

Exercise for anxiety disorders: systematic review

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ABSTRACT

Background Anxiety disorders are commonly treated with antidepressants and psychological treatments. Some patients may prefer alternative approaches such as exercise.

Objective To investigate the treatment effects of exercise compared with other treatments for anxiety disorders.

Data sources Randomised controlled trials (RCTs) of exercise interventions for anxiety disorders were identified by searching six online databases (July 2011). A number of journals were also hand searched.

Main results Eight RCTs were included. For panic disorder: exercise appears to reduce anxiety symptoms but it is less effective than antidepressant medication (1 RCT); exercise combined with antidepressant medication improves the Clinical Global Impression outcomes (1 RCT, $p < 0.05$); exercise combined with occupational therapy and lifestyle changes reduces Beck Anxiety Inventory outcomes (1 RCT, $p = 0.0002$). For social phobias, added benefits of exercise when combined with group cognitive behavioural therapy (CBT) were shown ($p < 0.05$). There was no significant difference between aerobic and anaerobic exercise groups (1 RCT, $p > 0.1$) with both seeming to reduce anxiety symptoms (1 RCT, $p < 0.001$). It remains unclear as to which type of exercise; moderate to hard or very light to light, is more effective in anxiety reduction (2 RCTs).

Conclusions Exercise seems to be effective as an adjunctive treatment for anxiety disorders but it is less effective compared with antidepressant treatment. Both aerobic and non-aerobic exercise seems to reduce anxiety symptoms. Social phobias may benefit from exercise when combined with group CBT. Further well-conducted RCTs are needed.

INTRODUCTION

Anxiety disorders are a common cause of morbidity and mortality. These disorders manifest as a range of cognitive, behavioural and physical symptoms. Prevalence varies among types of anxiety disorder,¹ but worldwide lifetime prevalence of anxiety disorders is generally estimated to be 16.6%, with considerable heterogeneity between studies.²

Anxiety disorders are commonly treated with antidepressants and psychological treatment methods.¹ However, concordance with antidepressant medication can be poor and it is associated with side effects. Patients may also not wish to follow psychological treatments due to the commitment of adhering to therapy and issues of stigma. There is preliminary evidence that an acute bout of exercise has an antipanic activity in healthy subjects.³ Smits and Zvolensky⁴ reported that physical inactivity is significantly associated with greater levels of anxiety sensitivity and can affect the

severity of panic disorder. Further, adults who are more likely to have a stressful lifestyle benefit more from the exercise training than those who do not.⁵ There have been a few hypothesised mechanisms of anxiety reduction following exercise; enhanced self-efficacy, experiences of mastery, distraction from anxiety-provoking stimuli, a method of exposure therapy, neurotransmitter changes, peptide changes and changes of self-concept have been proposed.^{6–7} Exercise might also provide exposure therapy by exposing agoraphobics to unsafe environments and may also produce more monoamine neurotransmitters leading to anxiety reduction.⁸

Petruzzello *et al*,⁹ conducted three separate meta-analyses and the results substantiate the claim that exercise is associated with reductions in anxiety. Meta-analysis conducted by Wipfli *et al*¹⁰ also showed larger reductions in anxiety among exercise groups than no-treatment control groups. Exercise training also seems to reduce anxiety symptoms among sedentary patients who have a chronic illness.¹¹

To our knowledge, there have been several formally conducted systematic reviews and meta-analyses published with regard to exercise effects on anxieties in healthy individuals^{5–9–10–12} but none on diagnosed clinical anxiety disorders alone. Our objectives are to examine the treatment effect of exercise on clinically diagnosed anxiety disorders where the diagnosis has been made following a formal assessment.

METHODS

Inclusion and exclusion criteria

Types of studies

A systematic review was conducted using all relevant published randomised controlled trials (RCTs) in which exercise was being used as an intervention for diagnosed clinical anxiety disorders.

Types of participants

Subjects were adult men and women with a clinical diagnosis of anxiety disorder according to International Classification of Disease,¹³ Diagnostic Statistical Manual,¹⁴ diagnostic tools, diagnostic questionnaires, research diagnostic criteria or any other validated criteria. Studies investigating mainly depressive disorder were also excluded.

Types of interventions

RCTs with following interventions were considered:

1. Exercise versus no intervention
2. Exercise versus other interventions
 - Exercise versus placebo pills
 - Exercise versus medication
 - Exercise versus cognitive behavioural therapy (CBT)

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Review

3. Exercise in combination with treatments versus other interventions
 - ▶ Exercise+occupational therapy+life style changes versus standard general practitioner care
 - ▶ Exercise+group CBT versus relaxation+group CBT
 - ▶ Exercise+antidepressant medication versus relaxation +placebo
4. Comparing different forms of exercise
 - ▶ Aerobic versus non-aerobic
 - ▶ Hard or strenuous or moderate to hard exercise versus light or very light exercise

Types of outcome measures

Main primary outcomes are

1. Clinically significant changes in anxiety symptoms— as define by each of the studies
2. Clinically relevant outcome/s such as ‘important improvement’ in general mental state
3. Clinically important improvement in quality of life
4. Relapse
5. Compliance with exercise treatment

Secondary outcomes include

1. Adverse effects associated with exercise treatment
2. Treatment satisfaction
3. Economic outcomes

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

We searched MEDLINE, EMBASE, PsycINFO, CINAHL, AMED and Cochrane database of systematic reviews (July 2011). Six journals were hand searched; *British Journal of Sports Medicine*, *British Medical Journal*, *The Psychiatrist*, *British Journal of Psychiatry*, *American Journal of Psychiatry* and *Archives of General Psychiatry*. For additional references, bibliographies of included trials and relevant review articles were examined. Attempts were also made to contact some authors for further clarification. Search terms are described in see online supplementary appendix 1.

