combined with resistance training and the skills of HR measurement at rest and after exercise. **Control group (another non-pharmacological intervention plus usual care)** Participants received usual care and information about the disease, but no exercise intervention. They were to maintain their usual lifestyle.
Outcomes	All outcomes measured at baseline and postintervention (12 weeks).

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Kao 2021 *(Continued)*

1. **Disease activity:** measured using SLEDAI-2K at baseline and after 12-week intervention. This gives a score range 0–101, higher score = higher the overall disease activity.
2. **Executive performance (reaction time and the performance index):** measured using the go/no-go test and Stroop Task.
   a. **Go/no go:** upon receiving an indicative stimulus for action (i.e. go signal), which was displayed on a computer screen, the participant pressed the assigned keyboard button as quickly as possible. Alternatively, upon receiving a distractor stimulus (i.e. no-go signal), the participant held their action. The participants performed a set of go (160 trials) and no-go (40 trials) stimuli. Reaction time measured as mean time required for pressing the button after the stimuli. Accuracy defined as the percentage of correct responses to both the indicative and distractor stimuli.
   b. **Stroop Task:** comprised a series of colour words presented on a screen. In the incongruent trial (100 trials in total), a mismatch existed between the name of the colour and the colour shown on the screen. In the congruent trials (100 trials in total), colour words were presented as a matching colour. All the words were written in the official national language and were displayed on the screen 1 at a time. The participants were asked to respond as quickly as possible by pressing the corresponding keyboard button that represented the actual colour and make as few errors as possible during this task. Reaction time measured as time required for pressing the button after the word appeared on the screen. Accuracy for each of the congruent and incongruent trials was calculated as the percentage of correctly pressed keyboard buttons.
3. **Physical fitness:** measured using a 2-km walking test. The faster the test was completed (lower time recorded), the better the result of the physical fitness test was. Recorded in minutes and seconds.

Notes	**Country:** Taiwan **Funding:** Tzu Chi Medical Mission Project 105–03–02 (TCMMP105–03–02), Buddhist Tzu Chi Medical Foundation, Taiwan **Trial registration:** unknown **Serious adverse events:** none reported **Other adverse events:** none reported **Total adverse events:** none reported **Data analysis:** contacted study authors to request missing data for SLEDAI; however, no response received.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Study was quasi-randomised; judged at high risk of bias. Quote: "The participants were allocated based on their willingness to either the exercise or control group".
Allocation concealment (selection bias)	Unclear risk	No allocation concealment reported; judged at unclear risk of bias.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Being an active exercise intervention, it is not possible to blind the participants and supervisors of the intervention; judged at high risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Assessor reported: unclear risk Exercise group were instructed by an exercise physiologist/professional exercise instructor. The participants were taught to measure their own HR range. Research team member contacted the home-based exercise participants privately to ensure compliance. Participants reported their own HR range each

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Kao 2021 *(Continued)*

		week. Unclear whether the outcome assessor was also the exercise instructor/exercise physiologist.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No evidence of selective reporting.
Selective reporting (reporting bias)	Low risk	All outcome measures were reported.
Other bias	Low risk	No other biases.

Keramiotou 2020

Study characteristics	
Methods	**Study design:** quasi-randomised 2-arm parallel controlled trial **Setting:** Greece **Time trial period:** unknown **Interventions:** exercise group (combined resistance and stretching) plus usual care vs another non-pharmacological intervention plus usual care **Sample size calculation:** a sample size of 32 participants per group was required for an 80% probability of demonstrating a difference of 15% between comparison groups (exercise: −25% (SD 20%) vs control: −10% (SD 20%)) in percentage change of DASH score from baseline to 12 weeks with a significance of < 5% (2-tailed test). Participants of pilot study were included in the final sample. The estimation of sample size was performed using G*Power V.3.1.9.2 programme. **Analysis:** data were expressed as mean ± SD or median (in case of violation of normality) for continuous variables and as percentages for categorical data. The Kolmogorov Smirnov test utilised for normality analysis of the parameters. The comparison of variables at each time point between interventions was performed using the independent samples t-test or non-parametric Mann-Whitney test. All tests were 2-sided, and statistical significance was set at $P < 0.05$. All analyses were carried out using the statistical package SPSS V.21.00 (IBM Corporation).
Participants	**Number of participants** 1. Screened: 293 (52 declined eligibility checks, 240 were assessed, 156 did not meet inclusion criteria, 9 declined to participate) 2. Randomised: 75 (39 in exercise group: 7 did not start, and not included in analysis, and 36 in control group: 6 did not start, and not included in analysis) 3. Included in 3-month analyses: start of intervention 62 participants. End of intervention 60 participants (2 participants from the exercise group abandoned study without reason). **Inclusion criteria** 1. Aged ≥ 18 years 2. Diagnosis of SLE according to the 2012 SLICC classification criteria for SLE 3. Upper limb arthralgias 4. Difficulty in performing activities of daily living (DASH score > 10) 5. Stable drug regimen for ≥ 12 weeks **Exclusion criteria** 1. Upper limb fracture or surgery in previous 6 months

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Keramiotou 2020 *(Continued)*

2. Physiotherapy programme in previous 6 months
3. Pregnancy

Baseline characteristics

All 62 participants were women.

Exercise group (combined resistance and stretching) (n = 32)

1. Mean age: 43.34 (SD 8.90) years
2. Female, n: 31 (96.9%)
3. Marital status, n: 10 (31.3%) single, 19 (59.4%) married
4. Education status, n: 30 (93.8%) secondary, 2 (6.3%) university
5. In employment, n: 25 (78.12%)
6. Dominant right hand, n: 32 (100%)
7. Median disease duration: 6 (IQR 10) years
8. Mean SLEDAI-2K: 4.25 (SD 3.24) points
9. Lupus low disease activity state: 18 (56.3%)
10. Mean SLICC: 0.34 (SD 0.60) points
11. Median symptomatic joint culture: 10 (IQR 11)
12. Mean swollen joint count: 1.39 (SD 3.05)
13. Arthritis, n: 5 (15.62%)
14. Fibromyalgia, n: 4 (12.5%)
15. Mean VAS: 5.81 (SD 1.67)
16. Corticosteroid use n: 20 (54.1%)
17. Mean prednisolone dosage: 4.63 (SD 5.55) mg
18. Hydroxychloroquine use n: 26 (81.3%)
19. Immunosuppressive agents use n: 15 (46.9%)
20. Biological agents use n: 1 (3.1%)
21. Mean DASH: 39.02 (SD 16.10)
22. Mean HAQ score: 0.81 (SD 0.45) points
23. Mean grip strength, DH: 22.86 (SD 8.77)
24. Mean pinch strength jaws DH: 4.27 (SD 2.01)
25. Mean Purdue DH: 13.25 (SD 2.05)
26. Mean LupusQOL: 56.44 (SD 22.62)
27. Mean LupusQOL Fatigue: 56.63 (SD 23.74)

Control group (n = 30)

1. Mean age: 48.77 (SD 12.38) years
2. Female, n: 27 (90%)
3. Marital status, n: 6 (20%) single, 20 (66.7%) married
4. Education status, n: 28 (93.3%) secondary, 2 (6.7%) university
5. In employment, n: 19 (63.33%)
6. Dominant right hand, n: 27 (90%)
7. Median disease duration: 11 (IQR 15)
8. Mean SLEDAI-2K: 4.20 (SD 3.58)
9. Lupus low disease activity state: 13 (43.3%)
10. Mean SLICC: 0.63 (SD 0.93)
11. Median symptomatic joint culture: 11 (IQR 7)
12. Mean swollen joint count: 1.43 (SD 2.53)
13. Arthritis, n: 6 (20%)
14. Fibromyalgia, n: 3 (10%)
15. Mean VAS: 6.03 (SD 1.77)

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Keramiotou 2020 *(Continued)*

16.Corticosteroid use n: 17 (46.0%)
17.Mean prednisolone dosage: 4.97 (SD 5.80) mg
18.Hydroxychloroquine use n: 25 (83.3%)
19.Immunosuppressive agents use n: 15 (50.0%)
20.Biological agents use n: 3 (10%)
21.Mean DASH: 43.08 (SD 16.39)
22.Mean HAQ score: 1.10 (SD 0.55)
23.Mean grip strength, DH: 21.42 (SD 9.75)
24.Mean pinch strength jaws DH: 3.91 (SD 2.19)
25.Mean Purdue DH: 12.27 (SD 2.36)
26.Mean lupus QoL: 51.25 (SD 20.62)
27.Mean lupus QoL fatigue: 49.44 (SD 21.03)

Pretreatment group differences: difference between groups in percentage changes of DASH, HAQ, grip strength, pinch strength, LupusQOL Physical Health and Fatigue, and VAS scores from baseline to 6, 12, and 24 weeks, and from baseline to 12 weeks for dexterity test ($P < 0.001$).

Interventions

Exercise group (combined resistance and stretching) plus usual care

1. **Frequency of exercise sessions:** 7 days/week
2. **Intensity of exercise:** moderate intensity. Initial intensity of exercise set at a moderate level and programme was reassessed, using a modified Borg Scale (a tool to measure a persons' perception of their effort and exertion, breathlessness, and fatigue during physical work) to maintain the same intensity, in every face-to-face session with the hand therapist at 0, 3, 6, and 9 weeks.
3. **Time of exercise session:** 30 min per session
4. **Type of exercise:** upper-limb exercises (9 strengthening and stretching exercises for the upper extremities with a stick, 10 strengthening and stretching exercises for the fingers, and 11 strengthening exercises against resistance with therapeutic putty).
5. **Duration of intervention:** 12 weeks (and 24 weeks' follow-up, we did not report these measurements)
6. **Supervision/setting:** none reported

Control group (another non-pharmacological intervention plus usual care)

Participants had 4 sessions of training in alternative methods of performing daily activities, use of aids, joint protection and energy conservation, additionally to assessment at baseline, 6, 12, and 24 weeks, in order to keep them also committed and motivated. All participants received the same training in alternative methods of performing daily activities, use of aids, joint protection, and energy conservation.

Outcomes

1. **Performance of daily activities:** measured using DASH at baseline, 6, 12, and 24 weeks. It was 30 items regarding symptoms and function. Items were scored on a scale from 1 (no difficulty) to 5 (extreme difficulty/unable to do). A high score indicates a decreased ability in performances of daily activities.
2. **Functional ability:** measured using the HAQ. Total score 0–3, in 0.125 increments. Lower scores indicate better function, and higher scores indicate worse function and greater disability. Measured at baseline, 6, 12, and 24 weeks.
3. **Grip and pinch strength:** measured using the Jamar dynamometer and pinch gauge tool using the DH at baseline, 6, 12, and 24 weeks. 3 trials were recorded, and the mean score was recorded after attempts complete by participants.
4. **Dexterity:** measured using the Purdue pegboard test at baseline, 6, 12, and 24 weeks. DH was required to be used. Participants were asked to take as many pins as possible in 30 s, out of a cup and place each 1 into a hole in a board. The greater the number of pins the better the result.
5. **QoL:** measured using the LupusQOL Questionnaire at baseline, 6, 12, and 24 weeks. Evaluating 8 domains, each domain is scored separately, score range 0–100, with greater values indicating better QoL.
6. **Pain:** measured using VAS Pain, scored on 0–10 scale, with a lower score indicating less pain. Measured at baseline, 6, 12, and 24 weeks.
7. **Fatigue:** measured using the LupusQOL Fatigue domain at baseline, 6, 12, and 24 weeks. Score range 0–100, higher the score indicates less fatigue.

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Keramiotou 2020 *(Continued)*

Notes	**Country:** Greece **Funding:** study authors have not declared a specific grant for this research from any funding agency in the public, commercial, or not-for-profit sectors. **Trial registration:** NCT03802578 **Serious adverse events:** none reported **Other adverse events:** none reported **Total adverse events:** none reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	RCT. Quote: "Block size 4 randomisation was used to allocate 75 patients".
Allocation concealment (selection bias)	Low risk	Allocation was unmasked to participants and therapists delivering the exercise programme. Rheumatologists working in the 2 hospitals evaluated all participants and were masked to group allocation.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Being an active exercise intervention, it is not possible to blind the participants and supervisors of the intervention; judged at high risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Assessor reported: unclear risk Quote: "A hand therapist (KK) assessed all patients at baseline, 6, 12 and 24 weeks. Rheumatologists working in the two hospitals evaluated all participants and were masked to group allocation. Clinical evaluation included tender and swollen joint count". It is unclear from this statement whether the hand therapist was also masked to group allocation; judged at unclear risk. Participant reported: high risk Participants were not blinded to the study, and outcomes were self-reported; judged at high risk of bias.
Incomplete outcome data (attrition bias) All outcomes	High risk	In the summary table of results, it was unclear how many participants were included in the postintervention outcome data, considering 2 participants withdrew from the exercise programme at 6 weeks, with no clear reason for dropout. Quote: "One patient in the exercise group was diagnosed with influenza and treated with oseltamivir". However, it was unclear whether this was the participant that dropped out, and they did not report anything regarding the second participant who dropped out.
Selective reporting (reporting bias)	High risk	The LupusQOL is used to assess QoL; however, authors did not report all domains. Only Physical Health and Fatigue domains were reported.
Other bias	Low risk	No other biases.

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Lopes-Souza 2021

Study characteristics	
Methods	**Study design:** randomised controlled 2-arm parallel trial **Setting:** Laboratorio de Vibracoes Mecanicas e Practicas Integrativas, Departamento de Biofisica, Instituto de Biologia Roberto Alcantara Gomes, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, RJ, Brazil **Time trial period:** recruited between May 2017 and November 2018 **Interventions:** WBVE plus usual care vs placebo (isometry) plus usual care **Sample size calculation:** performed by a previous study using the HAQ based on minimal clinically important difference of 0.22 in HAQ score (SD 0.19) between 2 groups. **Analysis:** descriptive analysis performed by mean ± SD for continuous variables, and absolute and relative frequency for categorical variables. To compare the variables between the intervention groups, the t test was used for the continuous variables and the Chi^2 test for the categorical variables. To evaluate the effect of the intra group intervention according to the moment of the evaluation (time) the paired t test was used, as well as 95% confidence intervals were calculated. The difference between the initial and final means of each group and the comparison of this difference between groups was performed using the paired t test. To minimise the effect of possible confounding variables on outcomes, the different variables between the groups at randomisation were considered as adjustment variables when comparing the intervention between the groups. The adjusted model was performed by multiple linear regression. For all analyses performed, the value of $P < 0.05$ was considered statistically significant.
Participants	**Number of participants** 1. Screened: 77 (56 excluded for unknown reasons, 24 excluded for not meeting inclusion criteria, and 32 declined to participate) 2. Randomised: 21 (11 in exercise group and 10 in isometry group) 3. Included in 6-week analyses: 19 participants (10 in exercise group and 9 in isometry group; 1 participant from WBVE group discontinued due to low back pain, and 1 participant discontinued from the isometry group for personal reasons) 4. Included in 12-week analyses: 17 participants (2 from exercise group discontinued for personal reasons) **Inclusion criteria** 1. Women aged 30–60 years 2. Diagnosis of SLE for ≥ 6 months 3. Chronic glucocorticoids use for ≥ 3 years 4. On stable drug therapy for ≥ 2 months 5. Had chronic diseases control 6. No activity or period of exacerbation and attended Department of Rheumatology **Exclusion criteria** 1. Current or prior smoking habits 2. History of alcohol abuse 3. Low impact fractures 4. Aseptic hip necrosis 5. Using assistive devises 6. Hip or knee replacement surgery 7. Pregnant 8. Comorbidities that could be affected by WBVE 9. Neurological or psychiatric disease

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Lopes-Souza 2021 *(Continued)*

Baseline characteristics

All 21 participants were women

WBVE group (n = 11)

1. Mean age: 48.5 (SD 4.7) years
2. Mean BMI: 26.9 (SD 5.3) kg/m^2
3. Caucasian (believed to be white people) n: 8 (73%)
4. Not Caucasian n: 3 (27%)
5. Diabetes n: 2 (18%)
6. Hypertension n: 7 (63%)
7. Dyslipidaemia n: 3 (27%)
8. Mean lupus diagnosis time: 13.5 (SD 5.2) years
9. Mean lupus treatment prednisone (change in daily dose): 5.3 (SD 5.3) mg
10. Mean lupus treatment prednisone (change in cumulative dose 6 months): 896 (SD 337) months
11. Mean lupus treatment time of prednisone use: 13.3 (SD 5.4) years
12. Lupus treatment hydroxychloroquine n: 8 (73%)
13. Lupus treatment immunosuppressants n: 10 (90%)
14. Mean skeletal mass index: 6.5 (SD 0.7) kg/m^2
15. Mean handgrip: 33.2 (SD 8.3) kg
16. Mean Timed Up and Go: 10.2 (SD 2.5) s

Isometry group (n = 10)

1. Mean age: 47.0 (SD 7.9) years
2. Mean BMI: 4.8 (SD 3.3) kg/m^2
3. Caucasian (believed to be white people) n: 6 (60%)
4. No Caucasian: 4 (40%)
5. Diabetes n: 2 (10%)
6. Hypertension n: 7 (70%)
7. Dyslipidaemia n: 2 (20%)
8. Mean lupus diagnosis time: 14.8 (SD 7.1) years
9. Mean lupus treatment prednisone (change in daily dose): 5.0 (SD 1.9) mg
10. Mean lupus treatment prednisone (change in cumulative dose 6 months): 963 (SD 950) months
11. Mean lupus treatment time of prednisone use: 14.8 (SD 7.1) years
12. Lupus treatment hydroxychloroquine n: 7 (70%)
13. Lupus treatment immunosuppressants n: 7 (70%)
14. Mean skeletal mass index: 5.9 (SD 0.6) kg/m^2
15. Mean handgrip: 33.2 (SD 6.2) kg
16. Mean Timed Up and Go: 9.1 (SD 1.5) s

Pretreatment group differences: groups were homogeneous for age, BMI, lupus diagnosis time, and indices related to sarcopenia at baseline.

Interventions	**Exercise group: WBVE plus usual care** Participants stood on a vibrating platform. 1. **Frequency of exercise sessions:** 2 times/week (24 hours between sessions) 2. **Intensity of exercise:** a. Week 1–4: 10 bouts of 30 s, frequency of 30 Hz, D 1.23 mm, and a peak of 2.22 g b. Week 5–8: 10 bouts of 60 s, frequency of 40 Hz, D 0.95 mm, and a peak of 3.06 g c. Week 9–12: 10 bouts of 60 s, frequency of 50 Hz, D 0.88 mm, and a peak of 4.40 g 3. **Time of exercise session:** a. Week 1–4: 2-min warm-up, 5 min

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Lopes-Souza 2021 *(Continued)*

b. Week 5–12: 2-min warm-up, 10 min WBVE

4. **Type of exercise:** WBVE is a subgroup of resistance training, better classified as muscle activation or neuromuscular training complementary to resistance training. The participants were positioned on the vibrating platform with 130° of knee flexion.
5. **Duration of intervention:** 12 weeks
6. **Supervision/setting:** unclear if there was supervision present during intervention.

