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*Published in:*
Cochrane Database of Systematic Reviews

*DOI:*
10.1002/14651858.CD004366.pub4

*Publication date:*
2010

*Document Version*
Publisher's PDF, also known as Version of record

# Exercise for depression (Review)

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This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2010, Issue 1

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[Intervention Review]

# Exercise for depression

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**Editorial group:** Cochrane Depression, Anxiety and Neurosis Group.
**Publication status and date:** Edited (no change to conclusions), comment added to review, published in Issue 1, 2010.
**Review content assessed as up-to-date:** 25 March 2007.

**Citation:** Mead GE, Morley W, Campbell P, Greig CA, McMurdo M, Lawlor DA. Exercise for depression. *Cochrane Database of Systematic Reviews* 2009, Issue 3. Art. No.: CD004366. DOI: 10.1002/14651858.CD004366.pub4.



## ABSTRACT

### Background

Depression is a common and important cause of morbidity and mortality worldwide. Depression is commonly treated with antidepressants and/or psychotherapy, but some people may prefer alternative approaches such as exercise. There are a number of theoretical reasons why exercise may improve depression.

### Objectives

To determine the effectiveness of exercise in the treatment of depression.

### Search methods

We searched Medline, Embase, Sports Discus, PsycINFO, the Cochrane Controlled Trials Register, and the Cochrane Database of Systematic Reviews for eligible studies in March 2007. In addition, we hand-searched several relevant journals, contacted experts in the field, searched bibliographies of retrieved articles, and performed citation searches of identified studies. We also searched www.controlled-trials.com in May 2008.

### Selection criteria

Randomised controlled trials in which exercise was compared to standard treatment, no treatment or a placebo treatment in adults (aged 18 and over) with depression, as defined by trial authors. We excluded trials of post-natal depression.

### Data collection and analysis

We calculated effect sizes for each trial using Cohen's method and a standardised mean difference (SMD) for the overall pooled effect, using a random effects model. Where trials used a number of different tools to assess depression, we included the main outcome measure only in the meta-analysis.

**Main results**

Twenty-eight trials fulfilled our inclusion criteria, of which 25 provided data for meta-analyses. Randomisation was adequately concealed in a minority of studies, most did not use intention to treat analyses and most used self-reported symptoms as outcome measures. For the 23 trials (907 participants) comparing exercise with no treatment or a control intervention, the pooled SMD was -0.82 (95% CI -1.12, -0.51), indicating a large clinical effect. However, when we included only the three trials with adequate allocation concealment and intention to treat analysis and blinded outcome assessment, the pooled SMD was -0.42 (95% CI -0.88, 0.03) i.e. moderate, non-significant effect. The effect of exercise was not significantly different from that of cognitive therapy. There was insufficient data to determine risks and costs.

**Authors' conclusions**

Exercise seems to improve depressive symptoms in people with a diagnosis of depression, but when only methodologically robust trials are included, the effect sizes are only moderate and not statistically significant. Further, more methodologically robust trials should be performed to obtain more accurate estimates of effect sizes, and to determine risks and costs. Further systematic reviews could be performed to investigate the effect of exercise in people with dysthymia who do not fulfil diagnostic criteria for depression.

## PLAIN LANGUAGE SUMMARY

**Exercise for depression**

Depression is a common and important illness affecting at least 1 in 5 people during their lifetime. Exercise has been advocated as an adjunct to usual treatment. This review identified all available randomised trials which compared exercise with either no treatment or an established treatment (e.g. talking therapy) for people with a clinical diagnosis of depression. Data from 25 trials were combined. We found exercise did seem to improve the symptoms of depression, but we cannot be sure exactly how effective it is, or the most effective type of exercise. The evidence suggests that exercise probably needs to be continued in the longer-term for benefits on mood to be maintained.

## BACKGROUND

### Description of condition

Depression refers to a wide range of mental health problems characterised by the absence of a positive affect (a loss of interest and enjoyment in ordinary things and experiences), low mood and a range of associated emotional, cognitive, physical and behavioural symptoms (NICE 2007). Depression is common, affecting 121 million people worldwide (Moussavi 2007). Depression is an important cause of morbidity and mortality and produces the greatest decrement in health compared with other chronic diseases such as angina or arthritis (Moussavi 2007).