DATA COLLECTION AND ANALYSIS

Selection of studies

KJ and SG inspected all the studies from the search and identified relevant abstracts. Any article considered relevant was accessed fully. Above inclusion and exclusion criteria were used to select suitable studies. Any discrepancies were resolved through a discussion with the other reviewer (figure 1).

Assessment of risk of bias in included studies

The Cochrane Collaboration Handbook criteria¹⁵ and the Cochrane Collaboration on Depression Anxiety and Neurosis (CCDAN) Quality Rating System^{16 17} were used to assess the methodological quality of included studies.

Data extraction and analysis

Data from included studies were extracted using a standardised extraction sheet. Cochrane Collaboration’s Review manager 5.1 was used to enter data using duplicate data entry facility. Attempts were made to calculate the weighted mean difference. Random effects model was used in all the analysis.

For continuous data, mean difference, 95% CI and probability value (p) were calculated when means and SDs were presented. We used the generic-inverse-variance method¹⁸ when means and SDs were not presented but the mean differences or standard mean differences were presented instead. In Merom *et al*,¹⁹ data were presented using effect size and CIs. Here we assumed ‘effect size=standard mean difference’ according to the Cochrane Hand

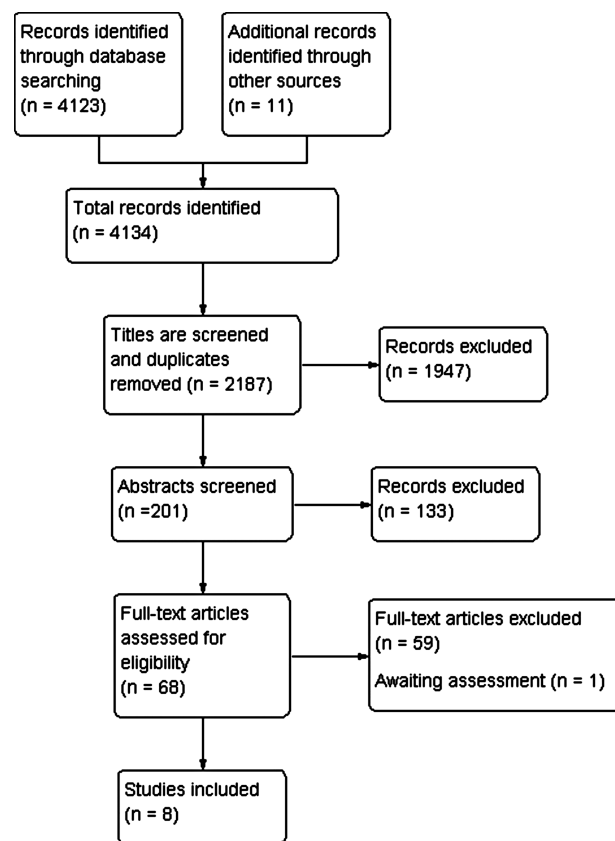


Figure 1 Study selection.

Book of Systematic Reviews on Interventions.²⁰ For Binary data, the ORs and 95% CIs were estimated with the p value.

When continuous data were not normally distributed, we applied the following two standards to all data before inclusion:

1. SDs and the means were reported or were obtained from authors
2. The SD when multiplied by two was less than mean (otherwise, mean is unlikely to be appropriate measure of the distribution).²¹ Data not meeting this standard were not entered to Review Manager for graphical presentation as this assumes normal distribution. These data were entered under the ‘other data’ tables using Other Data Entry Facility instead

The above two standards were applied to avoid the pitfall of applying parametric tests to non-parametric data.

Attempts were also made to do a subgroup analysis where data permitted. These included

1. Disease severity groups according to mild, moderate and severe
2. Comorbid physical illnesses

No subgroup analysis was done due to limited data availability. Attempts were also made to do a sensitivity analysis in order to examine the robustness of the observed findings but given limited data availability, this was not possible. We also used the GRADE approach to interpret findings²² and used the GRADE profiler V3.5 (GRADE PRO) to import data from Review Manager 5.1 to create ‘Summary of findings’ tables.

RESULTS

Search results

The initial search found 4134 records. The process of study selection is shown in figure 1.

Characteristics of included studies

Eight studies met the eligibility criteria and were included: Broocks *et al*,⁸ Esquivela *et al*,²³ Lambert *et al*,²⁴ Martinsen *et al*,⁶ Merom *et al*,¹⁹ Oeland *et al*,²⁵ Sexton *et al*²⁶ and Wedekind *et al*.²⁷ Study participants included patients diagnosed with an anxiety disorder from both sexes, with ages ranging from 18 to 65 years. Characteristics of the included studies are shown in table 1.

Excluded studies and studies awaiting assessment

Most studies were excluded on the basis of study design as they were not RCTs or failed to evaluate clinically diagnosed anxiety disorders.^{51–65} O'Connor⁶⁰ compared exercise with no intervention for patients with panic disorder. It was not clear as to whether its control group had an adequate wash-out period and was excluded. One study,⁶² evaluating the effects of exercise on post-traumatic stress disorder was excluded due to non-randomisation. Three studies assessing obsessive compulsive disorder^{63–65} were excluded because no control arm was found. One study⁶⁶ is awaiting assessment.