Control group: placebo (isometry) plus usual care

Participants stood on a vibrating platform (switched off).

1. **Frequency of exercise sessions:** 2 times/week (24 hours between sessions)
2. **Intensity of exercise:** light-to-moderate intensity, warm-up was performed in the same way as in the WBVE group.
3. **Time of exercise session:**
   a. Week 1–4: 2-min warm-up, 5 min stood on a vibrating platform
   b. Week 5–12: 2-min warm-up, 10 min stood on a vibrating platform
4. **Type of exercise:** participants were requested to maintain stance with 130° of knee flexion on the same vibrating platform (turned off). The deck panel remained covered. The cycles, working, and rest times corresponded to the weeks, consistent with the WBVE group, but without vibration.
5. **Duration of intervention:** 12 weeks
6. **Supervision/setting:** unclear if there was supervision present during intervention.

Outcomes

1. **Fatigue:** measured using the FACIT-Fatigue (version 4) is a 13-item questionnaire that uses a 5-point Likert-type response scale (0 = not at all; 1 = a little bit; 2 = somewhat; 3 = quite a bit; and 4 = very much), with scores ranging from 0 to 52 (higher scores indicating less fatigue). FACIT-Fatigue scale was completed before the intervention at weeks 0, 6, and 12.
2. **Functional capacity:** measured using the HAQ and the Timed Up and Go test.
   a. The HAQ consists of 20 questions, which represent common daily activities, and evaluates 8 categories: dress and physical presence, wake up, feed, walk, hygiene, reach, footprint, and other day-to-day activities. The answer alternatives for each question are 'no difficulty' (score = 0), with 'some difficulty' (score = 1), "very difficult" or 'using an auxiliary device' (score = 2) and 'unable to do' (score = 3). The highest score obtained for any question in a given subcategory determines the score for it. A final score is calculated based on the sum of the highest scores in each subcategory divided by the number of subcategories that were answered. Total score range from 0 (no disability) to 3 (severe disability). The HAQ questionnaire was completed by the women just before the intervention at 0, 6, and 12 weeks.
   b. The Timed Up and Go consisted of measuring the time use for participants to stand up from a chair, walking 3 m, turning, returning to the chair and sitting down. Instructed to walk in a comfortable and safe pace. The final score was the duration of time in which it took for the participant to complete this test, safely and correctly.
3. **QoL:** measured using the SF-36, which is a common tool for assessing QoL in chronic diseases, and it can be used in any disease, including SLE. It consists of 36 items, grouped into 8 domains covering physical and mental health. The 8 domains include: Functional Capacity, Physical Role Functioning, Pain, General Health, Vitality, Social Role Functioning, Emotional Role Limitations, and Emotional Wellbeing. The score of these domains ranges from 0 to 100, higher scores indicate better health. The SF-36 survey was completed by the women at 0, 6, and 12 weeks.
4. **Hand grip strength**: evaluated by a hand-held dynamometer performed through 3 evaluations, where the participant held the dynamometer (EMG830RF, EMG System, Sao Jose dos Campos/SP) with the DH 3 times in a row for 5 'seconds.' The best value of the 3 measurements was used to classify sarcopenia. Quote: "The higher the score, the better the strength".

Notes

Country: Brazil

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Lopes-Souza 2021 *(Continued)*

Funding: study authors received no financial support for the research, authorship, or publication of the article.

Trial registration: Brazilian Registry of Clinical Trials under number RBR-2b4bzq

Serious adverse events: none reported

Other adverse events: none reported

Total adverse events: none reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Study reported to be randomised in the manuscript, and was registered as an RCT; however, randomisation process was not reported.
Allocation concealment (selection bias)	Unclear risk	No allocation concealment was reported, and therefore it is unclear whether it was included.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Considering participants in both groups were on a vibrating platform, either turned on for those in the exercise group or turned off in the placebo group, we did not think that people in the placebo group could be truly blinded; judged at high risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Assessor reported: unclear risk The personnel conducting the outcomes or intervention (or both) were not clearly identified, and, therefore, it was unclear whether assessors were blinded to the intervention. Participant reported: high risk Assessors (i.e. participants) were not blinded to the self-reported outcome measures (i.e. fatigue); judged at high risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up reported.
Selective reporting (reporting bias)	High risk	Authors assessed QoL with the SF-36; however, the Mental Component Summary score and Physical Component Summary scores were not reported.
Other bias	Low risk	No other biases.

Miossi 2012

Study characteristics

Methods	**Study design:** randomised controlled 3-arm parallel trial **Setting:** Laboratory of Physical Conditioning for Rheumatologic Patients of the School of Medicine, University of São Paulo, São Paulo, Brazil **Time trial period:** May 2010 and April 2011 **Interventions:** exercise trained participants with SLE plus usual care vs non-trained participants with SLE vs healthy controls group

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Miossi 2012 *(Continued)*

Sample size calculation: not reported

Analysis: effect sizes were estimated for the postintervention assessments using the pooled SDs of the 2 independent samples at postintervention. The significance level was previously set at $P < 0.05$. All analyses were performed using SAS software, version 8.2. Data were presented as mean and SD. As the primary analysis, ITT analysis was used for each comparison irrespective of the compliance with exercise testing. Missing data were imputed using the unconditional mean imputation at 12 weeks and postintervention.

Participants

Number of participants

1. Screened: 45 (2 participants withdrew for personal reasons, and 3 failed follow-up from the SLE non-trained group. 1 participant failed follow-up from the SLE trained group. 3 participants withdrew for personal reasons and 2 failed follow-up from the control group)
2. Randomised: 45 (15 allocated to the SLE trained group, 15 allocated to the SLE non-trained group, and 15 allocated to the control group)
3. Included in final analysis: 32 (14 participants from the SLE trained group, 10 participants from the SLE non-trained group, and 8 participants from the control group)

Inclusion criteria

1. Aged 20–40 years
2. Disease activity < 4 according to SLEDAI
3. Physically inactive for ≥ 6 months before entering study

Exclusion criteria

1. Cardiovascular dysfunction
2. Rhythm and conduction disorders
3. Musculoskeletal disturbances
4. Kidney and pulmonary involvements
5. Peripheral neuropathy
6. Use of tobacco
7. Treatment with lipid-lowering drugs
8. Fibromyalgia
9. Use of chronotropic or antihypertensive drugs

Baseline characteristics

All 32 participants were women.

Trained group (participants with SLE) **(n = 14)**

1. Mean age: 31.4 (SD 5.9) years
2. Mean weight: 65.4 (SD 11.1) kg
3. Mean height: 1.6 (SD 0.05) m
4. Mean BMI: 25.3 (SD 4.7) kg/m^2
5. Mean SLEDAI disease activity: 0.9 (SD 1.5) points
6. Disease duration: 6.1 years
7. Drug prednisone n: 10 (66.7%)
8. Drug prednisone ≥ 20 mg/day n: 2 (13.3%)
9. Drug azathioprine n: 8 (53.3%)
10. Drug chloroquine n: 12 (80%)
11. Drug methotrexate n: 1 (6.7%)
12. Drug mycophenolate mofetil n: 4 (26.7%)
13. Drug cyclophosphamide n: 1 (6.7%)
14. Drug medroxyprogesterone n: 4 (26.7%)
15. Mean resting HR: 96.6 (SD 24.0) beats per min

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Miossi 2012 *(Continued)*

16.Mean peak HR: 170.7 (SD 13.4) beats per min
17.Mean VO_{2peak}: 24.8 (SD 4.8) mL/kg/min
18.Mean chronotropic reserve: 81.3 (SD 15.0)
19.Mean rest to VAT: 29.8% (SD 18%) relative change for HR
20.Mean respiratory compensation point: 64.6% (SD 26.1%) relative change for HR
21.Mean rest to peak HR: 81.1% (SD 21.8%) relative change for HR
22.Mean HR recovery 1 24.0 (SD 9.8)
23.Mean HR recovery 2: 39.5 (SD 10.3)
24.Mean chronotropic reserve before: 81.3 (SD 15.0)
25.Mean chronotropic reserve after: 95.4 (SD 9.2)
26.Mean rest to VAT before: 29.8% (SD 18.8%) relative change for HR
27.Mean rest to VAT after: 56.0% (22.2%) relative change for HR
28.Mean rest to RCP before: 69.6 (SD 26.1)
29.Mean rest to RCP after: 102.1 (SD 22.1)
30.Mean rest to peak exercise before: 81.1 (SD 21.8)
31.Mean rest to peak exercise after: 129.3 (SD 21.8)
32.Mean change in HR recovery 1 before: 24.1 (SD 9.8)
33.Mean change in HR recovery 1 after: 40.9 (SD 10.3)
34.Mean change in HR recovery 2 before: 39.5 (SD 10.3)
35.Mean change in HR recovery 2 after: 57.2 (SD 11.9)

Non-trained group (participants with SLE) **(n = 10)**

1. Mean age: 31.0 (SD 4.8) years
2. Mean weight: 58.7 (SD 7.2) kg
3. Mean height: 1.6 (SD 0.07) m
4. Mean BMI: 23.6 (SD 1.9) kg/m^2
5. Mean SLEDAI disease activity: 1.0 (SD 1.3) points
6. Disease duration: 6.4 years
7. Drug prednisone n: 8 (61.5%)
8. Drug prednisone ≥ 20 mg/day, n: 1 (7.1%)
9. Drug azathioprine n: 5 (38.4%)
10. Drug chloroquine n: 12 (92.3%)
11. Drug methotrexate n: 3 (23.0%)
12. Drug mycophenolate mofetil n: 2 (15.3%)
13. Drug cyclophosphamide n: 0 (0%)
14. Drug medroxyprogesterone n: 7 (53.8%)
15. Mean resting HR: 94.7 (SD 14.2) beats per min
16. Mean peak HR: 165.1 (SD 13.7) beats per min
17. Mean VO_{2peak}: 25.5 (SD 3.1) mL/kg/min
18. Mean chronotropic reserve: 76.1% (SD 18.1%)
19. Mean rest to VAT: 38.9% (SD 21.7%) relative change for HR
20. Mean RCP: 54.9% (SD 21.1%) relative change for HR
21. Mean rest to peak HR: 69.8% (SD 19.3%) relative change for HR
22. Mean HR recovery 1: 25.4 (SD 12.8)
23. Mean HR recovery 2: 37.9 (SD 13.1)
24. Mean chronotropic reserve before: 76.1 (SD 18.1)
25. Mean chronotropic reserve after: 75.6 (SD 16.6)
26. Mean rest to VAT before: 38.9% (SD 21.7%) relative change for HR
27. Mean rest to VAT after: 34.9% (SD 15.7%) relative change for HR
28. Mean rest to RCP before: 54.9 (SD 12.0)
29. Mean rest to RCP after: 68.7 (SD 25.3)

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Miossi 2012 *(Continued)*

30.Mean rest to peak exercise before: 69.8 (SD 19.3)
31.Mean rest to peak exercise after: 90.6 (SD 30.3)
32.Mean change in HR recovery 1 before: 25.4 (SD 12.8)
33.Mean change in HR recovery 1 after: 26.7 (SD 9.3)
34.Mean change in HR recovery 2 before: 37.8 (SD 13.1)
35.Mean change in HR recovery 2 after: 39.5 (SD 13.4)

Healthy control group (n = 8)

1. Mean age: 30.9 (SD 8.3) years
2. Mean weight: 61.3 (SD 7.7) kg
3. Mean height: 1.6 (SD 0.06) m
4. Mean BMI: 23.9 (SD 3.2) kg/m^2
5. Drug prednisone n: 1 (0%)
6. Drug prednisone ≥ 20 mg/day: 1
7. Drug azathioprine n: 0.47 (0%)
8. Drug methotrexate n: 0.3 (0%)
9. Drug mycophenolate mofetil n: 0.65 (0%)
10. Drug cyclophosphamide n: 1 (0%)
11. Drug medroxyprogesterone n: 0.2 (0%)
12. Mean resting HR: 90.4 (SD 9.2) beats per min
13. Mean peak HR: 182.6 (SD 5.5) beats per min
14. Mean VO_{2peak}: 31.0 (SD 4.8) mL/kg/min
15. Mean chronotropic reserve: 93.5% (SD 4.9%)
16. Mean rest to VAT: 49.2% (SD 15.4%) relative change for HR
17. Mean RCP: 85.0% (SD 19.8%) relative change for HR
18. Mean rest to peak HR: 103.6% (SD 18.3%) relative change for HR
19. Mean HR recovery 1: 33.8 (SD 6.6)
20. Mean HR recovery 2: 52.0 (SD 5.7)
21. Mean chronotropic reserve before: 93.5 (SD 4.9)
22. Mean chronotropic reserve after: 95.9 (SD 10.4)
23. Mean rest to VAT before: 49.2% (SD 15.4%) relative change for HR
24. Mean rest to VAT after: 49.6% (SD 21.5%) relative change for HR
25. Mean rest to RCP before: 85.0 (SD 19.8)
26. Mean rest to RCP after: 98.4 (SD 18.8)
27. Mean rest to peak exercise before: 103.6 (SD 18.3)
28. Mean rest to peak exercise after: 121.6 (SD 23.3)
29. Mean change in HR recovery 1 before: 33.8 (SD 6.6)
30. Mean change in HR recovery 1 after: 38.2 (SD 10.0)
31. Mean change in HR recovery 2 before: 52.0 (SD 5.7)
32. Mean change in HR recovery 2 after: 53.6 (SD 7.6)

Pretreatment group differences: the 3 groups were homogeneous for age, height, and resting HR at baseline.

Interventions	**Exercise: trained SLE plus usual care** 1. **Frequency of exercise sessions:** 2 times/week 2. **Intensity of exercise:** HR corresponding to the interval between VAT and 10% below RCP 3. **Time of exercise session:** 80 min per session 4. **Type of exercise:** training session composed of 5-min treadmill warm-up followed by 35–40 min of resistance training, 30 min of treadmill aerobic training, and 5 min of stretching. Resistance training included 7 exercises for the main muscle groups (e.g. bench press, leg press, leg extension). Participants were required to perform 4 sets of 8–12 RM, except during the first week, when a reduced volume

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Miossi 2012 *(Continued)*

of 2 sets of 15–20 RM for each exercise was performed (as an adaptation period to resistance training). Cardiorespiratory exercise test was performed on a treadmill (Centurion, Model 200, Micromed) using a maximal-graded exercise protocol.

5. **Duration of intervention:** 12 weeks
6. **Supervision/setting:** all sessions were monitored by 1 fitness professional.

Non-trained SLE group (another non-pharmacological intervention plus usual care)

Physically inactive women were advised to remain physically inactive. Participants received usual care and information about the disease, but no exercise intervention.

Heathy control group

1. **Frequency of exercise sessions:** 3 times/week
2. **Intensity of exercise:** HR corresponding to the interval between VAT and 10% below RCP.
3. **Time of exercise session:** 80 min per session
4. **Type of exercise:** training session composed of 5-min treadmill warm-up followed by 35–40 min of resistance training, 30 min of treadmill aerobic training, and 5 min of stretching. Resistance training included 7 exercises for the main muscle groups (e.g. bench press, leg press, leg extension). Participants were required to perform 4 sets of 8–12 RM, except during the first week, when a reduced volume of 2 sets of 15–20 RM for each exercise was performed (as an adaptation period to resistance training). Cardiorespiratory exercise test was performed on a treadmill (Centurion, Model 200, Micromed) using a maximal-graded exercise protocol.
5. **Duration of intervention:** 12 weeks
6. **Supervision/setting:** all sessions were monitored by 1 fitness professional.

Participants with SLE and healthy controls had not engaged in regular physical activity programme for ≥ 6 months before the commencement of study and were instructed to maintain their usual living activities and not to engage in any other regular exercise programme throughout the study.

Outcomes

1. **Cardiorespiratory fitness (VO_{2peak}):** oxygen consumption and carbon dioxide output were obtained through breath-by-breath sampling and expressed as a 30-s mean using an indirect calorimetry system (Cortex Model Metalyzer III B). This was measured using a maximal-graded exercise test on a treadmill. Measured at baseline and 12 weeks.
2. **Chronotropic reserve:** HR response during exercise was evaluated by the formula chronotropic reserve = [peak HR − resting HR/220 − age − resting HR] × 100. HRR was defined as the difference between HR at peak exercise and at both the first (HR recovery 1) and (HR recovery 2) minutes after exercise. Absolute change was used to calculate the difference between the HR at peak exercise and at the first and second minutes after the exercise test. Relative change for HR was calculated for the intervals between rest to VAT, rest to RCP, and rest to peak exercise. Measured at baseline and 12 weeks.

Notes

Country: Brazil

Funding: the Laboratory of Physical Conditioning for Rheumatologic Patients received an institutional grant from Bank of America Merrill Lynch. Dr Benatti's work was supported by the Fundaco de Amparo a Pesquisa do Estado de Sao Paulo. Dr Borba's work was supported by the Conselho Nacional de Desenvolvimento Cientıfico e Tecnologico and the Federico Foundation. Dr Bonfa's work was supported by the Fundacao de Amparon a Pesquisa do Estado de Sao Paulo and the Federico Foundation.

Trial registration: unknown

Serious adverse events: none reported

Other adverse events: none reported

Total adverse events: none reported

Risk of bias

Bias	Authors' judgement	Support for judgement

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Miossi 2012 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Reported as an RCT but unclear how randomisation was performed; judged at unclear risk of bias. Quote: "Physically inactive women with SLE were randomly assigned to participate in a supervised exercise training program (T group) or to remain physically inactive (NT group)".
Allocation concealment (selection bias)	Unclear risk	No allocation concealment was reported; judged at unclear risk of bias.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Being an active exercise intervention, it is not possible to blind the participants and supervisors of the intervention; judged at high risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Assessor reported: unclear risk No blinding of outcome assessments was reported; judged at unclear risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No evidence of selecting reporting.
Selective reporting (reporting bias)	Low risk	All outcome measures were reported.
Other bias	Low risk	No other biases.