CCDAN quality rating scores for included studies (table 2) are as follows:

Broocks *et al*⁸—27/46
Esquivela *et al*²³—22/46

Lambert *et al*²⁴—37/46
Martinsen *et al*⁶—26/46
Merom *et al*¹⁹—29/46
Oeland *et al*²⁵—33/46
Sexton *et al*²⁶—27/46
Wedekind *et al*²⁷—38/46

MAIN RESULTS

Exercise versus no intervention

One study²⁵ evaluated the effects of exercise versus no intervention. It compared exercise (both aerobic and non-aerobic) versus no exercise for patients with panic disorder and generalised anxiety disorder. Quality of life was increased in both exercise and no exercise groups from baseline at 20 and 32 weeks but the improvement was more prominent in exercise group, although the EuroQol 5D results were not significant (table 3).

Exercise versus placebo pill

One study⁸ found beneficial effects of structured exercise (running) including anxiety reduction compared with placebo pill in panic disorder with or without agoraphobia in all outcome scales. The results were statistically significant in six of nine outcome scales (table 3).

Table 1 Characteristics of included studies

Study	Participants	Interventions	Outcome scales (usable date only)
Broocks <i>et al</i> ⁸	Diagnosis: panic disorder±agoraphobia according to DSM-III-R or ICD-10 Age: 18–50 years (y), participant number (N): 46, setting: outpatients, duration: 10 weeks	Group 1: exercise (structured running) Group 2: clomipramine Group 3: placebo pill Clomipramine dose: 37.5–112.5 mg/day	Hamilton anxiety rating scale score, ²⁸ Clinical Global Impression score—observer rating, ²⁹ Panic and Agoraphobia scale score—observer rating, ³⁰ Panic and Agoraphobia scale score—patient rating, ³⁰ Beck Anxiety Inventory score, ³¹ Fear Questionnaire Score, ³² Montgomery-Asberg Depression Rating Score, ³³ Beck Depression Inventory score, ³⁴ Clinical Global Impression score—patient rating ²⁹
Wedekind <i>et al</i> ²⁷	Diagnostic criteria: panic disorder±agoraphobia (DSM-IV and ICD-10) Age: 31.9±8.1 years (average), N: 75 setting: outpatients, duration: 10 weeks	Group 1: exercise (aerobic)+paroxetine Group 2: relaxation+paroxetine Group 3: exercise (aerobic)+placebo Group 4: relaxation+placebo Paroxetine dose: 40 mg/day	Panic and Agoraphobia Scale ³⁰ Clinical Global Impression Scale ²⁹
Esquivela <i>et al</i> ²³	Diagnosis: panic disorder±agoraphobia (DSM-IV), Age:29.6 years (mean), N: 18 setting: outpatients, duration: one intervention session	Group 1: moderate or hard exercise Group 2: very-light exercise	Panic Symptom List—DSM-IV, ³⁵ Visual Analogue Anxiety Scale ³⁶
Sexton <i>et al</i> ²⁶	Diagnosis: anxiety diagnosis (DSM-III), age (mean): walkers: 39.2 years; joggers: 36.4 years, N:53, setting: inpatients, duration: 8 weeks (participants followed up until 6 months)	Group 1: walking exercise (light exercise) Group 2: jogging exercise (strenuous exercise)	Symptom Checklist 90R, ³⁷ State-Trait Anxiety Inventory, ³⁸ Brief Psychiatric Rating Scale, ³⁹ Global Assessment Scale ⁴⁰
Lambert <i>et al</i> ²⁴	Diagnosis: panic disorder±agoraphobia (DSM-IV), Age: 18–65 years, N: 170, Setting: outpatients, duration: 16 weeks (participants followed up until 10 months)	Group 1: occupational therapy+exercise+life style changes Group 2: standard general practitioner care	Beck anxiety inventory, ³¹ Panic attack frequency, severity and symptomatology, ⁴¹ Beck Depression Inventory II, ⁴² Fear Questionnaire, ⁴³ Short Form Health Survey Questionnaire, ⁴⁴ EuroQol Health Questionnaire ⁴⁵
Martinsen <i>et al</i> ⁶	Diagnosis: panic disorder, agoraphobia without panic attacks, social phobia, generalised anxiety disorder (DSM-III-R), mean age: aerobic—39.1 years; anaerobic—38.8 years, N: 79/setting, inpatients, duration: 8 weeks	Group 1: aerobic exercise Group 2: non-aerobic exercise	Comprehensive psycho-pathological Rating Scale; ⁴⁶ Phobic Avoidance Rating Scale; ⁴⁷ Agoraphobic Cognitions Scale ⁴⁸
Merom <i>et al</i> ¹⁹	Diagnosis: panic disorder, generalised anxiety disorder, social phobia (DSM-IV), mean age: 38.7 years (intervention), control group: 39.4 years, N:74, setting: outpatients, duration: 8 weeks (participants followed up until 10 weeks)	Group 1: exercise (walking)+group CBT Group 2: educational sessions+group CBT	Depression Anxiety and Stress Scale 21 ⁴⁹
Oeland <i>et al</i> , 2010 ²⁵	Diagnosis: panic disorder, generalised anxiety disorder (ICD-10), median age: exercise group 36 years control group 40 years, N: 48, setting: outpatients, duration: 20 weeks (followed up until 32 weeks)	Group 1: group exercise programme (aerobic training and non-aerobic weight lifting) Group 2: no exercise	Quality of life using EuroQol 5D scale ⁵⁰

Table 2 Cochrane Collaboration on Depression Anxiety and Neurosis (CCDAN) quality rating scores for included studies