Tench 2003

Study characteristics	
Methods	**Study design:** 3-arm RCT **Setting:** Bone and Joint Research Unit, Department of Psychological Medicine, Barts; the London, Queen Mary's School of Medicine and Dentistry; National Sports Medicine Institute; Barts and the London NHS Trust, London, UK **Time trial period:** unknown **Interventions:** aerobic exercise programme plus usual care vs another non-pharmacological intervention (relaxation exercise) plus usual care vs usual care alone **Sample size calculation:** in a previous study of exercise therapy and fibromyalgia, 50% of participants considered themselves moderately improved by the treatment compared with 10% of controls receiving flexibility training. By assuming similar treatment responses with a = 0.05 and a power of 90%, the study authors calculated that 30 participants would be required for each group. **Analysis:** statistical analysis used the SPSS 10.0 for Windows software package (SPSS, Chicago, IL, USA). All participants who underwent random allocation were analysed according to group assignment. The Clinical Global Impression Change score was analysed categorically; a score of 1 or 2 was considered clinically important. We compared the proportions of participants rating themselves clinically improved by ITT analysis by means of ×2 analysis with Fisher's exact test for small numbers. 1-way analysis of variance with Bonferroni correction or the Kruskal–Wallis test was used to compare means and medians of each variable in the 3 groups as appropriate.
Participants	**Number of participants**

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Tench 2003 *(Continued)*

1. Screened: 93
2. Randomised: 93 (33 in exercise group, 28 in relaxation group, and 32 in control group). 11 participants did not commence the intervention; 6 in exercise group, 4 in relaxation group, and 1 in control group dropped out of treatment (did not attend a single supervised exercise sessions or return any dairy sheets).
3. Included in the 12-week analyses: 79 (14 did not attend the 12-week physiological assessment; 4 in exercise group, 5 in relaxation group, and 5 in control group). 6/14 participants had dropped out of study, and 8/14 had completed the study but did not wish to repeat the walking test to exhaustion.

Inclusion criteria

1. Aged 16–55 years
2. Diagnosis of SLE according to ACR criteria

Exclusion criteria

1. Evidence of active severe myositis
2. Evidence of active severe nephritis
3. Neurological involvement
4. Cardiac disease
5. Pulmonary disease
6. Pregnancy

Baseline characteristics

All 93 participants were women. Mean age 39 (SD 0.8) years, median disease duration 30 (IQR 10–14) months, median SLAM score of 5 (IQR 3–8), and median SLICC/ACR damage index score of 0 (IQR 0–0).

Exercise group (n = 33)

1. CFS: mean 22 (SEM 1.3)
2. VAS: mean 33 (SEM 10)
3. FSS: mean 5.4 (SEM 0.2)
4. PSQI: median 8 (IQR 5–12)
5. HAD Anxiety: mean 9.0 (SEM 0.8)
6. HAD Depression: mean 5.0 (SEM 0.7)
7. SF-36 Physical Function: mean 62 (SEM 5)
8. SF-36 Role Physical: median 25 (IQR 0–63)
9. SF-36 Vitality: mean 37 (SEM 3)
10. SLAM: median 5 (IQR 3–8)
11. Test duration: mean 9.8 (SEM 0.6) min
12. Peak oxygen uptake: mean 23.1 (SEM 0.9) mL/kg/min
13. Maximum ventilation: mean 61.5 (SEM 3)
14. Maximum HR: median 173 (IQR 158–181) beats per min
15. Recovery HR: mean 99 (SEM 2.6) beats per min
16. BMI: median 25 (IQR 23–29) kg/m^2

Relaxation group (n = 28)

1. CFS: mean 24 (SEM 1.6)
2. VAS mean 290 (SEM 11)
3. FSS: mean 5.4 (SEM 0.2)
4. PSQI: median 8 (IQR 6–12)
5. HAD Anxiety: mean 9.9 (SEM 0.9)
6. HAD Depression: mean 7.9 (SEM 0.8)
7. SF-36 Physical Function: mean 61 (SEM 5)
8. SF-36 Role Physical: median 12.5 (IQR 0–75)

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Tench 2003 *(Continued)*

9. SF-36 Vitality: mean 32 (SEM 4)
10. SLAM: median 6 (IQR 3–8)
11. Test duration: mean 10.8 (SEM 0.8) min
12. Peak oxygen uptake: mean 24.2 (SEM 1.5) mL/kg/min
13. Maximum ventilation: mean 59.6 (SEM 4)
14. Maximum HR: median 168 (IQR 153–185) beats per min
15. Recovery HR: mean 104 (SEM 3.1) beats per min
16. BMI: median 24 (IQR 22–28) kg/m^2

Control group (n = 32)

1. CFS: mean 24 (SEM 1.7)
2. VAS: mean 286 (SEM 12)
3. FSS: mean 5.5 (SEM 0.2)
4. PSQI: median 7 (IQR 6–12)
5. HAD Anxiety: mean 8.8 (SEM 0.7)
6. HAD D: mean 6.4 (SEM 0.6)
7. SF-36 Physical Function: mean 61 (SEM 4)
8. SF-36 Role Physical: median 12.5 (IQR 0–50)
9. SF-36 Vitality: mean 36 (SEM 4)
10. SLAM: median 5 (IQR 4–8)
11. Test duration: mean 10.6 (SEM 0.7) min
12. Peak oxygen uptake: mean 22.5 (SEM 1.3) mL/kg/min
13. Maximum ventilation: mean 59.1 (SEM 3)
14. Maximum HR: median 166 (IQR 155–186) beats per min
15. Recovery HR: mean 100 (SEM 2.9) beats per min
16. BMI: median 26 (IQR 22–30) kg/m^2

Pretreatment group differences: the 3 groups were homogeneous for age, BMI, and disease duration at baseline.

Interventions

Exercise plus usual care

1. **Frequency of exercise sessions:** 3 times/week
2. **Intensity of exercise:** moderate intensity; HR corresponding to 60% of peak oxygen consumption
3. **Time of exercise session:** 30–50 min per session
4. **Type of exercise:** walking was encouraged, but participants were encouraged to take other forms of exercise such as cycling and swimming also
5. **Duration of intervention:** 12 weeks
6. **Supervision/setting:** participants were asked to exercise at home ≥ 3 times per week for 30–50 minutes and were seen by an exercise professional every 2 weeks for a supervised exercise session.

Another non-pharmacological intervention (relaxation) plus usual care

1. **Frequency of exercise sessions:** 3 times/week
2. **Intensity of exercise:** unclear
3. **Time of exercise session:** 30 min
4. **Type of exercise:** participants were asked to listen to a relaxation audiotape a minimum of 3 times/week for 30 min, in a darkened room where it was warm and quiet.
5. **Duration of intervention:** 12 weeks
6. **Supervision/setting:** participants were asked to listen to a 30-minute relaxation audio tape ≥ 3 times per week in a darkened, warm, and quiet room, and were seen every 2 weeks for a supervised relaxation session.

Control group (usual care alone)

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Tench 2003 *(Continued)*

	Participants were asked to continue with their normal daily activity pattern and specifically asked to avoid doing any extra physical activities. They were reviewed at follow-up but not seen at any other times.
Outcomes	1. **Fatigue:** measured using the FSS, CFS, and VAS a. **FSS:** FSS is a 9-item questionnaire, scored on a 7-point Likert scale with 1 = strongly disagree, and 7 = strongly agree. Minimum raw score is 9 and maximum score is 63. However, the mean of all scores can also be taken with a minimum score of 1 and a maximum score of 7. Higher score = greater fatigue severity. A change score of 1.9 points is considered a clinically important change. Measured at baseline and 12 weeks. b. **CFS:** was originally perceived as comprising 2 subscales that evaluate fatigue in the physical and mental domains. Items are rated on a 4-point Likert scale (0 = better than usual, 1 = no more than usual, 2 = worse than usual, 3 = much worse than usual), with higher scores indicating greater fatigue. Measured at baseline and 12 weeks. c. **VAS:** measured using VAS for fatigue. Study authors did not report which scale was used. However, lower scores on VAS usually indicate a better outcome. Measured at baseline and 12 weeks. 2. **Anxiety:** measured using the HADS questionnaire, which consists of 7 questions for anxiety and 7 questions for depression. Questions are compiled, but scored separately. Score range is 0–21. Lower scores indicate a better outcome (a score of 8–10 is mild, 11–14 moderate, and 15–21 severe). 3. **Depression:** measured using the HADS questionnaire, which consists of 7 questions for anxiety and 7 questions for depression. Questions are compiled, but scored separately. Score range is 0–21. Lower scores indicate a better outcome (a score of 8–10 is mild, 11–14 moderate, and 15–21 severe). 4. **Sleep:** measured using the PSQI, which is a self-rated questionnaire that assesses sleep quality and disturbances over a 1-month period. Consisting of 19 individual items, generating 7 'component' scores that include; subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. Score range from 0 (no difficulty) to 3 (severe difficulty). The component scores are summed to produce a final global score (ranging from 0 to 21). Higher scores indicate worse sleep quality. 5. **Disease activity:** measured using the SLAM, which includes both dimensions: disease activity and disease severity over the previous 4 weeks. It assesses 9 organ systems (subjective items include, fatigue, myalgia, arthralgia) and 7 laboratory items. There are 32 items. Score range from 0 to 83. Lower score indicates less disease activity. 6. **QoL:** measured using the SF-36, which is a common tool for assessing the QoL in chronic diseases, and it can be used in any disease, including SLE. It consists of 36 items, grouped into 8 domains covering physical and mental health. The 8 domains include: Functional Capacity, Physical Role Functioning, Pain, General Health, Vitality, Social Role Functioning, Emotional Role Limitations, and Emotional Wellbeing. The score of these domains ranges from 0 to 100, higher scores indicate better health. The study reported Physical Function, Physical Role, and Vitality domains. 7. **Self-rated CGI change:** this is a stand-alone assessment of the clinician's view of the patient's global functioning prior to and after initiating a study medication. Comprised of 2 companion 1-item measures evaluating severity of psychopathology from 1 to 7 and change from the initiation of treatment on a scale of 1 to 7. Rated on a 7-point scale, this indicates the severity of illness scale using a range of responses from 1 (normal) through to 7 (amongst the most severely ill patients).
Notes	**Country:** UK **Funding:** study author CMT was funded by the Arthritis Research Campaign (TO519), the Joint Research Board of St Bartholomew's Hospital (XMKY) and the British Medical Association Doris Hillier Award. **Trial registration:** unknown **Serious adverse events:** none reported **Other adverse events:** none reported **Total adverse events:** none reported

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Tench 2003 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation has been reported. Quote: "All 93 patients were randomly allocated to the exercise programme, the relaxation programme or to no intervention, using a minimisation protocol".
Allocation concealment (selection bias)	Unclear risk	No allocation concealment clearly reported, and, therefore, it was unclear whether this was concealed.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Being an active exercise intervention, it is not possible to blind the participants and supervisors of the intervention; judged at high risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Assessor reported: unclear risk No blinding of outcome assessment (disease activity) was clearly reported. Participant reported: high risk Participants completed self-reported outcomes, and participants knew which group they were in; judged a high risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Authors reported an ITT method of analysis.
Selective reporting (reporting bias)	High risk	Authors did not report scores for all 8 domains in the SF-36: Physical Functioning (10 items); Physical Role Limitations (4 items); Bodily Pain (2 items); General Health Perceptions (5 items); Energy/Vitality (4 items); Social Functioning (2 items); Emotional Role Limitations (3 items), and Mental Health (5 items). Authors also did not report the PCS score and the MCS score for this outcome.
Other bias	Low risk	No other biases.

ACR: American College of Rheumatology; ACR-DI: American College of Rheumatology Damage Index; ACSM: American College of Sports Medicine; BDI: Beck-Depression Index; BMI; body mass index; CES-D: Center for Epidemiologic Studies Depression Scale; CFS: Chandler Fatigue Scale; DASH: Disabilities of the Arm, Shoulder, and Hand; DH: dominant hand; dsDNA: double-stranded DNA; DEXA: dual-energy X-ray absorptiometry; ESR: erythrocyte sedimentation rate; FACIT-Fatigue: Fatigue Assessment of Chronic Illness Therapy – Fatigue subscale; FSS: Fatigue Severity Score; HAQ: Health Assessment Questionnaire; HDL: high-density lipoprotein; HR: heart rate; HRR: heart rate reserve; IFN: interferon; IL: interleukin; IQR: interquartile range; ITT: intention-to-treat; LDL: low-density lipoprotein; LupusQOL: Lupus Quality Of Life; MAC: Mental Adjustment to Cancer; MHR: maximum heart rate; MVPA: moderate-to-vigorous physical activity; n: number; NSAID: non-steroidal anti-inflammatory drug; PCS: Physical Component Score; POMS: Profile Of Moods State; PSQI: Pittsburgh Sleep Quality Index; $PWC_{75\%}$: 75% of the predicted maximal heart rate; QoL: quality of life; RA: rheumatoid arthritis; RCT: randomised controlled trial; RHR: resting heart rate; RM: repetitions maximum; SD: standard deviation; SEM: standard error of the mean; SF-36: 36-item Short Form; SLAM: Systemic Lupus Activity Measure; SLE: systemic lupus erythematosus; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; SLICC: Systemic Lupus International Collaborating Clinics; TNF: tumour necrosis factor; VAS: Visual Analogue Scale; VAT: ventilator anaerobic threshold; VLDL: very low-density lipoprotein; VO_{2max}: maximum rate of oxygen consumption; VO_{2peak}: peak oxygen consumption; WBC: white blood cell; WBVE: whole body vibration exercise.

Characteristics of excluded studies *[ordered by study ID]*

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Study	Reason for exclusion
Abrahao 2009	Conference abstract of 1 of the included studies (Abrahão 2016).
Ahn 2015	Ineligible study design (not an RCT) and ineligible intervention (not a structured exercise intervention).
Barnes 2010	Ineligible intervention (not a structured exercise intervention).
Bogdanovic 2015	Ineligible study design (not an RCT).
Bostrom 2013	Review of the literature (not a trial).
Cenedeze 2016	Ineligible intervention (single bout of exercise and not a structured exercise intervention).
Chapman 2020	Ineligible study design (not an RCT).
Clarke-Jenssen 2005	Ineligible study design (not an RCT).
Da Silva 2013	Ineligible intervention (study of an acute bout of exercise, and did not include an intervention of exercise over a period of time).
De Carvalho 2005	Ineligible study design (not an RCT).
Gavilan-Carrera 2020	Ineligible study design (study was a non-randomised clinical trial).
Gordon 2017	Ineligible study design (not an RCT).
Haglo 2021	Ineligible population: included people with SLE among other rheumatic diseases, and we were unable to distinguish results for the participants with SLE alone.
Hasni 2021	Ineligible study design: not an RCT. Single-group observational study.
Isenberg 1981	Ineligible intervention (study of an acute bout of exercise, and did not include an intervention of exercise over a period of time).
Mak 2020	Review of the literature (not a trial).
Martinez 2021	Ineligible study design (not an RCT). Abstract of the excluded study (Hasni 2021).
Martinez-Rosales 2020	Ineligible study design (not an RCT). Study part of another ineligible study (Soriano-Maldonado 2018).
Perandini 2014	Ineligible study design (not an RCT) and ineligible population (control group were healthy controls, and there was no control group of people with SLE).
Ramsey-Goldman 2000	Ineligible study design (not an RCT).
Sheikh 2019	Ineligible study design (not an RCT).
Sieczkowska 2022	Ineligible population: study of adolescents with juvenile idiopathic arthritis.
Soriano-Maldonado 2018	Ineligible study design (not an RCT).
Tench 2002	Indelible study design (cross-sectional design comparing outcomes in people with SLE and without SLE, and not an RCT of an exercise intervention).

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Study	Reason for exclusion
Youssef 2021	Ineligible study design: not an RCT.
Yuen 2011	Ineligible study design (not an RCT).
Zeppieri-Caruana 2018	Review of the literature (not a trial).

RCT: randomised controlled trial.

Characteristics of studies awaiting classification *[ordered by study ID]*

Boedecker 2020

Methods	**Study design:** 3-arm randomised controlled trial **Setting:** Division of Nephrology, Rheumatology, and Immunology outpatient clinic of the University Medical Center Mainz, Germany **Time trial period:** study registration in May 2019 and enrolment began in May 2019. **Interventions:** aerobic exercise vs anaerobic exercise vs usual care **Sample size calculation:** sample size determined after recruiting and screening multiple participants to determine if they fit the inclusion criteria. **Analysis:** data analysis is ongoing, and results were expected to be submitted for publication in January 2021.
Participants	**Number of participants** 1. Screened: 40 (10 did not meet inclusion criteria) 2. Randomised: 30: 10 in aerobic exercise group, 10 in anaerobic exercise group, and 10 in control group (1 participant withdrew before first performance test and before the programme due to a fracture; unclear which group this participant was randomised to). 3. Included in analyses: 25 participants were included in the 12-week analysis (1 participant has not yet completed the study, and 3 participants withdrew from the study: 1 due to repeated colds so that regular sport was not possible, 1 had a relapse of Crohn's disease during study, and 1 stated that continuing to exercise was not possible due to physical strain). **Inclusion criteria** 1. Aged 18–65 years 2. Diagnosis of SLE by the classification ACR criteria and the 2019 EULAR /ACR Classification Criteria for SLE 3. Positive antinuclear antibody titre (≥ 1:80) or anti-dsDNA c (≥ 200 IU/mL) or positive anti-dsDNA autoantibody (≥ 30 IU/mL) 4. SLE Disease Activity Index ≥ 4 5. For 30 days prior, stable immunosuppressive therapy with steroid (0–20 mg/day) or other immunosuppressive medication such as hydroxychloroquine, chloroquine, azathioprine, methotrexate, mycophenolate mofetil, ciclosporin, belimumab, rituximab. **Exclusion criteria** 1. Pregnancy 2. Active lupus nephritis, myocarditis, or pericarditis 3. Physical activity > 2 times a week **Baseline characteristics** All 30 participants were women.

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Boedecker 2020 *(Continued)*

	No other baseline characteristics were reported.
Interventions	**Anaerobic exercise programme** 1. **Frequency of exercise sessions:** 3 times/week 2. **Intensity of exercise:** each exercise session was to be adjusted (intensity) by interpreting of the training data and the rating of perceived pain and load every week. The recommendations are based on heart rate in training zones related to individual anaerobic threshold. 3. **Time of exercise session:** 20–50 min for each training session. Including 5-min warm-up and 5-min cool-down. Anaerobic training sessions are performed using an intermittent protocol with heart rate above the individual anaerobic threshold for 2–3 min per interval. The progression stages in the anaerobic exercise group range from 3 intervals (1 interval of 3 min + 2 intervals of 2 min each) up to 8 intervals (8 intervals of 3 min each) with a 2-min walking break between intervals. 4. **Type of exercise:** walking or running should be the main part of endurance training sessions. Performing 1 or 2 strength training session weekly or integrating specified strength training exercises into the endurance training (e.g. at the end of running or walking) was also suggested. 10 strength exercises for major muscle groups that can be trained separately with elastic resistance bands, 3 sets with 15 repetitions per exercise each week was created for compilation. The compilation also includes 10 relaxation exercises, recommended for after strength training sessions. 5. **Duration of intervention:** 12 weeks 6. **Supervision/setting:** every Monday, an individualised training schedule was sent to each participant in both intervention groups. Participants are given a weekly protocol, where all physical activities during the week, including all recommended (endurance and strength) and additional activities, should be recorded. After each week, a sports therapist analyses the training data to adapt the schedule for the following week according to participant self-reported values of pain and training load. **Aerobic exercise programme** 1. **Frequency of exercise sessions:** 3 times/week 2. **Intensity of exercise:** each exercise session was to be adjusted (intensity) by interpreting of the training data and the rating of perceived pain and load every week. The recommendations are based on heart rate in training zones related to individual anaerobic threshold. 3. **Time of exercise session:** 20–50 min for each training session. Including 5-min warm-up and 5-min cool-down. Anaerobic training sessions are performed by using an intermittent protocol with heart rate above the individual anaerobic threshold for 2–3 min per interval. The aerobic exercise group performs aerobic training sessions for the whole programme. 4. **Type of exercise:** walking or running should be the main part of endurance training sessions. Performing 1 or 2 strength training session weekly or integrating specified strength training exercises into the endurance training (e.g. at the end of running or walking) was also suggested. 10 strength exercises for major muscle groups that can be trained separately with elastic resistance bands, 3 sets with 15 repetitions per exercise each week was created for compilation. The compilation also includes 10 relaxation exercises, recommended for after strength training sessions. 5. **Duration of intervention:** 12 weeks 6. **Supervision/setting:** every Monday, an individualised training schedule was sent to each participant in both intervention groups. Participants are given a weekly protocol, where all physical activities during the week, including all recommended (endurance and strength) and additional activities, should be recorded. After each week, a sports therapist analyses the training data to adapt the schedule for the following week according to participant self-reported values of pain and training load. **Usual care** To assess the effect of the intervention programme, the control group (treatment as usual) will participate in voluntary exercise that is assessed using a questionnaire for habitual physical activity. These participants also received a smartwatch.
Outcomes	**Primary outcomes**

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Boedecker 2020 *(Continued)*

1. **VO_{2peak}:** measured using spiroergometry at weeks 0 and 12.

Secondary outcomes

1. **Fatigue Scale for Motor and Cognitive Functions:** scale consists of 20 items using a 5-point Likert scale, from absolutely agree to absolutely disagree, to assess cognitive fatigue (10 items) and motor fatigue (10 Fatigue Scale for Motor and Cognitive Functions items). The scores for cognitive and motor fatigue are added for the sum score. A cutoff value of 43 indicates mild fatigue, whereas higher values are associated with moderate fatigue (≥ 53) or severe fatigue (≥ 63). Outcome measured at weeks 0, 12, and 24.
2. **Beck-Depression Inventory:** questionnaire consists of 21 sets of statements, which are ranked in terms of severity from 0 to 3. The sum (range 0–63) indicates the severity of depression. The standardised scale is 0–8, no depression; 9–13, minimal depression; 14–19, mild depression: 20–28, moderate depression, 29–63: severe depression. Outcome measured at weeks 0, 12, and 24.
3. **SLE disease activity index:** index consists of 24 items including clinical and laboratory variables to measure disease activity within the previous 10 days. Maximum score 105, scores > 3 indicate a mild or moderate flare, and scores ≥ 12 indicate a severe flare. Outcome measured at weeks 0, 12, and 24.
4. **Disease Activity Score-28:** score indicates rheumatoid arthritis disease activity and treatment response. It is composed of 4 measures including the number of swollen or tender joints, C-reactive protein level, and patient's health assessment. A total score is calculated using the formula. Values range from 2.0 to 10, where a higher value indicates higher disease activity. The score is a valuable tool to assess the severity of joint involvement and activity in SLE. Outcome measured at weeks 0, 12, and 24.
5. **Work Ability Index:** self-assessment questionnaire used to assess the work ability of the patients. The questionnaire covers 6 dimensions including current work ability, as well as past 2-year estimation amongst others: 7–27 points indicates poor, 28–36 points indicates moderate, 37–43 points indicates good, and 44–49 points indicates very good work ability. Outcome measured at weeks 0, 12, and 24.
6. **Revised Cutaneous Lupus Erythematosus Disease Area and Severity Index:** scoring system includes a score to measure the activity of skin lesions and a score to measure the damage to skin lesions in people with discoid lupus erythematosus and cutaneous lupus erythematosus. The score is used as a follow-up parameter. It has been shown that scores correlate well with the physician's and patient's global assessment of disease activity. Outcome measured at weeks 0, 12, and 24.
7. **Autoantibody titres:** DNA b (standard value ≤ 20 IU). Outcome measured at weeks 0, 12, and 24.
8. **Complement level:** C3c and C4 levels (standard values: C3c: 0.9–1.8 g/L; C4: 0.1–0.4 g/L). Outcome measured at weeks 0, 12, and 24.
9. **Circulating, cell-free DNA levels:** concentration of circulating, cell-free DNA (ng/mL) measured before, during, and after laboratory standardised stepwise exercise test from capillary and venous blood samples. After centrifugation of the samples, the circulating cell-free DNA is determined by a direct quantitative real-time polymerase chain reaction method from plasma without previous DNA extraction. Compared to healthy participants, participants with SLE show higher circulating cell-free DNA plasma levels. Outcome measured at weeks 0 and 12.
10. **Extracellular vesicles:** relative amount of extracellular vesicle subpopulations analysed using bead isolation and size exclusion chromatography followed by protein marker characterisation. Outcome measured at weeks 0 and 12.
11. **Lactate levels:** to estimate the lactate threshold, capillary blood samples were taken from the fingertips using end-to-end capillary with a defined volume of 20 µL sodium heparin (EKF-Diagnostics GmbH) before analysis using the Biosen S-Line (EKF-Diagnostics GmbH). In this study, capillary blood samples were taken at the beginning of the test, after each step of treadmill walking, and 3 min after exhaustion. All samples were quantified directly after the test. To define the anaerobic lactate acid threshold or individual anaerobic threshold the Dickhuth model (baseline) +1.5 mmol/L model was used. Outcome measured at weeks 0 and 12.
12. **Ventilatory threshold:** change in ventilatory threshold after 12 weeks compared to baseline. Outcome measured at weeks 0 and 12.
13. **Muscle mass:** muscle mass measured in absolute mass (kilograms) including internal organs using bioelectrical impedance analysis. Outcome measured at weeks 0 and 12.

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Boedecker 2020 *(Continued)*

14. **Borg's scale:** ratings of perceived exertion with the Borg 15-grade scale (range 6–20) within the last 30 s of each stage of walking recorded. Higher scores indicate higher perceived exertion. Outcome measured at weeks 0 and 12.
15. **Smartwatch data:** evaluation of the physical strain and performance during the weekly training sessions measured by heart rate and distance covered during running. Outcome measured at weeks 0 and 12.

Notes	**Country:** Germany **Funding:** University of Mainz, Germany **Trial registration:** DERR1-10.2196/18291 **Serious adverse events:** none reported **Other adverse events:** none reported **Total adverse events:** not reported

ACR: American College of Rheumatology; anti-dsDNA: antidouble stranded DNA; EULAR: European League Against Rheumatism; min: min; SLE: systemic lupus erythematosus.

DATA AND ANALYSES

Comparison 1. Exercise plus usual pharmacological care versus placebo plus usual pharmacological care (exercises versus placebo)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Fatigue (FACIT fatigue, score 0–52, lower scores indicate less fatigue)	1	17	Mean Difference (IV, Random, 95% CI)	-5.00 [-13.29, 3.29]
1.2 Functional capacity (SF-36 Function Capacity domain, score 0–100, higher scores indicate better functional capacity)	1	17	Mean Difference (IV, Random, 95% CI)	-2.50 [-23.78, 18.78]
1.3 Pain (SF-36 Pain domain, score 0–100, lower scores indicate less pain)	1	17	Mean Difference (IV, Random, 95% CI)	-9.00 [-28.88, 10.88]
1.4 Withdrawals for any reason	1	21	Risk Ratio (M-H, Random, 95% CI)	2.73 [0.34, 22.16]

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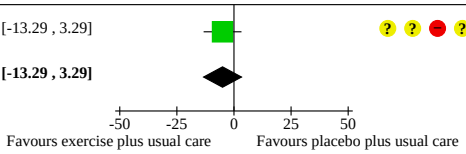
Analysis 1.1. Comparison 1: Exercise plus usual pharmacological care versus placebo plus usual pharmacological care (exercises versus placebo), Outcome 1: Fatigue (FACIT fatigue, score 0–52, lower scores indicate less fatigue)

Study or Subgroup	Exercise plus usual care Mean	SD	Total	Placebo plus usual care Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Lopes-Souza 2021 (1)	-43	7.21	8	-38	10.12	9	100.0%	-5.00 [-13.29 , 3.29]
Total (95% CI)			**8**			**9**	**100.0%**	**-5.00 [-13.29 , 3.29]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.18 (P = 0.24)
Test for subgroup differences: Not applicable



Risk of Bias: A B C D E F G

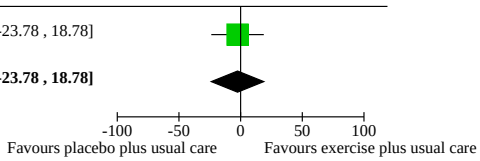
Footnotes
(1) FACIT: Functional Assessment of Chronic Illness Therapy.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.2. Comparison 1: Exercise plus usual pharmacological care versus placebo plus usual pharmacological care (exercises versus placebo), Outcome 2: Functional capacity (SF-36 Function Capacity domain, score 0–100, higher scores indicate better functional capacity)

Study or Subgroup	Exercise plus usual care Mean	SD	Total	Placebo plus usual care Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Lopes-Souza 2021 (1)	67.5	22.2	8	70	22.5	9	100.0%	-2.50 [-23.78 , 18.78]
Total (95% CI)			**8**			**9**	**100.0%**	**-2.50 [-23.78 , 18.78]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.23 (P = 0.82)
Test for subgroup differences: Not applicable

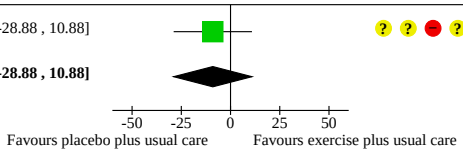


Footnotes
(1) SF-36: 36-item Short Form questionnaire.

Analysis 1.3. Comparison 1: Exercise plus usual pharmacological care versus placebo plus usual pharmacological care (exercises versus placebo), Outcome 3: Pain (SF-36 Pain domain, score 0–100, lower scores indicate less pain)

Study or Subgroup	Exercise plus usual care Mean	SD	Total	Placebo plus usual care Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Lopes-Souza 2021 (1)	34	16.18	8	43	25.13	9	100.0%	-9.00 [-28.88 , 10.88]
Total (95% CI)			**8**			**9**	**100.0%**	**-9.00 [-28.88 , 10.88]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.89 (P = 0.37)
Test for subgroup differences: Not applicable



Risk of Bias: A B C D E F G

Footnotes
(1) SF-36: 36-item Short Form.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

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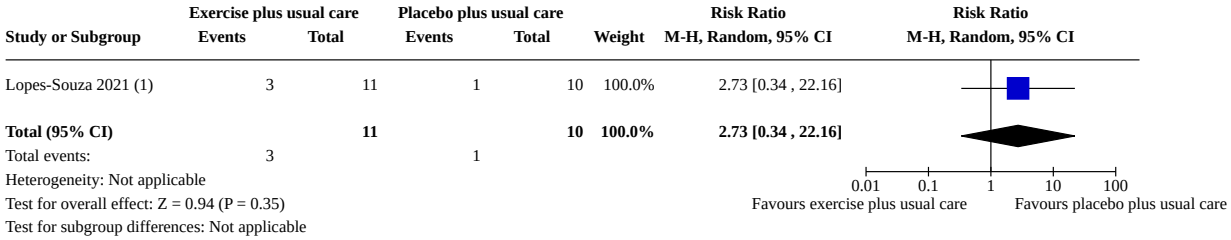
Analysis 1.4. Comparison 1: Exercise plus usual pharmacological care versus placebo plus usual pharmacological care (exercises versus placebo), Outcome 4: Withdrawals for any reason



Footnotes

(1) Exercise plus usual care group: 1 discontinued due to low back pain, and 2 for personal reasons. Placebo plus usual care: 1 discontinued for personal reasons.

Comparison 2. Exercise plus usual pharmacological care versus usual pharmacological care alone (exercise versus usual care alone)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Fatigue (Fatigue Severity Scale, score 1–7, lower score indicates less fatigue)	2	104	Mean Difference (IV, Random, 95% CI)	-0.59 [-1.40, 0.22]
2.2 Functional capacity (SF-36 Physical Function domain, score 0–100, higher scores indicate better functional capacity)	2	96	Mean Difference (IV, Random, 95% CI)	5.39 [-5.97, 16.75]
2.3 Disease activity (various scales, lower scores indicate less disease activity)	2	100	Mean Difference (IV, Random, 95% CI)	-0.26 [-3.69, 3.17]
2.4 Pain (SF-36 Pain domain, score 0–100, lower scores indicate less pain)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.5 Withdrawals for any reason	6	235	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.53, 1.60]
2.6 Aerobic capacity (peak oxygen uptake, higher scores indicate better aerobic capacity)	3	109	Mean Difference (IV, Random, 95% CI)	1.27 [-0.59, 3.12]
2.7 Depression (various scales, lower score indicates less depression)	1	65	Std. Mean Difference (IV, Random, 95% CI)	-0.29 [-0.78, 0.20]
2.8 Anxiety (HADS Anxiety, score 0–21, lower score indicates less anxiety)	1	65	Mean Difference (IV, Random, 95% CI)	-0.80 [-3.02, 1.42]

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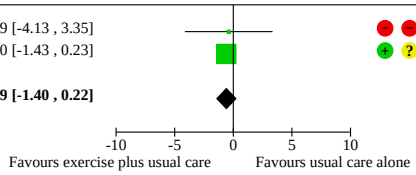
Analysis 2.1. Comparison 2: Exercise plus usual pharmacological care versus usual pharmacological care alone (exercise versus usual care alone), Outcome 1: Fatigue (Fatigue Severity Scale, score 1–7, lower score indicates less fatigue)

Study or Subgroup	Exercise plus usual care Mean	SD	Total	Usual care alone Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Avaux 2016 (1)	5.11	5.39	31	5.5	4.65	8	4.7%	-0.39 [-4.13 , 3.35]
Tench 2003	4.8	1.723369	33	5.4	1.697056	32	95.3%	-0.60 [-1.43 , 0.23]
Total (95% CI)			**64**			**40**	**100.0%**	**-0.59 [-1.40 , 0.22]**

Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.91); I² = 0%
Test for overall effect: Z = 1.42 (P = 0.15)
Test for subgroup differences: Not applicable



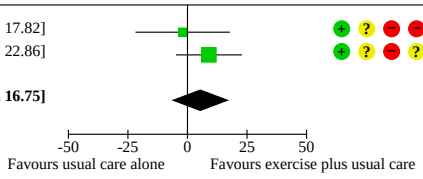
Footnotes
(1) Result is the combined mean and standard deviation of the two exercise groups.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 2.2. Comparison 2: Exercise plus usual pharmacological care versus usual pharmacological care alone (exercise versus usual care alone), Outcome 2: Functional capacity (SF-36 Physical Function domain, score 0–100, higher scores indicate better functional capacity)

Study or Subgroup	Exercise plus usual care Mean	SD	Total	Usual care alone Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Bostrom 2016 (1)	63	25.93	17	65	29.63	14	32.8%	-2.00 [-21.82 , 17.82]
Tench 2003 (1)	69	28.73	33	60	28.28	32	67.2%	9.00 [-4.86 , 22.86]
Total (95% CI)			**50**			**46**	**100.0%**	**5.39 [-5.97 , 16.75]**

Heterogeneity: Tau² = 0.00; Chi² = 0.79, df = 1 (P = 0.37); I² = 0%
Test for overall effect: Z = 0.93 (P = 0.35)
Test for subgroup differences: Not applicable



Footnotes
(1) SF-36 Physical Function domain (higher value = better function (scale 0–100)).

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

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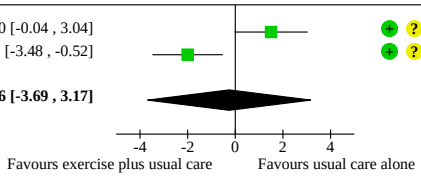
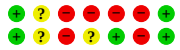
Analysis 2.3. Comparison 2: Exercise plus usual pharmacological care versus usual pharmacological care alone (exercise versus usual care alone), Outcome 3: Disease activity (various scales, lower scores indicate less disease activity)

Study or Subgroup	Exercise plus usual care Mean	SD	Total	Usual care alone Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Bostrom 2016 (1)	2	2.96	18	0.5	1.48	17	49.8%	1.50 [-0.04 , 3.04]
Tench 2003 (2)	4	3.7	33	6	2.22	32	50.2%	-2.00 [-3.48 , -0.52]
Total (95% CI)			**51**			**49**	**100.0%**	**-0.26 [-3.69 , 3.17]**

Heterogeneity: Tau² = 5.53; Chi² = 10.34, df = 1 (P = 0.001); I² = 90%
Test for overall effect: Z = 0.15 (P = 0.88)
Test for subgroup differences: Not applicable



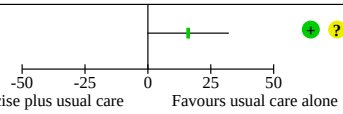


Footnotes
(1) SLEDAI: Systemic Lupus Erythematosus Disease Activity Index (lower scores indicate less disease activity (score range 0–105).
(2) SLAM: Systemic Lupus Activity Measure (lower scores indicate less disease activity (score range 0–83).