Study reference	8	23	24	6	19	25	26	27
Included studies	Broocks <i>et al</i> (1998)	Esquivela <i>et al</i> (2007)	Lambert (2007)	Martinsen (1989)	Merom (2008)	Oeland (2010)	Sexton (1989)	Wedekind, 2010
CCDAN Criteria Question								
Objectives and specification, main outcomes a priori; 0=objectives unclear/ 1=objectives clear but main outcomes not specified a priori/2=objectives clear with priori specification of main outcomes	2	2	2	2	2	2	2	2
Sample size; 0=<50/1=50–100/2=>100	0	0	2	1	1	0	0	1
Appropriate duration of trial including follow-up; 0=too short/ 1=reasonable length/2=long enough for assessment of long-term outcomes	1	1	2	1	1	2	2	1
Power calculation; 0=not reported/1=mentioned without details 2=details of calculations provided	0	0	2	0	0	0	0	0
Method of allocation; 0=unrandomised and likely to be biased/1=partially or quasi randomised with some bias possible/2=randomised allocation	2	2	2	1	2	2	2	2
Concealment of allocation; 0=not done or not reported/1=partial concealment reported/2=done adequately	0	0	2	0	0	2	0	2
Clear description of treatment and adjunctive treatment; 0=main treatments not clearly described/ 1=inadequate details of main or adjunctive treatments/2=full details of main and adjunctive treatments	2	2	2	2	2	2	2	2
Blinding of subjects; 0=not done/1=done but no test of blind/2=done and integrity of blind tested	1	0	0	0	0	0	0	2
Source of subjects described and representative sample recruitment; 0=source of subjects not described/ 1=source of subjects but unrepresentative sample, for example, volunteers/2=source of subjects described plus representative sample taken	2	1	2	2	2	2	2	2
Use of diagnostic criteria or clear specification of inclusion criteria; 0=none 1=diagnostic criteria or clear inclusion criteria/2=diagnostic criteria plus specification of severity	2	2	2	2	2	2	2	2
Record of exclusion or inclusion criteria and number of exclusions and refusals reported; 0=Criteria and number not reported/1=criteria or number of exclusions & refusals not reported/2=criteria and number of exclusions and refusals reported	2	1	2	2	2	2	2	2
Description of sample demographics; 0=little/no info/1=basic details/2=full description	1	1	1	2	2	2	2	2
Blinding of assessor; 0=not done/1=done but no test of blind/2=done and integrity of blind tested	1	0	0	0	0	0	0	2
Assessment of compliance with experimental treatment; 0=not assessed/ 1=assessed for some experimental treatments/2=assessed for all experimental treatments	0	0	0	0	2	2	0	2
Details of side effects; 0=inadequate details/1=recorded by group but details inadequate/2=full side effect profiles by group	2	0	1	1	0	1	0	2
Record of number and reasons for withdrawal by group; 0=no info on withdrawals by group /1=withdrawals by group reported without reason/2=withdrawals and reason by group	1	0	2	1	1	1	1	2
Outcome measures described clearly or use of validated instruments; 0=outcomes not described clearly/ 1=some outcomes not clearly described/2=outcomes described or valid and reliable instruments used	1	2	2	2	1	2	2	2
Information on comparability and adjustment for differences in analysis; 0=no info on comparability/ 1=some info on comparability with appropriate adjustment 2=sufficient comparability info with appropriate adjustment	1	1	1	2	2	1	2	2
Inclusion of withdrawals in analysis; 0=not included or not reported/1=withdrawals included in analysis by estimation of outcome/2=withdrawals followed up and included in analysis	1	0	2	0	2	0	0	0
Presentation of results with inclusion of data for reanalysis of main outcome; 0=little information presented/1=adequate information/2=comprehensive	1	1	2	0	1	2	2	0
Appropriate statistical analysis; 0=inadequate/1=adequate/2=comprehensive and appropriate	2	2	2	2	2	2	2	2
Conclusions justified; 0=no/1=partially/2=yes	2	2	2	1	2	2	2	2
Declaration of interests; 0=no/2=yes	0	2	2	2	0	2	0	2
Total	27	22	37	26	29	33	27	38

Table 3 Results summary

Comparison	Number of RCTs	Results					Significance	Conclusions
		Outcome scales	How measured	Intervention	Control			
Exercise vs no exercise	1	EuroQol 5D scale	Baseline to 20 weeks	Exercise (median)	No exercise (median)	p=0.47	Better quality of life in the exercise group compared to no exercise group	
				25	15			
Exercise vs placebo pill	1	Hamilton Anxiety scale	Baseline to 32 weeks	Exercise (median)	No exercise (median)	p=0.39	More anxiety reduction in the exercise group compared to placebo pill group	
				40	20			
Exercise vs placebo pill	1	Beck Anxiety Inventory	At 10 weeks	Exercise (mean)	Placebo pill (mean)	p=0.02	More anxiety reduction in the exercise group compared to placebo pill group	
				11.3	21.7	p=0.0006		
				Beck Depression Inventory	14.9	35.4		p=0.01
				Montgomery-Asberg Depression Rating scale	6.8	15.8		p=0.0002
				Observer-Rating Clinical Global Impression scale	7.8	15.9		p=0.008
				Panic and Agoraphobia Observer Rating	2.4	3.8		p=0.03
				Patient Rated Panic and Agoraphobia scale	14.8	21.1		p=>0.05
				Fear Questionnaire scale	17.2	23.7		p=>0.05
				Patient Rated Clinical Global Impression scale	41.2	65.8		p=>0.05
					2.8	3.9		p=>0.05
Exercise vs antidepressant medication	1	Observer Rating Clinical Global Impression scale	At 10 weeks	Exercise (mean)	Antidepressant (mean)	p=0.0002	More anxiety reduction in the antidepressant group compared to exercise group	
				2.4	1.6	p=0.02		
				Observer Rating Panic and Agoraphobia scale	14.8	7.6		p=0.02
				Patient Rating Panic and Agoraphobia scale	17.2	9.7		p=0.02
				Patient Rating Clinical Global Impression scale	2.8	1.8		p=0.005
				Fear Questionnaire scale	41.2	30.2		p=0.03
				Hamilton Anxiety Rating scale	11.3	8.5		p=>0.05
				Montgomery-Asberg Depression Rating Scale	7.8	6.1		p=>0.05
				Beck Anxiety Inventory	14.9	15.6		p=>0.05
				and Beck Depression Inventory scale	6.8	7.2		p=>0.05
Exercise + antidepressant vs relaxation + placebo	1	Clinical Global Impression Scale	At 10 weeks	Exercise+antidepressant	Relaxation+placebo	p=<0.05	More improvement in the exercise + antidepressant group	
				No data given	No data given			
Exercise + placebo pill vs relaxation + placebo pill	1	Clinical Global Impression Scale	At 10 weeks	Exercise+placebo pill	Relaxation+placebo pill	p=0.06	Inconclusive	
				No data given	No data given			
	1			Exercise+group CBT	Educational sessions +group CBT	p=0.61		