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 2.4. Comparison 2: Exercise plus usual pharmacological care versus usual pharmacological care alone (exercise versus usual care alone), Outcome 4: Pain (SF-36 Pain domain, score 0–100, lower scores indicate less pain)

Study or Subgroup	Exercise plus usual care Mean	SD	Total	Usual care alone Mean	SD	Total	Mean Difference IV, Random, 95% CI
Bostrom 2016 (1)	54	21.91	17	38	23.64	14	16.00 [-0.18 , 32.18]



Footnotes
(1) SF-36 Pain (higher score indicates less pain; score range 0–100). We inversed this to match other comparisons. Data extracted from 3-month analyses.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

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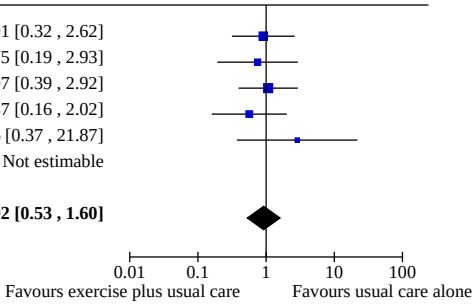
Analysis 2.5. Comparison 2: Exercise plus usual pharmacological care versus usual pharmacological care alone (exercise versus usual care alone), Outcome 5: Withdrawals for any reason

Study or Subgroup	Exercise plus usual care Events	Total	Usual care alone Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Avaux 2016 (1)	10	33	3	9	27.1%	0.91 [0.32 , 2.62]
Benatti 2015 (2)	3	20	4	20	16.4%	0.75 [0.19 , 2.93]
Benatti 2018 (3)	5	14	5	15	30.2%	1.07 [0.39 , 2.92]
Bostrom 2016 (4)	3	18	5	17	18.9%	0.57 [0.16 , 2.02]
Hashemi 2022 (5)	4	14	1	10	7.3%	2.86 [0.37 , 21.87]
Tench 2003 (6)	0	33	0	32		Not estimable
Total (95% CI)		**132**		**103**	**100.0%**	**0.92 [0.53 , 1.60]**
Total events:	25		18			

Heterogeneity: Tau² = 0.00; Chi² = 1.93, df = 4 (P = 0.75); I² = 0%
Test for overall effect: Z = 0.29 (P = 0.77)
Test for subgroup differences: Not applicable



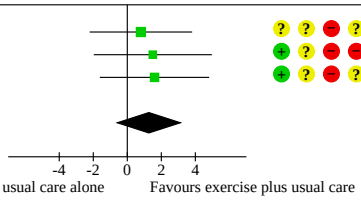
Footnotes

(1) Exercise plus usual care: reasons for withdrawal not clear for each group.
(2) Exercise plus usual care: 3 withdrew for personal reasons; usual care alone: 4 withdrew for personal reasons.
(3) Exercise plus usual care: 5 withdrew (see text); usual care alone: 5 withdrew (see text).
(4) Exercise plus usual care: 3 withdrew (see text); usual care alone: 3 withdrew after 2 weeks, and then another 2 withdrew (see text).
(5) Authors did not report why 5 participants (1 in usual care alone, and 4 in exercise plus usual care) were not included in analyses.
(6) Authors did not clearly report how many withdrew from each group.

Analysis 2.6. Comparison 2: Exercise plus usual pharmacological care versus usual pharmacological care alone (exercise versus usual care alone), Outcome 6: Aerobic capacity (peak oxygen uptake, higher scores indicate better aerobic capacity)

Study or Subgroup	Exercise plus usual care Mean	SD	Total	Usual care alone Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Benatti 2018 (1)	24.6	2.99	9	23.8	3.7	10	38.0%	0.80 [-2.21 , 3.81]	? ? − ? − − +
Bostrom 2016 (2)	23.7	4.16	12	22.2	4.69	13	28.6%	1.50 [-1.97 , 4.97]	+ ? − − − − +
Tench 2003 (3)	23.8	5.74	33	22.2	7.35	32	33.4%	1.60 [-1.61 , 4.81]	+ ? − ? + − +
Total (95% CI)			**54**			**55**	**100.0%**	**1.27 [-0.59 , 3.12]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 2 (P = 0.93); I² = 0%
Test for overall effect: Z = 1.34 (P = 0.18)
Test for subgroup differences: Not applicable



Footnotes

(1) VO 2peak (mL/kg/min) used (higher scores indicate better aerobic capacity).
(2) VO 2max (mL/kg/min) used (higher scores indicate better aerobic capacity).
(3) Peak oxygen uptake (mL/kg/min) used (higher scores indicate better aerobic capacity).

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

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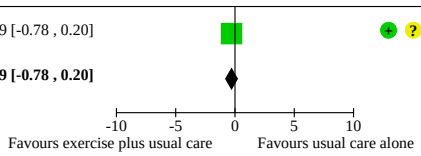
Analysis 2.7. Comparison 2: Exercise plus usual pharmacological care versus usual pharmacological care alone (exercise versus usual care alone), Outcome 7: Depression (various scales, lower score indicates less depression)

Study or Subgroup	Exercise plus usual care Mean	SD	Total	Usual care alone Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Tench 2003 (1)	4.6	4.02	33	5.7	3.4	32	100.0%	-0.29 [-0.78 , 0.20]
Total (95% CI)			**33**			**32**	**100.0%**	**-0.29 [-0.78 , 0.20]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.17 (P = 0.24)
Test for subgroup differences: Not applicable



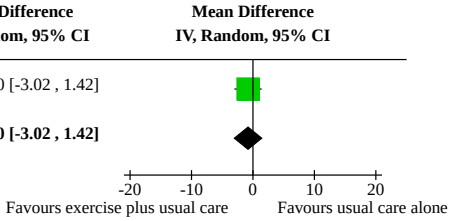
Footnotes
(1) Hospital Anxiety and Depression Scale – Depression used (lower scores indicate less depression (score range 0–21)).

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 2.8. Comparison 2: Exercise plus usual pharmacological care versus usual pharmacological care alone (exercise versus usual care alone), Outcome 8: Anxiety (HADS Anxiety, score 0–21, lower score indicates less anxiety)

Study or Subgroup	Exercise plus usual care Mean	SD	Total	Usual care alone Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Tench 2003 (1)	7.4	4.59565	33	8.2	4.525483	32	100.0%	-0.80 [-3.02 , 1.42]
Total (95% CI)			**33**			**32**	**100.0%**	**-0.80 [-3.02 , 1.42]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.71 (P = 0.48)
Test for subgroup differences: Not applicable



Footnotes
(1) Hospital Anxiety and Depression Scale – Anxiety.

Comparison 3. Exercise plus usual pharmacological care versus another non-pharmacological intervention plus usual pharmacological care (exercise versus active control)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Fatigue (various scales, lower score indicate less fatigue)	2	119	Std. Mean Difference (IV, Random, 95% CI)	-0.51 [-0.88, -0.14]
3.2 Functional capacity (various scales, higher scores indicate better functional capacity)	3	182	Mean Difference (IV, Random, 95% CI)	13.20 [6.17, 20.22]
3.3 Disease activity (various scales, lower scores indicate less disease activity)	4	184	Std. Mean Difference (IV, Random, 95% CI)	0.02 [-0.28, 0.32]
3.4 Pain (various scales, lower score indicates less pain)	2	121	Mean Difference (IV, Random, 95% CI)	-1.59 [-2.46, -0.71]
3.5 Withdrawals for any reason	7	317	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.13, 5.94]

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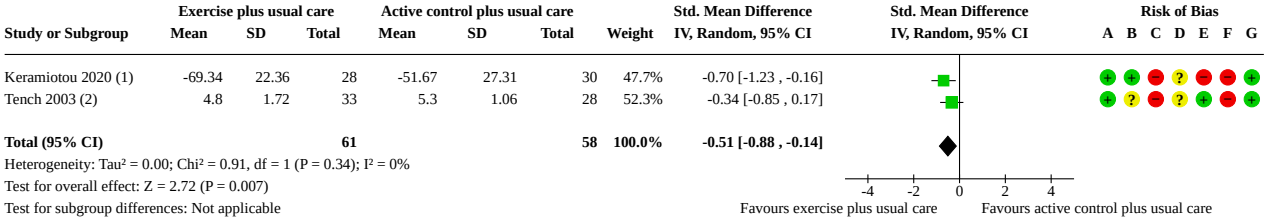
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.6 Aerobic capacity (peak oxygen uptake, higher scores indicate better aerobic capacity)	2	99	Mean Difference (IV, Random, 95% CI)	1.19 [-1.64, 4.02]
3.7 Depression (BDI, score 0–63, lower scores indicate less depression)	1	61	Mean Difference (IV, Random, 95% CI)	-1.40 [-4.61, 1.81]
3.8 Anxiety (HADS Anxiety, score 0–21, lower score indicates less anxiety)	1	61	Mean Difference (IV, Random, 95% CI)	-1.10 [-3.61, 1.41]

Analysis 3.1. Comparison 3: Exercise plus usual pharmacological care versus another non-pharmacological intervention plus usual pharmacological care (exercise versus active control), Outcome 1: Fatigue (various scales, lower score indicate less fatigue)



Footnotes

(1) LupusQOL Fatigue used (higher score indicates less fatigue (scale 0–100)). Control group received joint aids and information about their disease.
(2) Krupp Fatigue Severity Scale used (lower scores indicate less fatigue severity (scale 1–7)). Control group received relaxation therapy.

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

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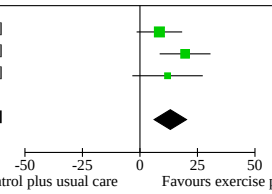
Analysis 3.2. Comparison 3: Exercise plus usual pharmacological care versus another non-pharmacological intervention plus usual pharmacological care (exercise versus active control), Outcome 2: Functional capacity (various scales, higher scores indicate better functional capacity)

Study or Subgroup	Exercise plus usual care Mean	SD	Total	Active control plus usual care Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Abrahão 2016 (1)	49.85	22.93	42	41.4	15.7	19	44.0%	8.45 [-1.45 , 18.35]	+ + − ? + − +
Keramiotou 2020 (2)	72.95	21.54	30	53.33	22.12	30	36.2%	19.62 [8.57 , 30.67]	+ + − ? − − +
Tench 2003 (3)	69	28.72	33	57	31.75	28	19.9%	12.00 [-3.31 , 27.31]	+ ? − ? + − +
Total (95% CI)			**105**			**77**	**100.0%**	**13.20 [6.17 , 20.22]**	

Heterogeneity: Tau² = 3.74; Chi² = 2.21, df = 2 (P = 0.33); I² = 9%
Test for overall effect: Z = 3.68 (P = 0.0002)
Test for subgroup differences: Not applicable



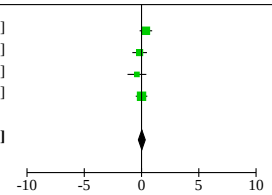
Footnotes
(1) SF-36 Physical Function domain used (higher scores indicate better functional capacity (scale 0–100)). Control group included education.
(2) LupusQOL Physical domain used (higher scores indicate better functional capacity (scale 0–100)). Control group received joint aids and information about their disease.
(3) SF-36 Physical Function domain used (higher scores indicate better functional capacity (scale 0–100)). Control group received relaxation therapy.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.3. Comparison 3: Exercise plus usual pharmacological care versus another non-pharmacological intervention plus usual pharmacological care (exercise versus active control), Outcome 3: Disease activity (various scales, lower scores indicate less disease activity)

Study or Subgroup	Exercise plus usual care Mean	SD	Total	Active control plus usual care Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Abrahão 2016 (1)	1.45	0.73	42	1.2	0.4	19	29.8%	0.38 [-0.17 , 0.93]	+ + − ? + − +
Dos Reis-Neto 2013 (1)	2.4	2.3	18	3.1	5.3	20	21.9%	-0.16 [-0.80 , 0.47]	− ? − − − + +
Miossi 2012 (1)	0.8	1.2	14	1.3	1.2	10	13.3%	-0.40 [-1.22 , 0.42]	? ? − ? + + +
Tench 2003 (2)	4	12.85	33	4	10.58	28	35.0%	0.00 [-0.50 , 0.50]	+ ? − ? + − +
Total (95% CI)			**107**			**77**	**100.0%**	**0.02 [-0.28 , 0.32]**	

Heterogeneity: Tau² = 0.00; Chi² = 3.02, df = 3 (P = 0.39); I² = 1%
Test for overall effect: Z = 0.16 (P = 0.87)
Test for subgroup differences: Not applicable



Footnotes
(1) SLEDAI used (lower scores indicate less disease activity (scale 0–105)). Control group received information about their disease.
(2) SLAM used (lower scores indicate less disease activity (score 0–83)). Control group received relaxation therapy.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

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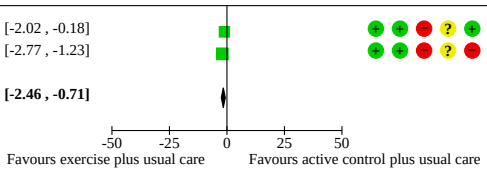
Analysis 3.4. Comparison 3: Exercise plus usual pharmacological care versus another non-pharmacological intervention plus usual pharmacological care (exercise versus active control), Outcome 4: Pain (various scales, lower score indicates less pain)

Study or Subgroup	Exercise plus usual care Mean	SD	Total	Active control plus usual care Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Abrahão 2016 (1)	6.4	2.3	42	7.5	1.4	21	46.1%	-1.10 [-2.02 , -0.18]		+ + - ? + - +
Keramiotou 2020 (2)	2.97	1.45	28	4.97	1.56	30	53.9%	-2.00 [-2.77 , -1.23]		+ + - ? - - +
Total (95% CI)			**70**			**51**	**100.0%**	**-1.59 [-2.46 , -0.71]**		

Heterogeneity: Tau² = 0.22; Chi² = 2.16, df = 1 (P = 0.14); I² = 54%
Test for overall effect: Z = 3.53 (P = 0.0004)
Test for subgroup differences: Not applicable



Footnotes

(1) SF-36 Bodily Pain domain used (lower scores indicates less pain (score 0–100)). Control group received information about their disease.
(2) VAS Pain used (lower scores indicate less pain (scores 0 to 10)). Control group received joint aids and information about their disease.

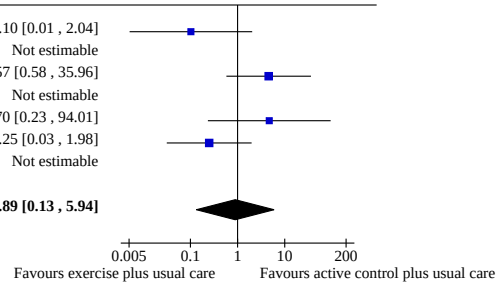
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.5. Comparison 3: Exercise plus usual pharmacological care versus another non-pharmacological intervention plus usual pharmacological care (exercise versus active control), Outcome 5: Withdrawals for any reason

Study or Subgroup	Exercise plus usual care Events	Total	Active control plus usual care Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Abrahão 2016 (1)	0	42	2	21	21.0%	0.10 [0.01 , 2.04]	
Daltroy 1995 (2)	0	16	0	18		Not estimable	
Dos Reis-Neto 2013 (3)	5	23	1	21	29.0%	4.57 [0.58 , 35.96]	
Kao 2021 (4)	0	12	0	11		Not estimable	
Keramiotou 2020 (5)	2	32	0	30	21.0%	4.70 [0.23 , 94.01]	
Miossi 2012 (6)	1	15	4	15	28.9%	0.25 [0.03 , 1.98]	
Tench 2003 (7)	0	33	0	28		Not estimable	
Total (95% CI)		**173**		**144**	**100.0%**	**0.89 [0.13 , 5.94]**	
Total events:	8		7				

Heterogeneity: Tau² = 2.12; Chi² = 7.04, df = 3 (P = 0.07); I² = 57%
Test for overall effect: Z = 0.12 (P = 0.91)
Test for subgroup differences: Not applicable



Footnotes

(1) Active control plus usual care: 2 people abandoned the study without reason. Control group received information about their disease.
(2) Authors did not clearly report dropouts for participants with SLE alone. Control group received information about their disease.
(3) Exercise plus usual care: 5 withdrew. Control group received information about their disease.
(4) No withdrawals reported. Control group received information about their disease.
(5) Exercise plus usual care: 2 people withdrew after 6 weeks for no reported reason. Control group received joint aids and information about their disease.
(6) Control group received information about their disease.
(7) Authors did not clearly report dropouts within each group. Control group received relaxation therapy.

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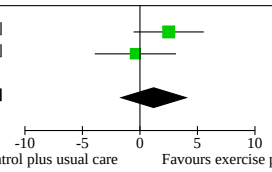
Analysis 3.6. Comparison 3: Exercise plus usual pharmacological care versus another non-pharmacological intervention plus usual pharmacological care (exercise versus active control), Outcome 6: Aerobic capacity (peak oxygen uptake, higher scores indicate better aerobic capacity)

Study or Subgroup	Exercise plus usual care Mean	SD	Total	Active control plus usual care Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Dos Reis-Neto 2013	28	4.5	18	25.5	5.1	20	54.9%	2.50 [-0.55 , 5.55]		− ? − − − + +
Tench 2003	23.8	5.74	33	24.2	7.94	28	45.1%	-0.40 [-3.93 , 3.13]		+ ? − ? + − +
Total (95% CI)			**51**			**48**	**100.0%**	**1.19 [-1.64 , 4.02]**		

Heterogeneity: Tau² = 1.37; Chi² = 1.48, df = 1 (P = 0.22); I² = 33%
Test for overall effect: Z = 0.83 (P = 0.41)
Test for subgroup differences: Not applicable

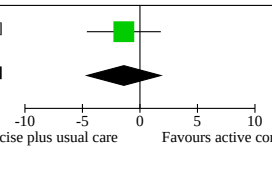


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.7. Comparison 3: Exercise plus usual pharmacological care versus another non-pharmacological intervention plus usual pharmacological care (exercise versus active control), Outcome 7: Depression (BDI, score 0–63, lower scores indicate less depression)

Study or Subgroup	Exercise plus usual care Mean	SD	Total	Active control plus usual care Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Abrahão 2016 (1)	18.7	6	42	20.1	5.9	19	100.0%	-1.40 [-4.61 , 1.81]		+ + − ? + − +
Total (95% CI)			**42**			**19**	**100.0%**	**-1.40 [-4.61 , 1.81]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.85 (P = 0.39)
Test for subgroup differences: Not applicable



Footnotes
(1) BDI: Beck Depression Inventory.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

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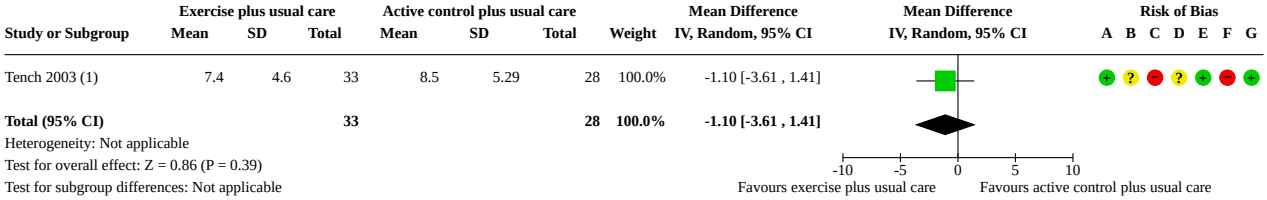
Analysis 3.8. Comparison 3: Exercise plus usual pharmacological care versus another non-pharmacological intervention plus usual pharmacological care (exercise versus active control), Outcome 8: Anxiety (HADS Anxiety, score 0–21, lower score indicates less anxiety)