Continued

Table 3 Continued

Comparison	Number of RCTs	Outcome scales	How measured	Results		Significance	Conclusions						
				Intervention	Control								
Exercise + group CBT vs Educational sessions + group CBT		Depression and Anxiety Stress Scale 21—Anxiety		Standard mean difference —0.16 CI—0.77 to 0.45			Added benefits of exercise+group CBT for social phobics						
		Depression and Anxiety Stress Scale—Stress		Standard mean difference —0.32 CI—0.93 to 0.29		p=0.30							
		Depression and Anxiety Stress Scale: Depression		Standard mean difference —0.67 CI—1.30 to—0.04		p=0.04							
Exercise + occupational therapy + life style changes vs Standard general practice care	1	Beck Anxiety Inventory	20 weeks	Exercise+occupational therapy+life style mean difference—9.8 CI –15 to –4.6	Standard general practice		p=0.0002	Significant anxiety reduction by exercise+occupational therapy+life style changes					
			10 months	28/29 (events)	25/34 (events)	p=0.03							
		Panic free	20 weeks	23/36 (events)	17/42 (events)	p=0.04	More panic free in the exercise arm						
			10 months	21/31 (events)	17/36 (events)	p=0.09							
Light/very light exercise vs Moderate/Strenuous/hard exercise	2	State-Trait Anxiety Inventory—Trait State-Trait Anxiety Inventory—State Symptom Checklist 90R Beck Depression Inventory Brief Psychiatric Rating Scale Global Assessment Scale Visual Analogue Anxiety Scale Panic Symptom List panic rate	At 8 weeks After one intervention session	light/very light exercise mean (SD) 46.2 (12) 47.4 (15.3) 0.94 (0.67) 11.9 (10.7) 25 (1.8) 63.5 (17.2) 36.2 (17.9) 7.7 (6.2) 5/8 (events)	Moderate/Strenuous/hard mean (SD) 41.2 (11.3) 42.2 (12.9) 0.88 (0.67) 9.8 (10.8) 24.8 (6.1) 68.5 (11.9) 9 (15.4) –1.5 (10.4) 1/10 (events)		p=0.18 p=0.24 p=>0.05 p=>0.05 p=0.90 p=0.28 p=<0.01 p=<0.01 p=0.03	Inconclusive about the type of exercise that is more effective in anxiety reduction					
				Aerobic vs non-aerobic exercise	1	Comprehensive Psycho-pathological Rating Scale Phobic Avoidance Rating Scale	8 weeks		Aerobic exercise No data given	Non-aerobic exercise No data given		p=>0.1	Both types reduces anxiety symptoms, no significant difference among two groups
									No data given	No data given	p=>0.1		

Exercise versus antidepressant medication

One RCT⁸ compared structured exercise (running) with antidepressant medication (clomipramine 37.5–112.5 mg/day) for patients with panic disorder with or without agoraphobia. Beneficial effects of this medication including a significant anxiety reduction were observed in five of nine outcome scales (table 3).

Exercise+antidepressant medication versus relaxation+placebo

One study²⁷ examined the effect of combined exercise plus antidepressant medication (paroxetine 40 mg/day) against relaxation plus placebo pill for patients with panic disorder with or without agoraphobia (table 3). Here, the outcome was assessed using Clinical Global Impression scale at 10 weeks. There was a significant improvement in Clinical Global Impression in the exercise plus antidepressant (paroxetine) group (F value=8.61, $p<0.05$).

This study²⁷ also compared exercise plus placebo pill against relaxation plus placebo pill using the same outcome scale (Clinical Global Impression scale). There was a greater non-significant improvement in Clinical Global Impression in the exercise plus placebo pill group (F value=3.7, $p=0.06$).

Exercise versus CBT

None of the studies compared exercise with CBT. Heiden *et al*⁶¹ compared CBT with exercise (included in physical activity programme). It broadly looked at patients diagnosed with a stress-related illness including anxiety but not anxiety disorders.

Exercise+group CBT versus educational sessions+group CBT

For generalised anxiety disorder, social phobia and panic disorder, one RCT¹⁹ showed a non-significant reduction in anxiety symptoms following exercise plus group CBT compared with educational sessions plus group CBT (table 3), and there was a significant reduction in depressive symptoms in the Depression and Anxiety Stress Scale: Depression. Added benefits of exercise

when combined with group CBT were shown for social phobics ($p<0.05$) when considering the results of regression coefficients of analysis of covariance (ANCOVA).