Footnotes
(1) HADS: Hospital Anxiety and Depression Scale – Anxiety.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

ADDITIONAL TABLES

Table 1. Characteristics of interventions in included studies

Study ID	Description of usual care	Description of exercise group	Description of control group
Trials with a placebo plus usual care control			
Lopes-Souza 2021	The SLE treatment outlined at baseline for each intervention group included: **Exercise group (n = 11)** 1. Mean lupus treatment prednisone (change in daily dose) 5.3 (SD 5.3) mg 2. Mean lupus treatment prednisone (change in cumulative dose 6 months) 896 (SD 337) months 3. Mean lupus treatment time of prednisone use: 13.3 (SD 5.4) years Number (%) of participants on the following medications: 1. hydroxychloroquine: 8 (73%) 2. immunosuppressants: 10 (90%) **Control group (n = 10)**	Participants received usual care and whole body vibration exercise 2 times/week (24 hours between sessions) for 12 weeks. WBVE is a subgroup of resistance training, better classified as muscle activation or neuromuscular training complementary to resistance training. The participants were positioned on the vibrating platform (turned on) with 130° of knee flexion. It is unclear whether this was supervised. **Intensity of exercise** **Week 1–4:** 10 bouts of 30 s, frequency 30 Hz, D 1.23 mm, and a peak of 2.22 g. **Week 5–8:** 10 bouts of 60 s, frequency 40 Hz, D 0.95 mm, and a peak of 3.06 g. **Week 9–12:** 10 bouts of 60 s, frequency 50 Hz, D 0.88 mm, and a peak of 4.40 g. **Time of exercise session** **Week 1–4:** 2-min warm-up, 5-min WBVE. **Week 5–12:** 2-min warm-up, 10-min WBVE. 3 participants dropped out; 1 withdrew before 6-week analysis due to low back pain ("not related directly with the intervention"), and 2 withdrew before 12-week analysis for personal reasons.	Participants received usual care and isometry[a] (they did not receive any vibration), 2 times/week (24 hours between sessions) for 12 weeks. [a]Participants were requested to maintain stance with 130° of knee flexion on the same vibrating platform (vibration turned off). It is unclear whether this was supervised. **Intensity of exercise:** light-to-moderate intensity, warm-up performed in the same way as in WBVE group. Cycles, working, and rest times corresponded to the weeks,

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Table 1. Characteristics of interventions in included studies *(Continued)*

	1. Mean lupus treatment prednisone (change in daily dose) 5.0 (SD 1.9) mg 2. Mean lupus treatment prednisone (change in cumulative dose 6 months) 963 (SD 950) months 3. Mean lupus treatment time of prednisone use: 14.8 (SD 7.1) years Number (%) of participants on the following medications: 1. hydroxychloroquine: 7 (70%) 2. immunosuppressants: 7 (70%) No further information about their usual care was reported.		consistent with the WBVE group, but without vibration. **Time of exercise session** **Week 1–4:** 2-min warm-up, 5-min stood on platform. **Week 5–12:** 2-min warm-up, 10-min stood on platform. 1 participant withdrew before the 6-week analysis for personal reasons.
Trials with a **usual care alone control**			
Avaux 2016	No information about their usual care was reported.	Participants received usual care plus an exercise programme that was supervised or performed independently at home. All participants were asked to perform 3 hours of exercise per week for 12 weeks. At start of programme, the home-training group and supervised training group participated in a multidisciplinary information session about the benefits of exercise in SLE, during which practical information was also delivered. Participants in both groups were asked to record their number of training hours. **Exercise group 1: home training** Participants performed endurance exercise (walking or bicycle) and strengthening exercises (elastic band or weights for upper and lower limbs), at home unsupervised. The targeted intensity was moderate (60–80% of theoretical maximal HR). The modified Borg scale was used to determine participant's perception of exertion at PWC75%. **Exercise group 2: supervised training** Participants performed the same exercise programme; endurance exercise (walking or bicycle) and strengthening exercises (elastic band or weights for upper and lower limbs), in the hospital-based revalidation centre under the supervision of the multidisciplinary team. Targeted intensity was moderate (60–80% of theoretical maximal HR). The modified Borg scale was used to determine participant's perception of exertion at PWC75%.	Participants did not attend the information session and were asked not to change their level of physical activity. No further information reported.

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Table 1. Characteristics of interventions in included studies *(Continued)*

Benatti 2015	The SLE treatment outlined at baseline for each intervention group. **Exercise group (n = 17)** 1. Mean cumulative prednisone dose: 31.2 (SD 33.7) g 2. Mean prednisone dose: 11.5 (SD 12.8) mg 3. Number of participants on the following medications: a. prednisone: 12 (70.6%) b. azathioprine: 9 (52.9%) c. chloroquine: 11 (64.7%) d. methotrexate: 1 (5.9%) e. mycophenolate mofetil: 5 (29.4%) f. cyclophosphamide: 2 (11.8%) **Control group (n = 16)** 1. Mean cumulative prednisone dose: 21.8 (SD 15.6) g 2. Mean prednisone dose: 7.2 (SD 8.6) mg 3. Number of participants on the following medications: a. prednisone: 10 (62.5%) b. azathioprine: 7 (43.7%) c. chloroquine: 10 (62.5%) d. methotrexate: 4 (25.0%) e. mycophenolate mofetil: 2 (12.5%) f. cyclophosphamide: 0 (0%) No further information about their usual care reported.	Participants received usual care plus a combined resistance and cardiovascular supervised exercise training programme for 12 weeks. Participants performed approximately 30 min of cardiovascular endurance exercise and strength exercise, 2 times/week. Intensity was set at the HR corresponding to the interval between ventilatory anaerobic threshold and 10% below respiratory compensation point.	Participants remained physically inactive. No further information reported.
Benatti 2018	The SLE treatment outlined at baseline for each intervention group. **Exercise group (n = 9)**	Participants received usual care plus a supervised aerobic exercise programme in an intrahospital gymnasium for 12 weeks. Participants performed 40–60 min of aerobic exercise (5-min warm-up, followed by 30–50 min	Participants were strongly instructed to maintain their usual living activi-

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Table 1. Characteristics of interventions in included studies *(Continued)*

	1. Mean cumulative glucocorticoid dose: 42.1 (SD 31.8) g/kg 2. Mean current glucocorticoid dose: 1.7 (SD 3.5) mg 3. Number participants on the following medications: a. Glucocorticoid: 2 (22%) b. Hydroxychloroquine: 5 (56%) c. Methotrexate: 2 (22%) d. Azathioprine: 5 (56%) e. Mycophenolate: 1 (11%) f. Cyclophosphamide: 0 (0%) g. Oral contraceptive: 6 (67%) **Control group (n = 10)** 1. Mean cumulative glucocorticoid dose: 32.4 (SD 19.1) g/kg 2. Mean current glucocorticoid dose: 2.0 (SD 4.2) mg 3. Number of participants on the following medications: a. glucocorticoid: 2 (20%) b. hydroxychloroquine: 7 (70%) c. methotrexate: 2 (20%) d. azathioprine: 4 (40%) e. mycophenolate: 2 (20%) f. cyclophosphamide: 0 (0%) g. oral contraceptive: 6 (60%) No further information about their usual care reported.	of treadmill walking, and 5-min cool-down), 2 times/week. Walking duration was gradually increased every 4 weeks, from 30 min to 50 min. Intensity was set at the HR corresponding to the interval between ventilatory anaerobic threshold and 10% below respiratory compensation point.	ties throughout the study. No further information reported.
Bostrom 2016	The SLE treatment outlined at baseline for each intervention group. **Exercise group (N=18)** 1. Median prednisolone: 3.1 (quartiles Q1–Q3 0–5) mg 2. Number of participants who are on:	Participants received usual care plus a supervised combined aerobic and resistance exercise programme for 12 weeks. Participants performed 60-min exercise programme 2 times/week. Participants were also followed up with exercise for 12 months; however the level of exercise supervision decreased over time. Programme consisted of 3 phases **Phase 1 (0–3 months)**	Participants were asked not to change their physical activity lifestyle during the study period. They were not given any specific information related to the study.

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Table 1. Characteristics of interventions in included studies *(Continued)*

	a. beta-blockers: 3 **Control group (n = 17)** 1. Median prednisolone: 1.3 (quartiles Q1–Q3 0–5) mg 2. Number of participants who are on: a. beta-blockers: 1 No further information about their usual care reported.	Consisted mainly aerobic exercise (about 20 min) and muscle strength and endurance exercise (about 15 min). Intensity was set as high (65–80% of maximum HR or a rating of 13–16 out of 20 on the BORG rating of perceived exertion scale) *Note: participants could alternatively choose any preferred self-managed high-intensity physical activity, as some participants lived far from the hospital.* Phase also included a 1-hour education session held by a rheumatologist and another by a physiotherapist to educate them on: their disease, the risk for cardiovascular disease, the treatment of the disease, and the importance of, and how to perform, physical activity and exercise. It also included education on how to use a HR monitor, how to assess intensity according to RPE scale, and how to document physical activity with modes, frequency, durations, and intensities. This phase also included supervised exercise training, 30 min of individual coaching of physical activity at 6 and 12 weeks, loan and use of HR monitor, and use of a physical activity diary. **Phase 2 (4–9 months)** During this period, the physical activity was self-managed with the help of videotapes or sound cassettes (or both) from the high-intensity aerobic group exercise programme performed during the first 3 months. As an alternative, any physical activity at high intensity could be chosen. This phase included: 30-min of individual coaching of physical activity at 6 and 9 months, use of HR monitor, and use of the physical activity diary. Participants also received 10 min of telephone support which reduced towards the end of the 12 months. **Phase 3 (9–12 months)** This phase included: use of the HR monitor, and use of physical activity diary.	No further information reported.
Hashemi 2022	No information about their usual care described.	Participants received usual care plus a combined aerobic and anaerobic supervised exercise programme for 8 weeks. Participants performed 60 min of exercise (commencing with 40 min in week 1), 3 times/week. The exercise programme included a 10-min warm-up, 10-min of running on a treadmill, and 10 min of cycling, both at an intensity of 50–60% of their VO_{2max}, followed by 60 min of Pilates training uses bodyweight resistance, and a 10-min cool-down.	No information about the control group reported. Assumed that control group continued with their usual care alone.
Tench 2003	No information about their usual care described.	Participants received usual care plus a partially supervised aerobic exercise programme for 12 weeks. Participants were encouraged to perform 30–50 min of aerobic exercise (consisting of walking, cycling, or swimming) 3 times/week. The target intensity was moderate; HR corresponding to 60% of peak oxygen consumption. Participants were seen by an exercise pro-	Participants were asked to continue with their normal daily activity pattern and specifically asked to avoid doing any extra physical activities

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Table 1. Characteristics of interventions in included studies *(Continued)*

		fessional every 2 weeks for a supervised exercise session. Comparator group included participants who received usual care plus a different non-pharmacological intervention (relaxation practice). Participants listened to a relaxation audiotape in a quiet, warm, and darkened room for 30 min, 3 times/week. Participants were seen by an exercise professional every 2 weeks for a supervised relaxation session. This intervention is included as a control group comparator in the description below under 'trials with another non-pharmacological intervention plus usual care control.'	They were reviewed at follow-up but not seen at any other times. No further information reported.
Trials with **another non-pharmacological intervention plus usual care control**			
Abrahão 2016	There was no clear information about their usual care, including the medications taken by participants. However, authors reported that there were changes in the use of medication to control disease activity in the control group, but without significant differences amongst groups (P = 0.34). It is also reported that the 2 exercise intervention groups (group 1: cardiovascular training, group 2: resistance training) had no changes in the use of medications.	Participants in the 2 exercise groups received their usual care plus they performed 1 type of exercise, described below, 3 times/week, for 50 min for 12 weeks. Both exercise groups were supervised by trained professional in the Rheumatology Services at the Interlagos Specialty Outpatient Clinic. **Exercise group 1: cardiovascular training group** Participants received walking and bicycle ergometer interventions (Model CLB 10 Classic, Caloi, São Paulo, Brazil) consisting of a 10-min warm-up, 30 min of exercise at target HR, and 10-min cool-down. The targeted intensity was moderate (65–75% of maximum HR according to the ACSM guidelines), determined by the HR reserve. **Exercise group 2: resistance training group** Participants received a resistance training programme comprised of 8 exercises; holds (crucifix) with free weights, extension-machine exercises, rowing exercise with an elastic band, knee flexion with ankle weights, 2-arm biceps curls, adduction exercises with an elastic band, French curls, and abdominal exercises. The training involved small and large muscle group exercises. Participants performed 3 sets of 15 repetitions with rest intervals of 1 min between sets. The targeted intensity was moderate (65–75% of 1 repetition maximum according to the ACSM guidelines). To establish the training intensity for each participant, their 1 repetition maximum for each exercise was determined. Training intensity changed over time as the participants progressed.	Participants received usual care and information about the disease, but no exercise intervention. They were informed that they would receive the intervention after the study was finished, and they would be invited to participate in the intervention that proved the most effective. No further information reported.
Daltroy 1995	The SLE treatment outlined at baseline for each intervention group. **Exercise group (n = 16)** 1. % of participants taking steroids: 38% 2. % of participants taking NSAIDs: 31%	Participants received usual care plus unsupervised home aerobic exercise for 12 weeks. Participants performed 30 min of aerobic exercise (cycling on a stationary bike that was set up in their home) 3 times/week. The target intensity was moderate to high (60–80% of maximum HR achieved on the exercise tolerance test). A physiotherapist contacted the participant once a week to update their exercise log, report any symptoms, and ask about their perceived fatigue. Pulse oximeters were provided to help participants monitor	Participants received usual care plus they were contacted by the research team once per week as an attention control group. They were also asked to fill out questionnaires, and

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Table 1. Characteristics of interventions in included studies *(Continued)*

	Control group (n = 18) 1. % of participants taking steroids: 61% 2. % of participants taking NSAIDs: 67% No further information about their usual care described.	their heart rates and as a compliance-enhancing strategy. The physiotherapist instructed the participant at home when setting up the bike, and made a second visit 2–3 weeks later at an exercise session to check the participants' ability to follow the regimen correctly.	were encouraged to maintain their current level of activity during the 12-week programme. No further information reported.
Dos Reis-Neto 2013	The SLE treatment outlined at baseline for each intervention group. **Exercise group (n = 18)** Number (%) of participants on the following medications: 1. prednisone: 10 (55%) a. median current prednisone dose: 2 (minimum–maximum 0–40) mg 2. antimalarials: 13 (72.2%) 3. immunosuppressives: 8 (44.4%) 4. antihypertensives: 3 (16.7%) 5. aspirin: 2 (11.1%) 6. contraceptives: 3 (16.7%) **Control group (n = 20)** Number (%) of participants on the following medications: 1. prednisone: 13 (65%) a. median of current prednisone dose: 5 (minimum–maximum 0–30) 2. antimalarials: 16 (80%) 3. immunosuppressives: 14 (70%) 4. antihypertensives: 7 (35%) 5. aspirin: 3 (15%) 6. contraceptive: 8 (40%) No further information about their usual care reported.	Participants received usual care plus an aerobic exercise programme for 16 weeks. Participants performed 60 min of outdoor walking (10-min warm-up, 40 min of walking, 10-min cool-down), 3 times/week. Target intensity set at a HR corresponding to the ventilatory 1 threshold obtained from ergospirometry and monitored by frequency meter. Participants met in the morning at a public park, supervised by a physical educator or physician.	Participants received usual care and information about the disease, but no exercise intervention. They received clear instruction not to start any exercise programme for the next 16 weeks. No further information reported.
Kao 2021	No information about their usual care reported.	Participants received usual care plus a home-based exercise programme for 12 weeks. Participants performed approximately 40 min of combined aerobic and	Participants received usual care and information

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Table 1. Characteristics of interventions in included studies *(Continued)*

		resistance exercise (3–5 min warm-up, 30 min combined aerobic and resistance exercises, 5 min relaxation and stretching; the exercise programme comprised a 7- to 8-min set of combined aerobic and resistance exercise such as high knees/shuffle runs/biceps curls etc., and participants had to perform 4 sets). The target intensity was moderate, determined by the HR reserve. The research team member contacted participants periodically by telephone or text messages to ensure their compliance. Each week the participants reported their maximal HR after each exercise session using written logs. Instructed by an exercise physiologist/professional exercise instructor on the performance of aerobic exercise combined with resistance training and the skills of HR measurement at rest and after exercise.	about the disease, but no exercise intervention. They were to maintain their usual lifestyle. No further information reported.
Keramiotou 2020	The SLE treatment outlined at baseline for each intervention group. **Exercise group (n = 32)** Number (%) of participants on the following medications: 1. corticosteroids: 20 (54.1%) **note that the percentage seems to be reported incorrectly in the study.* a. Mean prednisolone dosage: 4.63 (SD 5.55) mg 2. hydroxychloroquine: 26 (81.3%) 3. immunosuppressive agents: 15 (46.9%) 4. biological agents: 1 (3.1%) **Control group (n = 30)** Number (%) of participants on the following medications: 1. corticosteroids: 17 (46%) **note that the percentage seems to be reported incorrectly in the study.* a. Mean prednisolone dosage: 4.97 (SD 5.80) mg 2. hydroxychloroquine: 25 (83.3%) 3. immunosuppressive agents: 15 (50%) 4. biological agents: 3 (10%)	Participants received usual care plus an upper limb combined resistance and stretching exercise programme for 12 weeks, and were followed up at 24 weeks. Participants performed 30 min of upper limb exercises (9 strengthening and stretching exercises for the upper extremities with a stick, 10 strengthening and stretching exercises for the fingers, and 11 strengthening exercises against resistance with therapeutic putty) daily. The initial intensity was set at a moderate level, and the programme was reassessed using a modified Borg Scale (a tool to measure a persons' perception of their effort and exertion, breathlessness, and fatigue during physical work) to maintain the same intensity, in every face-to-face session with the hand therapist at 0, 3, 6, and 9 weeks. It is unclear whether this programme was supervised.	Participants received usual care plus they 4 sessions of training in alternative methods of performing daily activities, use of aids, joint protection, and energy conservation, additionally to assessment at baseline, 6, 12, and 24 weeks, in order to keep them committed and motivated. All participants received the same training in alternative methods of performing daily activities, use of aids, joint protection and energy conservation.