Exercise+occupational therapy+life style changes versus standard general practitioner (GP) care

One study²⁴ compared exercise in combination with occupational therapy (including life style changes) against standard general practitioner care for patients with panic disorder with or without agoraphobia (figure 2). To measure the panic attack frequency, severity and symptomatology, it also used Anxiety Disorder Interview Schedule-IV.⁶⁷ At 20 weeks in Beck Anxiety Inventory (Supplementary File for editors only figure 3), it showed a significant reduction in anxiety in the exercise arm (which included occupational therapy and life style changes) compared with standard general practitioner care (table 3). Even at 10 months, exercise arm patients remained improved compared with general practitioner care (OR 0.10, 95% CI 0.01 to 0.84, $p=0.03$). At 20 weeks, exercise arm patients had been more panic free compared with those receiving general practitioner care (OR 0.38, 95% CI 0.15 to 0.96, $p=0.04$). At 10 months, again exercise arm patients remained more panic free non-significantly (OR 0.43, 95% CI 0.16 to 1.16, $p=0.09$). Its GRADE PRO summary of findings is shown in table 4.

Moderate, strenuous or hard exercise versus very light or light exercise

Two studies^{26 23} compared moderate, hard or strenuous exercise versus very light or light exercise (table 3). These two studies used different exercise programmes and outcome scales causing significant heterogeneity, and were not combined for meta-analysis. Nonetheless the data were extracted and were entered in to the Review Manager.

Sexton *et al*²⁶ compared light exercise (walking) against strenuous or hard exercise (jogging) for patients with an anxiety diagnosis (figure 3). A greater non-significant reduction in anxiety symptoms were observed in the jogging group compared

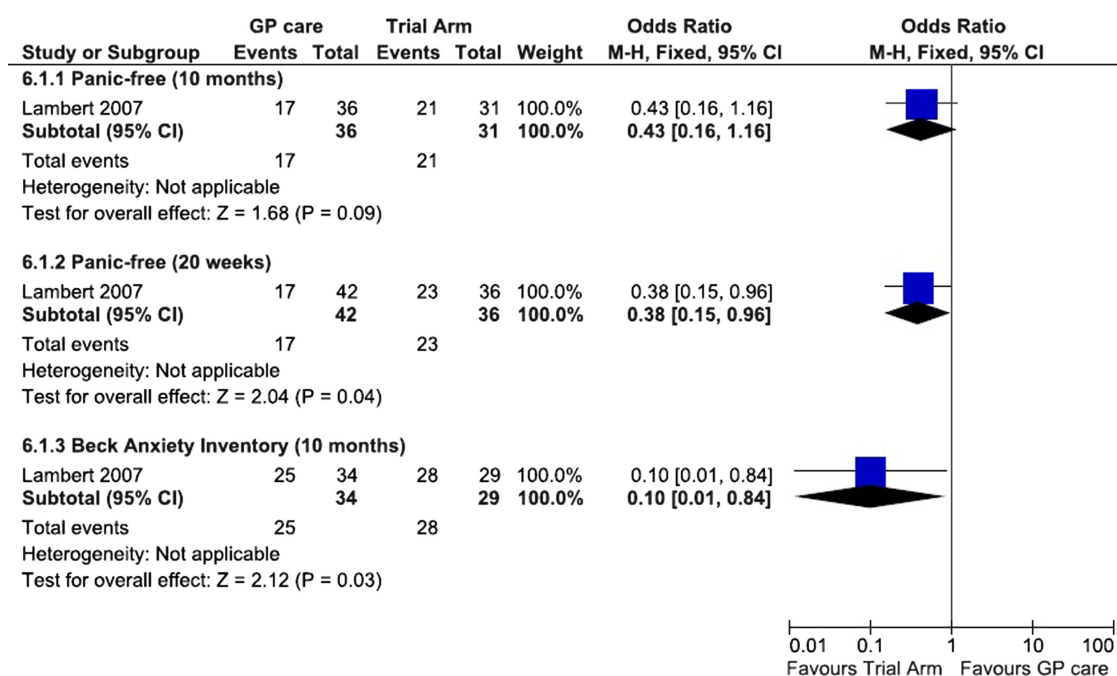


Figure 2 Exercise+occupational therapy+life style changes versus standard general practitioner care.

Table 4 Summary of findings table; exercise+occupational therapy+life style changes versus standard general practitioner care

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE) Comments
	Assumed risk	Corresponding risk			
	Control	Exercise+occupational therapy +life style changes vs standard general practitioner care			
Beck Anxiety Inventory (10 months) Follow-up: 10 months	Study population		RR 0.76 (0.62 to 0.94)	63 (1 study)	⊕⊕⊕⊖ Moderate†,‡
	966 per 1000	734 per 1000 (599 to 908)			
	Medium risk population				
Panic-free (20 weeks) Follow-up: 10 months	Study population		RR 0.63 (0.41 to 0.99)	78 (1 study)	⊕⊕⊕⊖ Moderate†,§
	639 per 1000	403 per 1000 (262 to 633)			
	Medium risk population				
Panic-free (10 months) Follow-up: 10 months	Study population		RR 0.7 (0.46 to 1.06)	67 (1 study)	⊕⊕⊕⊖ Low†,¶, **
	677 per 1000	474 per 1000 (311 to 718)			
	Medium risk population				
	677 per 1000	474 per 1000 (311 to 718)			

Patient or population: patients with anxiety disorders; Settings: outpatients; Intervention: exercise+occupational therapy+life style changes; Comparison: standard general practitioner care.

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

*The basis for the assumed risk (eg, the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

†Unblinded trial.

‡95% CI -14.99 to -4.61.

§95% CI 0.15 to 0.96.

¶95% CI 0.16 to 1.16.