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Table 1. Characteristics of interventions in included studies *(Continued)*

	No further information about their usual care reported.		
Miossi 2012	The SLE treatment outlined at baseline for each intervention group. **Exercise group (n = 14)** Number of participants on the following medications: 1. prednisone: 10 (66.7%) 2. prednisone ≥ 20 mg/day: 2 (12.3%) 3. azathioprine: 8 (53.3%) 4. chloroquine: 12 (80%) 5. methotrexate: 1 (6.7%) 6. mycophenolate mofetil: 4 (26.7%) 7. cyclophosphamide: 1 (6.7%) 8. medroxyprogesterone: 4 (26.7%) **Control group (n = 10)** Number of participants on the following medications: 1. prednisone: 8 (61.5%) 2. prednisone ≥ 20 mg/day: 1 (7.1%) 3. azathioprine: 5 (38.4%) 4. chloroquine: 12 (92.3%) 5. methotrexate: 3 (23.0%) 6. mycophenolate mofetil: 2 (15.3%) 7. cyclophosphamide: 0 (0%) 8. medroxyprogesterone: 7 (53.8%) No further information about their usual care described.	The participants received usual care plus a supervised combined resistance and aerobic exercise programme for 12 weeks. Participants performed approximately 80 min of exercise (5-min treadmill warm-up, 35–40 min of resistance training, 30 min of treadmill aerobic training, and 5 min of stretching). Resistance training included 7 exercises for the main muscle groups (e.g. bench press, leg press, leg extension); 2 sets of 15–20 repetition maximum for each exercise in week 1, and 4 sets of 8–12 repetitions maximum every week after that, 2 times/week. Intensity was set at a HR corresponding to the interval between Ventilatory anaerobic threshold and 10% below respiratory compensation point. All sessions were monitored by 1 fitness professional.	Participants received usual care plus information about their disease, but no exercise intervention. They were advised to remain physically inactive. No further information reported.
Tench 2003	No information about their usual care described.	Participants received usual care plus a partially supervised aerobic exercise programme for 12 weeks. Participants were encouraged to perform 30–50 min of aerobic exercise (consisting of walking, cycling, or swimming) 3 times/week. Target intensity was moderate; HR corresponding to 60% of peak oxygen consumption. Participants were seen by an exercise professional every 2 weeks for a supervised exercise session.	Participants received usual care plus a different non-pharmacological intervention (relaxation practice). Participants listened to a relaxation audiotape in a quiet, warm, and darkened room for

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Table 1. Characteristics of interventions in included studies *(Continued)*

			30 min, 3 times/ week. Participants were seen by an exercise professional every 2 weeks for a supervised relaxation session. This intervention was included as a control group comparator in the description above under 'Trials with a usual care alone control.'

ACSM: American College of Sports Medicine; HR: heart rate; NSAID: non-steroidal anti-inflammatory drug; PWC75%: 75% of the predicted maximal heart rate; RPE: rating of perceived exertion; SD: standard deviation; SLE: systemic lupus erythematosus.

Table 2. Characteristics of exercise intervention in included studies

Study ID	Dosage of exercise (frequency, intensity, time, type), duration of exercise intervention, progressions to programme (if any), and equipment used	Setting of exercise (supervision, provider expertise, setting of exercise, individual or group)	Country
Trials that compared exercise plus usual care to a placebo plus usual care			
Lopes-Souza 2021	**Frequency of exercise sessions:** 2 times/week (24 hours between sessions). **Intensity of exercise** 1. Weeks 1–4: 10 bouts of 30 s, frequency 30 Hz, D 1.23 mm, and a peak of 2.22 g. 2. Weeks 5–8: 10 bouts of 60 s, frequency 40 Hz, D 0.95 mm, and a peak of 3.06 g. 3. Weeks 9–12: 10 bouts of 60 s, 50 Hz, D 0.88 mm, and a peak of 4.40 g. The "low" amplitude was maintained in all sessions. **Time of exercise session** 1. Weeks 1–4: 2-min warm-up on a cycle ergometer pedalling continuously with no defined load, and 5-min WBVE. 2. Weeks 5–12: 2-min warm-up on a cycle ergometer pedalling continuously with no defined load, and 10-min WBVE. **Type of exercise:** WBVE is a subgroup of resistance training, better classified as muscle activation or neuromuscular training complementary to resistance training. The participants were positioned on the vibrating platform with 130° of knee flexion. **Duration of intervention:** 12 weeks **Progressions:** described above	**Supervision:** unclear if there was supervision present during the intervention. **Provider:** not reported **Setting of exercise:** not clearly reported. **Individual or group:** given that participants were positioned on a single vibration platform, this exercise intervention was performed individually; however, it was unclear whether multiple participants performed this together in a clinic, or unsupervised at home.	Brazil

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Table 2. Characteristics of exercise intervention in included studies *(Continued)*

	Equipment used: vertical vibrating platform used in the study was of the triaxial type, where the base moves vertically and horizontally directions (with predominantly vertical displacement), model Power Plate Pro5 (Power Plate International, Performance Health Systems, USA).		
Trials that compared exercise plus usual care to usual care alone			
Avaux 2016	At the start of the programme, the 2 groups (supervised training group and home training group) participated in a multidisciplinary information session about the benefits of exercise in SLE, during which practical information was also delivered. **Frequency of exercise sessions:** not clearly reported. However, participants were advised to perform 3 hours of exercise per week. **Intensity of exercise:** moderate to high (60–80% of predicted maximal heart rate) **Time of exercise session:** not clearly reported. However, participants were advised to perform 3 hours of exercise per week. **Type of exercise:** participants were advised to perform cardiovascular endurance exercise (walking or cycling), or strengthening exercises. **Duration of intervention:** 12 weeks **Progression:** not clearly reported. **Equipment used:** 1. Endurance exercises (walking or bicycle) 2. Strengthening exercises (elastic band or weights for both upper and lower limbs) Note that the intervention dosage were the same in both groups. The groups only differed by the level of supervision and setting of exercise.	**Exercise intervention group 1 (supervised training group)** 1. **Supervision:** yes 2. **Provider:** participant were supervised by a multidisciplinary team in the hospital 3. **Place of exercise:** hospital-based revalidation centre 4. **Individual or group:** not clearly reported **Exercise intervention group 2 (home training group)** 1. **Supervision:** no 2. **Place of exercise:** home 3. **Individual or group:** not clearly reported	Belgium
Benatti 2015	**Frequency of exercise sessions:** 2 times/week **Intensity of exercise:** heart rate corresponding to the interval between ventilatory anaerobic threshold and 10% below respiratory compensation point. **Time of exercise session:** cardiovascular endurance exercise = 30 min and strength exercise = time not specified, per session. **Type of exercise:** cardiovascular endurance exercise (treadmill walking) and strength exercises (7 exercises for major muscle groups: 4 sets of 8–12 repetitions maximum for each exercise) **Duration of intervention:** 12 weeks **Progression:** not reported	**Supervision:** yes **Provider:** not reported **Place of exercise:** not reported **Individual or group:** not reported	Brazil

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Table 2. Characteristics of exercise intervention in included studies *(Continued)*

	Equipment used: not reported		
Benatti 2018	**Frequency of exercise sessions:** 2 times/week **Intensity of exercise:** heart rate corresponding to the interval between ventilatory anaerobic threshold and 10% below respiratory compensation point **Time of exercise session:** 40–60 min (including a 5-min warm-up and 5-min cool-down) **Type of exercise:** cardiovascular endurance (treadmill walking) **Duration of exercise intervention:** 12 weeks **Progression:** walking duration gradually increased every 4 weeks, from 30 min to 50 min **Equipment used:** treadmill	**Supervision:** yes **Provider:** not reported **Place of exercise:** intrahospital gymnasium (Laboratory of Assessment and Conditioning in Rheumatology, School of Medicine, University of São Paulo) **Individual or group:** not clearly reported. However, given that participants were walking on a treadmill, it was assumed to be individual. Whether participants performed treadmill walking with other participants in the clinic was not clear	Brazil
Bostrom 2016	**Frequency of exercise sessions:** 2 times/week (supervised) **Intensity of exercise:** high (65–80% of MHR, or 13–16 rate of perceived exertion) **Time of exercise session:** 60 min (20 min aerobic and 15 min strength) **Type of exercise** 1. **0–3 months:** education about the disease and exercise (1-off 1-hour workshop), supervised aerobic and strength exercise, individual coaching of physical activity (30 min of individual coaching at the start and after 6 weeks and 12 weeks), loan and use of heart rate monitor, and use of a physical activity diary. 2. **4–9 months:** individual coaching of physical activity, use of heart rate monitor, and the use of a physical activity diary, self-managed aerobic and strength exercise. 3. **10–12 months:** use of heart rate monitor and the use of a physical activity diary, self-managed aerobic and strength exercise. **Duration of exercise intervention** 1. Phase 1: 0–3 months 2. Phase 2: 4–12 months **Progression:** participants were asked to successively increase their physical activity during the programme to achieve: 1. high intensity, ≥ 30 min per session, 2–3 days/week, and 2. low-to-moderate intensity, ≥ 30 min per session, 4–5 days/week. **Equipment used:** treadmill, heart rate monitor, activity diary.	**Supervision/support** 1. Phase 1: more supervision; education about the disease and exercise was offered in a 1-hour workshop at the start. 2 supervised high-intensity aerobic exercise sessions were offered during the first 3 months in the hospital gymnasium. However, participants could choose to perform their own 2 high-intensity exercise sessions if the hospital was not convenient for them to get to. Participants were also encouraged to perform low-to-moderate exercise 4–5 days per week on their own during this time. Individual coaching for 30 min was offered at the start, and 6 and 12 weeks. 2. Phase 2: less supervision; this was assisted by videotapes and cassettes of the 2 high-intensity exercise sessions performed during phase 1. Participants were also encouraged to perform low-to-moderate exercise 4–5 days/week on their own during this time. Individual	Sweden

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Table 2. Characteristics of exercise intervention in included studies *(Continued)*

		coaching for 30 min was also offered at months 6 and 9. They also received telephone support for approximately 10 min and the frequency of this was reduced during the 4- to 12-month period (months 4–6, every third week; months 7–9, once per month; months 10–12, no support). 3. **Provider:** physiotherapist provided the education, individual coaching, and the supervision of the exercise. A rheumatologist was also present during the education session at the start of the programme. 4. **Place of exercise:** hospital gymnasium, at home/their choice of location. 5. **Individual or group:** group-based when under supervision, individual or group if they were performing exercise at home/their choice of location.	
Hashemi 2022	**Frequency of exercise sessions:** 3 times/week **Intensity of exercise:** stage 2 of the session (aerobic exercise programme, including 10 min of cycling and 10 min of running, both at intensity of 50–60% maximum, as predetermined in the peak oxygen uptake measurements). **Time of exercise session:** 60 min per session (40 min for the first week, to allow for acclimatisation, but increased thereafter) **Type of exercise:** Pilates exercise, which is classified as low-intensity resistance exercise. Each exercise session consisted of 4 stages, including 10-min warm-up, 10-min aerobic exercise programme (10 min cycling and 10 min running), 60-min Pilates training using bodyweight as the resistive load, and 10-min cool-down. Borg's scale was used to assess the participants' perceptions of physical exertion during the aerobic exercises that were used in stage 2. **Duration of intervention:** 8 weeks	**Supervision:** not reported **Provider:** not reported **Setting of exercise:** not reported **Individual or group:** not reported	Iran
Tench 2003	**Frequency of exercise sessions:** 3 times/week **Intensity of exercise:** heart rate corresponding to 60% of peak oxygen consumption	**Supervision:** yes **Provider:** not clearly reported.	UK

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Table 2. Characteristics of exercise intervention in included studies *(Continued)*

	Time of exercise session: 30–50 min **Type of exercise:** home-based cardiovascular exercise (mainly walking, swimming, or cycling) with a supervised exercise session every 2 weeks **Duration of exercise intervention:** 12 weeks **Progression:** not reported **Equipment used:** not reported	**Place of exercise:** home-based, with a supervised exercise session every 2 weeks. **Individual or group:** not clearly reported	
Trials that compared exercise plus usual care to another non-pharmacological intervention plus usual care			
Abrahão 2016	**Frequency of exercise sessions:** 3 times/week **Intensity of exercise:** moderate intensity (65–75% of MHR according to the ACSM guidelines). Exercise intensity was determined by HRR, which was calculated by HRR = MHR – RHR. MHR determined using: MHR = 205 – (0.42 × age). **Time of exercise session:** 50 min per session **Type of exercise** 1. Cardiovascular exercise; walking and bicycle ergometry interventions. Each training session consisted of a 10-min warm-up followed by 30 min of exercise at the target heart rate, and 10-min cool-down. 2. Resistance training exercise. Each session consisted of 8 exercises, including holds (crucifix) with free weights, extension-machine exercises, rowing exercise with an elastic band, knee flexion with ankle weights, 2-arm biceps curls, adduction exercises with an elastic band, French curls, and abdominal exercises. The training involved small and large muscle group exercises. Participants performed 3 sets of 15 repetitions with rest intervals of 1 min between sets. **Duration of exercise intervention:** 12 weeks **Progression:** training intensity changed over time as the participants progressed. Progression unknown. **Equipment used:** bicycle ergometry (Model CLB 10 Classic, Caloi, Sao Paulo, Brazil), free weights, extension-machine, and elastic bands	**Supervision:** yes **Provider:** trained professional (profession unknown) **Place of exercise:** in the Rheumatology Services at the Interlagos Specialty Outpatient Clinic **Individual or group:** not clearly reported	Brazil
Daltroy 1995	**Frequency of exercise sessions:** 3 times/week **Intensity of exercise:** moderate–high (60–80% of MHR achieved on the exercise tolerance test) **Time of exercise session:** 30 min per session **Type of exercise:** aerobic exercise performed on a stationary bike that was set up in their home. **Duration of exercise intervention:** 12 weeks **Progression:** not reported **Equipment used:** stationary bike	**Supervision:** yes **Provider:** a physiotherapist contacted the participant once a week to update logs of exercise, report of symptoms, and perceived fatigue. The physiotherapist instructed the participant at home when setting up the bike, and made a second visit 2–3 weeks later at an exercise session to check the participants' ability to	US

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Table 2. Characteristics of exercise intervention in included studies *(Continued)*

		follow the regimen correctly. **Place of exercise:** participants' homes **Individual or group:** individual (participants completed their sessions in their own homes, independently)	
Dos Reis-Neto 2013	**Frequency of exercise sessions:** 3 times/week **Intensity of exercise:** heart rate corresponding to the ventilatory 1 threshold obtained from ergospirometry and monitored by frequency meter (Poland Electro, Kempele, Finland). **Time of exercise session:** 60 min per session (10-min warm-up, 40-min of walking and 10-min cool-down) **Type of exercise:** walking, outdoors in the morning **Duration of exercise intervention:** 16 weeks **Progression:** not reported **Equipment used:** none	**Supervision:** yes **Provider:** physical educator or physician **Place of exercise:** park, outdoors **Individual or group:** not clearly reported	Brazil
Kao 2021	**Frequency of exercise sessions:** 5 times/week **Intensity of exercise:** moderate intensity determined by HRR 50–50%, according to the ACSM guidelines. HRR = MHR − RHR. MHR determined using formula: MHR = 205 − (0.42 × age). **Time of exercise session:** 30 min per session (3- to 5-min warm-up session, 4 sets of combined exercise session for approximately 30 min in total, and a final set of 3- to 5-min of relaxation and stretching). Each set of combined exercise lasting for 7 min 15 s, with a brief break between sets. **Type of exercise:** aerobic exercise combined with bodyweight or 500–620 mL of dumbbell water weights for resistance training. Combined exercise sessions consisted of various styles of basic exercises, alternating workouts of legs with trunk movement, and arm exercises. **Duration of exercise intervention:** 12 weeks **Progression:** not reported **Equipment used:** 500–620 mL of dumbbell water weights	**Supervision:** yes **Provider:** instructed by an exercise physiologist/professional exercise instructor on the performance of aerobic exercise combined with resistance training and the skills of heart rate measurement at rest and after exercise. The research team member contacted participants periodically by telephone or text message to ensure their compliance. Each week, the participants reported their maximal heart rate after each exercise session by written logs. **Place of exercise:** participant's home **Individual or group:** individual (considering each participant was performing the exercise intervention in their own home)	Taiwan
Keramiotou 2020	**Frequency of exercise sessions:** 7 days/week	**Supervision:** not reported	Greece

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Table 2. Characteristics of exercise intervention in included studies *(Continued)*

	Intensity of exercise: moderate intensity. The initial intensity of exercise was set at a moderate level and the programme was reassessed, using a modified Borg Scale (a tool to measure a persons' perception of their effort and exertion, breathlessness, and fatigue during physical work) to maintain the same intensity, in every face-to-face session with the hand therapist at 0, 3, 6, and 9 weeks. **Time of exercise session:** 30 min per session **Type of exercise:** upper limb resistance and range of motion exercise (9 strengthening and stretching exercises for the upper extremities with a stick, 10 strengthening and stretching exercises for the fingers and 11 strengthening exercises against resistance with therapeutic putty). **Duration of exercise intervention:** 12 weeks (with a follow-up assessment at 24 weeks) **Progression:** not reported **Equipment used:** therapeutic putty (soft or medium resistance)	**Provider:** team of hand therapists. Frequency of visits to the hand therapist, unknown. **Place of exercise:** home-based programme **Individual or group:** individual (taking into account participants were performing their exercise programme at home)	
Miossi 2012	**Frequency of exercise sessions:** 2 times/week **Intensity of exercise:** heart rate corresponding to the interval between ventilatory anaerobic threshold and 10% below respiratory compensation point. **Time of exercise session:** 80 min per session (5-min treadmill warm-up, 35–40 min of resistance training, 30 min of treadmill aerobic training, and 5-min of stretching). **Type of exercise:** cardiovascular exercise (treadmill walking for 30 min), and resistance training included 7 exercises for the main muscle groups (e.g. bench press, leg press, leg extension). **Duration of exercise intervention:** 12 weeks **Progression:** participants were required to perform 4 sets of 8–12 repetitions maximum, except during the first week, when a reduced volume of 2 sets of 15–20 repetitions maximum for each exercise was performed (as an adaptation period to resistance training). Overload progression was implemented when the participant could perform > 12 repetitions on the last training set for 2 consecutive workouts. Aerobic training intensity was set at the corresponding heart rate between the ventilatory anaerobic threshold and 10% below the respiratory compensation point. Cardiorespiratory exercise test was performed on a treadmill (Centurion, Model 200, Micromed) using a maximal-graded exercise protocol. The recovery period was set at 2 min using the initial workload (1.7 miles per hour).	**Supervision:** yes **Provider:** 1 fitness professional **Place of exercise:** hospital gymnasium **Individual or group:** not clearly reported	Brazil

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Table 2. Characteristics of exercise intervention in included studies *(Continued)*

	Equipment used: treadmill and resistance training equipment (e.g. machine weights or dumbbells); however, this was not clearly reported.		
Tench 2003	**Frequency of exercise sessions:** 3 times/week **Intensity of exercise:** heart rate corresponding to 60% of peak oxygen consumption **Time of exercise session:** 30–50 min **Type of exercise:** home-based cardiovascular exercise (mainly walking, swimming, or cycling) with a supervised exercise session every 2 weeks **Duration of exercise intervention:** 12 weeks **Progression:** not reported **Equipment used:** not reported	**Supervision:** yes **Provider:** not clearly reported **Place of exercise:** home-based, with a supervised exercise session every 2 weeks **Individual or group:** not clearly reported	UK

ACSM: American College of Sports Medicine; HRR: heart rate reserve; MHR: maximum heart rate; RHR: resting heart rate; SLE: systemic lupus erythematosus; WBVE: whole body vibration exercise.