**Test for overall effect: Z=1.68 (p=0.09).

RR, risk ratio.

with the walking group in the State—Trait Anxiety Inventory—Trait scale (mean difference 5, 95% CI -2.27 to 12.27, p=0.18) and the State—Trait Anxiety Inventory—State scale (mean difference 5.20, 95% CI -3.56 to 13.96, p=0.24). Similarly, there was no significant outcome difference between these two groups in the Brief Psychiatric Rating Scale (mean difference 0.29, 95% CI -2.79 to 3.19, p=0.90). To the contrary, the Global Assessment Scale outcome results non-significantly favoured walking (mean difference 5, 95% CI 14.02 to 4.02, p=0.28). The GRADE PRO summary of findings table comparing moderate, hard or strenuous exercise against light or very light exercise is shown in online supplementary table S4.

Esquivela *et al*²⁶ compared moderate with hard exercise with very light exercise by having patients exercised on a bicycle ergometer with different workloads, for patient with panic disorder with or without agoraphobia. Outcomes were assessed using the Panic Symptom List (PSL-IIIR) consisting of 13 symptoms of a panic attack (as described by DSM III-R) on a scale from 0 to 4.³⁵ Also, the frequency and the severity of panic attacks were assessed using Visual Analogue Anxiety Scale after provoking panic attacks using 35% carbon dioxide panic provocation challenge.³⁶

The Visual Analogue Anxiety Scale showed a significant reduction in anxiety symptoms in moderate to hard exercise compared with very light exercise (p<0.01). The panic rate (Supplementary File for editors only figure 5) was also lower significantly in moderate to hard exercise group than the light exercise group (OR 0.07, 95% CI 0.01 to 0.82, p=0.03).

Aerobic versus non-aerobic exercise

One study⁶ compared the effects of aerobic and non-aerobic exercise on panic disorder, agoraphobia without panic attacks, social phobia and generalised anxiety disorder (table 3). At the end of the study, both groups had achieved significant reductions in scores compared with admission values in the Comprehensive Psycho-pathological Rating Scale and Phobic Avoidance Rating Scale (p<0.001). The difference between aerobic and non-aerobic groups was small and non-significant (p>0.1).

Exercise for obsessive compulsive disorder and post-traumatic stress disorder

Our search identified a protocol for a one RCT evaluating the effects of exercise on post traumatic stress disorder.⁶⁸ No RCTs were found evaluating the effects of exercise on obsessive compulsive disorder. However, there were other study designs evaluating the effect of exercise on obsessive compulsive disorder^{63–65} and post-traumatic stress disorder.⁶²

Exercise for adjustment disorder and acute stress disorder

This review did not find any RCTs specifically evaluating the effects of exercise for adjustment disorder or acute stress disorder. Again, we found other study designs evaluating this effect.⁶⁹

DISCUSSION

The strengths of this review include: thorough searching for evidence; systematic appraisal of the quality of included studies

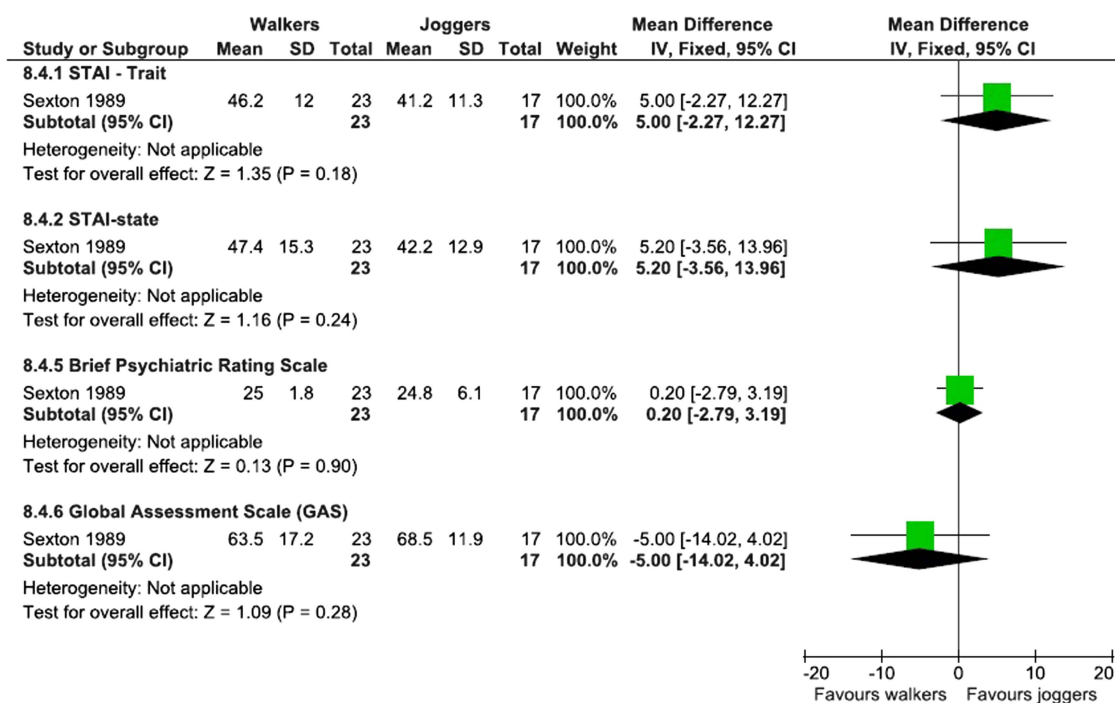


Figure 3 Moderate, strenuous or hard exercise (jogging) versus very light or light exercise (walking): continuous data.

using the CCDAN quality assessment tool; and grading of evidence (GRADE PRO). Furthermore, attempts were made to cover a wide range of anxiety disorders and a total of 563 subjects were included.

There was a significant reduction in anxiety symptoms following structured exercise (running) for patients with panic disorder with or without agoraphobia in comparison with placebo pill treatment.⁸ However, some limitations were identified in this study. It can be argued that running exercise induces prolonged exposure to feared agoraphobic situations which might act as a graded exposure technique. As the authors note, ‘running exposes patients to the internal feared cues of palpitations, sweating, rapid breathing, and the like that are induced by exercise’.⁷⁰ On the other hand, it could also be argued that running exercise may not induce exposure to ‘all of the cues that panic disorder or agoraphobic sufferers fear’—and in that sense it may have additional benefits than just a graded exposure technique. Marks⁷⁰ commenting on this study⁸ reported, ‘The study may have achieved even more improvement had its exposure been tailored to involve all of the patients’ feared cues systematically rather than just incidental to the exercise schedule’.⁷⁰

One study²⁴ concluded that exercise and ‘occupational therapy led life style treatment’ may provide a clinically effective intervention at least as effective as routine general practice care for patients with panic disorder. It is not clear about the type of treatment patients had as routine general practitioner care which would have affected the outcomes.

One study¹⁹ suggests that there is no benefit of exercise plus group CBT upon educational sessions plus group CBT for social phobia, panic disorder and generalised anxiety disorder. Possible explanations for this could be that the strategies used with group CBT may also be applied to exercise training. The authors state, “these may include situational analysis, goal setting, self monitoring, home work activities, and supportive follow up.”⁷¹ However, when considering the results of regression coefficients of ANCOVA, added benefits of exercise when

combined with group CBT were shown for social phobics ($p < 0.05$).¹⁹ In this study, attendance rates were high for patients with social phobia compared to the other two diagnoses. Here, the effects of unmeasured confounders were not accounted for analysis.¹⁹ “The study had a limited statistical power to demonstrate significant effects.” As a positive note, assessors had used audio-taped recordings to assess the inter-rater reliability.

It remains uncertain as to how effective exercise is when it comes to hard or light exercise. Our review found two studies evaluating this:^{23 26} one²³ highlighted the beneficial effects of moderate to hard exercise for patients with panic disorder in the Visual Analogue Anxiety scale, Panic Symptom List and Panic Rate (statistically significant result). One of the strengths in this study²³ was that the effects of comorbid disorders across the two treatment arms (confounders) were minimised after effective randomisation. However, in the second study, Sexton *et al*²⁶ failed to show a significant difference among light exercise (walking) and hard exercise (Jogging). In fact, all the outcome scales used in this study delivered a non-significant result. The authors commented: “There was an un-equal distribution of confounders at the baseline when substance misuse was taken in to consideration. There was also a high dropout rate in jogging group.”²⁶ It remains unclear as to why these two studies contradict each other. Possible explanations include that the two studies used different patient groups, different exercising methods and different outcome scales. For instance, Esquivela *et al*²³ used patients with panic disorder while Sexton *et al*²⁶ used patients with an anxiety disorder; also Esquivela *et al*²³ used exercising on a bicycle ergometer while Sexton *et al*²⁶ used walking or jogging. In contrast to the aforementioned findings, Dishman and Buckworth⁷² reported that moderate intensity activities such as walking are more successful than vigorous physical activity programmes for anxiety and depression.

In terms of aerobic and non-aerobic exercise, one study⁶ indicated that both aerobic and non-aerobic groups achieve similar

and significant reductions in anxiety scores. The patients in this study⁶ were hospitalised, and had received traditional psychiatric treatment in addition to exercise, which could have affected the outcomes. Carrera *et al*⁷³ reported that people with panic disorder rate their quality of life as lower than that of healthy people. Our review found one RCT²⁵ showing a non-significant improvement in quality of life in the exercise group (at 20 and 32 weeks) compared with a 'no exercise' group for patients with panic disorder and generalised anxiety disorder. When exercise combined with an antidepressant for patients with panic disorder,²⁷ combined group (exercise+antidepressant) showed a greater improvement in Clinical Global Impression outcomes compared with relaxation plus placebo ($p<0.05$). In CCDAN quality rating this study scored 38 of 46 but it should also be noted that Wedekind *et al*²⁷ were unable to establish true double-blind conditions.

Limitations

We considered English language reported articles only. There were very few studies to enter into a meaningful funnel graph to assess publication bias. Most of the included studies were of shorter duration with methodological limitations. It can be argued that studying treatment effects of anxiety disorders brings unique difficulties; distressed patient experiencing anxiety symptoms may not wait till the end of exercise treatment programme and thus drop out. Patients may request medication or other psychological treatment options to deal with their acutely distressing symptoms at an earlier stage rather than waiting to see exercise effects.

Clinical implications

Considering the results from above eight included studies, it seems that exercise shows a treatment effect beyond the placebo effect. Although it appears that the antianxiety effects of exercise are lesser than antidepressants for clinical anxiety disorders, it can still be beneficial as an adjunctive treatment. Medical clearance is needed for these patients to proceed with exercise programme.⁷ The Physical Activity Readiness Questionnaire is a simple screening instrument commonly used in preparticipation screening for moderate intensity physical activity programme.⁷⁴ Exercise prescription or motivational messages in printed form or by computer seem to be more effective than face-to-face counselling alone.⁷² Further, interventions that target specific groups or are tailored to the individual seem more effective than more generic interventions for anxiety and depression.⁷⁵⁻⁷⁸

What this study adds

- ▶ Treatment effects of exercise for patients with clinical anxiety disorders.
- ▶ Identification of less-researched areas such as; treatment effects of exercise on different types of clinical anxiety disorders; comparing treatment effects exercise versus psychological treatment methods for clinical anxiety disorders.

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Contributors KJ participated in protocol development, searching, study selection, data extraction, data analysis and report writing. SG participated in protocol development, data analysis, statistical expertise, searching, study selection and data extraction. CH participated in protocol development, searching, study selection and report writing.

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Exercise for anxiety disorders: systematic review

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