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Table 3. Major outcomes reported in included studies

Study ID	Fatigue	Functional capacity	Disease activity	Quality of life	Pain	Serious adverse events	Withdrawals due to adverse events
Trials that compared exercise plus usual care to placebo plus usual care							
Lopes-Souza 2021	**Yes** **The Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F)** 1. Score range: score 0–52, higher scores indicate less fatigue SF-35 Vitality domain was also used; however, this was not used in our analyses.	**Yes** **SF-36 Functional Capacity domain** 1. Score range 0–100, higher scores indicate better functional capacity HAQ and TUG test were also used to assess functional capacity; however, these were not used in our analyses.	Not measured	Partially reported. SF-36 was used to measure quality of life; however, authors did not report the MCS and PCS scores, so this was not used in our analyses.	**Yes** **SF-36 Pain domain** 1. Score range 0–100, higher scores indicate less pain	No serious adverse events were reported.	No withdrawals due to adverse events were reported.
Trials that compared exercise plus usual care to usual care alone							
Avaux 2016	**Yes** **Krupp FSS** 1. Score range: 1–7, lower score indicates less fatigue	Not measured	Not measured	Not measured	Not measured	No serious adverse events were reported.	Yes. 1 participant withdrew from study due to a disease flare; however, unclear which group they were part of, and, therefore, unable to be included in meta-analysis. It is also important to note that it is unclear whether the disease flare was due to the intervention, the severity of the

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Table 3. Major outcomes reported in included studies *(Continued)*

							disease flare, or whether they were hospitalised.
Benatti 2015	Not measured	Not measured	Not measured	Not measured	Not measured	No serious adverse events were reported.	No withdrawals due to adverse events were reported.
Benatti 2018	Not measured	Not measured	Not measured	Not measured	Not measured	No serious adverse events were reported.	**Yes** **2 participants withdrew from the study.** 1. 1 from the control group due to a disease flare 2. 1 from the exercise group due to a disease flare However, it is important to note that it was unclear whether the disease flare was due to the intervention, the severity of the disease flare, or whether they were hospitalised.
Bostrom 2016	Not measured. SF-36 Vitality domain was used; however, this was not used in our analyses.	**Yes** **SF-36 Physical Function domain** 1. Score range 0–100, higher scores indicate better functional capacity	**Yes** **SLEDAI** 1. Score range: 0–105, lower scores indicate less disease activity	Partially reported. Used SF-36 to measure quality of life; however, authors did not report MCS and PCS scores, and, therefore, this was not used in our analyses.	**Yes** **SF-36 Pain** 1. Score range 0–100, higher scores indicate less pain	No serious adverse events were reported.	No withdrawals due to adverse events were reported.

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Table 3. Major outcomes reported in included studies *(Continued)*

Hashemi 2022	Not measured	Not measured	Not measured	Not measured	Not measured	No serious adverse events were reported.	No withdrawals due to adverse events were reported.
Tench 2003	**Yes** **Krupp FSS** 1. Score range 1–7, lower score indicates less fatigue Chalder Fatigue Scale, Visual Analogue Scale, and SF-36 Fatigue and Vitality domains were also used; however, these were not used in our analyses.	**Yes** **SF-36 Physical Function domain** 1. Score range 0–100, higher scores indicate better functional capacity	**Yes** **Systemic Lupus Activity Measure** 1. Score range 0–83, lower scores indicate less disease activity	Partially reported. Used SF-36 to measure quality of life; however, authors did not report the MCS score, PCS score, and all 8 domains, and, therefore, this was not used in our analyses.	Not reported. Used SF-36 to measure quality of life, but authors did not report the Pain domain, and, therefore, this was not used in our analyses.	No serious adverse events were reported.	No withdrawals due to adverse events were reported.
Trials that compared exercise plus usual care to another non-pharmacological intervention plus usual care							
Abrahão 2016	Not measured	**Yes** **SF-35 Physical Function domain** 1. Score range 0–100, higher scores indicate better functional capacity	**Yes** **SLEDAI** 1. Score range: 0–105, lower scores indicate less disease activity	Partially reported. SF-36 used to measure quality of life; however, authors did not report the MCS and PCS scores, and, therefore, this was not used in our analyses.	**Yes** **SF-36 Pain domain** 1. Score range 0–100, higher scores indicate less pain	No serious adverse events were reported.	No withdrawals due to adverse events were reported.
Daltroy 1995	Yes, the Mental Adjustment to Cancer questionnaire, and the Profile Of Moods State Fatigue questionnaire were used; however, these were not included in our analy-	Not measured	Not measured	Not measured	Not measured	No serious adverse events were reported.	No withdrawals due to adverse events were reported.

Table 3. Major outcomes reported in included studies *(Continued)*

	ses because the results for the participants with SLE were not presented separately from the results for participants with rheumatoid arthritis.						
Dos Reis-Neto 2013	Not measured	Not measured	**Yes** **SLEDAI** 1. Score range: 0–105, lower scores indicate less disease activity	Not measured	Not measured	No serious adverse events were reported.	No withdrawals due to adverse events were reported.
Kao 2021	Not measured	Not measured	Yes, used SLEDAI; however, authors did not report the mean and standard deviation, and, therefore, we were unable to use in our analyses.	Not measured	Not measured	No serious adverse events were reported.	No withdrawals due to adverse events were reported.
Keramiotou 2020	**Yes** **Lupus quality of life Fatigue domain** 1. Score range 0–100, higher scores indicate less fatigue	Not measured	Yes, used SLEDAI; however, authors do not report the mean and standard deviation, and, therefore, we were unable to use in our analyses.	Partially reported Used Lupus Quality of Life questionnaire; however, only Physical Health and Fatigue domains were reported, and, therefore, this was not used in our analyses.	**Yes** **Visual Analogue Scale Pain** 1. Score range 0–10, lower scores indicate less pain	No serious adverse events were reported.	No withdrawals due to adverse events were reported.
Miossi 2012	Not measured	Not measured	**Yes** **SLEDAI**	Not measured	Not measured	No serious adverse events were reported.	No withdrawals due to adverse events were reported.

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Table 3. Major outcomes reported in included studies *(Continued)*

			1. Score range: 0–105, lower scores indicate less disease activity.				
Tench 2003	**Yes** **Krupp FSS** 1. Score range 1–7, lower score indicates less fatigue Chalder Fatigue Scale, Visual Analogue Scale, and SF-36 Fatigue and Vitality domains were also used; however, these were not used in our analyses.	**Yes** **SF-36 Physical Function domain** 1. Score range 0–100, higher scores indicate better functional capacity	**Yes** **Systemic Lupus Activity Measure** 1. Score range 0–83, lower scores indicate less disease activity	Partially reported. SF-36 was used to measure quality of life; however, authors did not report MCS score, PCS score, and all 8 domains, and, therefore, this was not used in our analyses.	Not reported. SF-36 was used to measure quality of life but authors did not report the Pain domain, and, therefore, this was not used in our analyses.	No serious adverse events were reported.	No withdrawals due to adverse events were reported.

FACIT-F: Functional Assessment of Chronic Illness Therapy – Fatigue; FSS: Fatigue Severity Scale; HAQ: Health Assessment Questionnaire; MCS: Mental Component Score; PCS: Physical Component Score; SF-36: 36-item Short Form; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; TUG: Timed Up and Go.

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Table 4. Minor outcomes reported in included studies

Study ID	Composite responder rate	Aerobic capacity	Depression	Anxiety	Withdrawals due to any reason
Trials that compared exercise plus usual care to placebo plus usual care					
Lopes-Souza 2021	Not measured	Not measured	Not measured	Not measured	**Yes** **4 participants withdrew from the intervention** 1. 3 from the exercise group (1 before the 6-week analysis due to low back pain, and 2 before the 12-week analysis for personal reasons) 2. 1 from the control group before the 6-week analysis due to personal reasons
Trials that compared exercise plus usual care to usual care alone					
Avaux 2016	Not measured	Not measured	Not measured	Not measured	Yes, 2 participants withdrew from the intervention for personal reason; however, it is unclear which group they were part of, and, therefore, not included in our analyses.
Benatti 2015	Not measured	Not measured	Not measured	Not measured	No withdrawals due to any reason reported.
Benatti 2018	Not measured	Not measured	Not measured	Not measured	**Yes** **8 participants withdrew from the intervention.** 1. 4 from the control group (1 pregnant, 3 for personal reasons) 2. 4 from the exercise group (1 fractured limb outside of training sessions, 3 for person reasons)
Bostrom 2016	Not measured	**Yes** **Maximum oxygen consumption (VO_{2max} in L/min)** 1. Higher scores indicate better aerobic capacity	Not measured	Not measured	**Yes** **3 participants withdrew from the control group (1 depression/cognitive impairment, 1 untreated dementia, 1 suspected relapse breast cancer)**
Hashemi 2022	Not measured	Not measured	Not measured	Not measured	No withdrawals due to any reason reported.
Tench 2003	Not measured	**Yes**	**Yes**	**Yes**	**Yes**

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Table 4. Minor outcomes reported in included studies *(Continued)*

		Peak oxygen consumption (VO_{2peak} in mL/kg/min) 1. Higher scores indicate better aerobic capacity	**Hospital Anxiety and Depression Scale – Depression subscale** 1. Score range 0–21, lower scores indicate a better outcome	**Hospital Anxiety and Depression Scale – Anxiety subscale** 1. Score range 0–21, lower scores indicate a better outcome	**14 participants withdrew from the study.** 1. 4 from the exercise group 2. 5 from the active control group (relaxation) 3. 5 from the usual care control group Note that 6 participants dropped out of treatment and 8 participants completed the study but did not wish to repeat the walking test to exhaustion at the end of the intervention.
Trials that compared exercise plus usual care to another non-pharmacological intervention plus usual care					
Abrahão 2016	Not measured	Not measured	**Yes** **Beck-Depression Inventory** 1. Score range 0–63, lower scores indicate a better outcome	Not measured	**Yes** **2 participants withdrew from the control group for an unknown reason**
Daltroy 1995	Not measured	Yes, the 12-min walking test was used to measure aerobic capacity; however, this was not used in our analyses.	**Yes** **Center for Epidemiologic Studies – Depression Scale** 1. Score range 0–60, lower scores indicate a better outcome	Not measured	No withdrawals due to any reason were clearly reported.
Dos Reis-Neto 2013	Not measured	**Yes** **Peak oxygen consumption (VO_{2peak} in mL/kg/min)** 1. Higher scores indicate better aerobic capacity.	Not measured	Not measured	No withdrawals due to any reason were clearly reported.
Kao 2021	Not assessed	Not measured	Not measured	Not measured	No withdrawals due to any reason were reported.
Keramiotou 2020	Not measured	Not measured	Not measured	Not measured	**Yes** **2 participants from the exercise intervention group withdrew; however, the reasons were not reported.**

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Table 4. Minor outcomes reported in included studies *(Continued)*

Miossi 2012	Not measured	Not measured	Not measured	Not measured	No withdrawals due to any reason were reported.
Tench 2003	Not measured	**Yes** **Peak oxygen consumption (VO_{2peak} in mL/kg/min)** 1. Higher scores indicate better aerobic capacity	**Yes** **Hospital Anxiety and Depression Scale – Depression subscale** 1. Score range 0–21, lower scores indicate a better outcome	**Yes** **Hospital Anxiety and Depression Scale – Anxiety subscale** 1. Score range 0–21, lower scores indicate a better outcome	**Yes** **14 participants withdrew from the study** 1. 4 from the exercise group 2. 5 from the active control group (relaxation) 3. 5 from the usual care control group Note that 6 participants dropped out of treatment and 8 participants completed the study but did not wish to repeat the walking test to exhaustion at the end of the intervention.

VO_{2peak}: peak oxygen consumption.

APPENDICES

Appendix 1. CENTRAL (via Ovid) search strategy

1.	Lupus.mp.
2.	exp Lupus Erythematosus, Systemic/
3.	SLE.mp.
4.	or/1-3
5.	Exercise Therapy/ or Exercise/ or exercis*.mp.
6.	physical activity.mp. or Exercise/
7.	physical activities.mp. or Exercise/
8.	exp Physical Therapy Modalities/
9.	or/5-8

Appendix 2. MEDLINE (via Ovid) search strategy

1.	Lupus.mp.
2.	exp Lupus Erythematosus, Systemic/

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(Continued)

3.	SLE.mp.
4.	or/1-3
5.	Exercise Therapy/ or Exercise/ or exercis*.mp.
6.	physical activity.mp. or Exercise/
7.	physical activities.mp. or Exercise/
8.	exp Physical Therapy Modalities/
9.	or/5-8
10.	randomized controlled trial.pt
11.	controlled clinical trial.pt
12.	randomized.ab
13.	placebo.ab
14.	drug therapy.fs
15.	randomly.ab
16.	trial.ab
17.	groups.ab
18.	or/10-17
19.	exp animals/ not humans.sh
20.	18 not 19
21.	9 AND 20

Appendix 3. Embase (via Ovid) search strategy

1 lupus.mp.

2 systemic lupus erythematosus.mp. or exp systemic lupus erythematosus/

3 SLE.mp.

4 or/1-3

5 Exercise Therapy.mp.

6 exp exercise/ or exercis*.mp.

7 physical activity.mp. or exp physical activity/

8 physical activities.mp.

9 Physical Therapy Modalities.mp.

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10 or/5-9

11 random$.tw.

12 factorial$.tw.

13 crossover$.tw.

14 cross over.tw.

15 cross-over.tw.

16 placebo$.tw.

17 (doubl$ adj blind$).tw.

18 (singl$ adj blind$).tw.

19 assign$.tw.

20 allocat$.tw.

21 volunteer$.tw.

22 crossover procedure/

23 double blind procedure/

24 randomized controlled trial/

25 single blind procedure/

26 or/11-25

27 4 and 10 and 26

Appendix 4. CINAHL (via EBSCO) Search strategy

(Lupus OR SLE OR "systemic Lupus Erythematosus") AND (exercis* OR "physical activity" OR "physical activities)

Appendix 5. SPORTDiscus (via EBSCO) Search strategy

(Lupus OR SLE OR "systemic Lupus Erythematosus") AND (exercis* OR "physical activity" OR "physical activities)

Appendix 6. Web of Science Search strategy

1.	lupus.mp.
2.	systemic lupus erythematosus.mp. or exp systemic lupus erythematosus/
3.	SLE.mp.
4.	or/1-3
5.	Exercise Therapy.mp.
6.	exp exercise/ or exercis*.mp.
7.	physical activity.mp. or exp physical activity/
8.	physical activities.mp.
9.	Physical Therapy Modalities.mp.

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(Continued)

10.	or/5-9

HISTORY

Protocol first published: Issue 10, 2021

CONTRIBUTIONS OF AUTHORS

All review authors contributed to each stage of the review including screening of articles, extraction of study characteristics, extraction of outcomes, review of risk of bias, GRADE assessment, writing, and proofreading the review.

SF: screening included and excluded studies, extraction of study characteristics, extraction of outcomes, risk of bias, GRADE, summary of findings table, writing the review, proofreading the review.

SO: review of risk of bias, summary of findings, review of the results and discussion.

EN: screening included and excluded studies and extraction of characteristics of studies, and review of the additional tables.

DG: reviewed and corroborated risk of bias.

MC: review of risk of bias, summary of findings table, review of the results and discussion.

DECLARATIONS OF INTEREST

SF: none.

SO: none.

EN: none.

DG: none.

MC: none.

SOURCES OF SUPPORT

Internal sources

- University of Southern Queensland, Australia

  The University of Southern Queensland provided in-kind support in the form of time release, library support, and computer and print access for SF and MC to complete this review.

External sources

- New Source of support, Other

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We made the following changes from the protocol (Frade 2021).

We clarified the definition of usual care: "Usual pharmacological care could include, but was not limited to, the following standard pharmacological drug treatments; antimalarials such as hydroxychloroquine, NSAIDs, glucocorticoids such as prednisone, immunosuppressives such as mycophenolate, biologicals such as belimumab or rituximab. Other non-pharmacological measures may also have included sun avoidance, commonly prescribed supplementation (i.e. vitamin D), and education about the disease or managing comorbidities such as hypertension, for example (Fanouriakis 2019)".

We changed the preferred order of the data synthesis to reflect the hierarchy of the control group:

1. Exercise plus usual care versus placebo plus usual care
2. Exercise plus usual care versus usual care alone
3. Exercise plus usual care versus another non-pharmacological intervention (e.g. education about exercise, counselling about exercise, relaxation exercises) plus usual care

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We changed the major outcome: 'withdrawals due to adverse events' to 'withdrawals due to any reason,' inclusive of any adverse events. We removed withdrawals from the minor outcomes.

The review authors who screened the titles and abstracts, and full-text, has been changed to SF and EN. The third review author has been changed to MC.

Extraction of study characteristics has been changed from one author (SF) to two authors (SF, EN) who will both spot-check for accuracy.

We clarified the definition of end time point of data extraction to be when the structured exercise intervention had completed (i.e. the exercise intervention went for 12 weeks; however, participants were advised to continue to exercise and were followed up).

We did not do the following: in the 'Effects of interventions' results section and the 'What happens' column of the summary of findings table, we provided the absolute percent change and the NNTB or NNTH (the NNTB or NNTH was provided only when the outcome shows a clinically significant difference).

INDEX TERMS

Medical Subject Headings (MeSH)

*Exercise; Exercise Therapy [methods]; Fatigue [etiology] [therapy]; *Lupus Erythematosus, Systemic [complications] [therapy]; Pain; Quality of Life

MeSH check words

Adult; Humans

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