### Description of intervention

Depression is commonly treated with antidepressants or psychological therapies or a combination of both. However, a recent Cochrane review (Moncrieff 2003) found only small differences between antidepressant medications and active placebos. Furthermore, antidepressants may have adverse side effects, adherence can be poor, and there is a lag time between starting antidepressants and improvements in mood. Psychological treatments are generally free from side effects, but some people may not wish to attend psychotherapy because of perceived stigma. Depression is a well-recognised reason for seeking alternative therapies (Astin 1998). Whilst this may reflect dissatisfaction with conventional treatments, another possibility is that alternative therapies may be more in line with people's own beliefs and philosophies (Astin 1998). There has been increasing interest in the potential role of alternative therapies such as music therapy, light therapy, acupuncture, family therapy, marital therapy, relaxation and exercise for the management of depression.

The effect of exercise on depression has been the subject of research for several decades and is believed by a number of researchers and clinicians to be effective in the treatment of depression (Beesley 1997). For example, a report for the National Service Framework for Mental Health suggested that exercise should be included as a treatment option for people with depression (Donaghy 2000). The recent UK National Institute of Clinical Excellence (NICE)

guideline for depression recommended structured, supervised exercise programmes, three times a week (45 minutes to 1 hour) for 10 to 12 weeks for mild depression (NICE 2007). This recommendation was graded 'C' i.e. expert committee reports, or opinions and/or clinical experience of respected authorities. Exercise programmes can be offered in the UK through Exercise Referral Systems (DOH 2001). These schemes direct someone to a service offering an assessment of need, development of a tailored physical activity programme, monitoring of progress and follow-up. However, a recent systematic review of Exercise on Prescription Schemes found limited evidence about their effectiveness and recommended further research (Sorensen 2006). NICE (NICE 2006) concluded that there was insufficient evidence to recommend Exercise Referral Schemes other than as part of research studies to evaluate their effectiveness.

**How the intervention might work**

There is evidence from population studies that depression is related to low levels of physical activity (Biddle 2000; Goodwin 2003). Whilst an association between two variables does not necessarily imply causality, there are plausible reasons why physical activity and exercise may improve mood. Exercise may act as a diversion from negative thoughts, and the mastery of a new skill may be important (LePore 1997). Social contact may be part of the mechanism. Physical activity may have physiological effects such as changes in endorphin and monoamine levels, or reduction in the levels of the stress hormone cortisol (Duclos 2003) which all may improve mood. Recent studies have suggested that exercise stimulated growth of new nerve cells and release of proteins known to improve health and survival of nerve cells, e.g. brain-derived growth neurotrophic factor (Cotman 2002; Ernst 2005).

**Why it is important to do this review**

Several meta-analyses (Craft 1998; Carlson 1991; North 1990; Lawlor 2001; Stathopoulou 2006; Sjosten 2006) have looked at the effect of exercise on depression and all found that exercise was of benefit. However, three of these reviews pooled data from a range of study types that included uncontrolled studies and randomised as well as non-randomised controlled trials, and pooled data from trials that compared exercise and no treatment with data from trials that compared exercise and other forms of treatment (Craft 1998; Carlson 1991; North 1990). One included only trials in older people (Sjosten 2006). One meta-analysis (Stathopoulou 2006) included only publications from peer-reviewed journals even though it is widely acknowledged that positive trials are more likely to be published than negative or inconclusive trials. The Cochrane Handbook recommends comprehensive searching for all trials, including unpublished ones, to avoid bias. Two meta-analyses which included assessments of study quality both cautiously concluded that exercise may be effective, but recommended that further well-designed trials are required (Sjosten 2006; Lawlor 2001).

We have become aware that futher randomised trials have been published since these systematic reviews and meta-analyses. Hence, another systematic review, which includes these new trials and which seeks to determine the effect of study quality on the effectiveness of exercise, is now required.

## OBJECTIVES

1. To determine the effectiveness of exercise in the treatment of depression.

2. To update a previously published systematic review in this area (Lawlor 2001).

## METHODS

### Criteria for considering studies for this review

#### Types of studies

Randomised controlled trials. A trial was defined as a randomised controlled trial if the allocation of participants to intervention and comparison groups is described as randomised (including terms such as "randomly", "random", and "randomisation").

#### Types of participants

Adult men and women aged 18 and over (with no upper age limit). Studies were included if the participants were defined by the author of the trial as having depression (by any method of diagnosis and with any severity of depression).The effects of exercise on depressive symptoms in participants with emotional distress (but not fulfilling a diagnosis of depression) or those who are heathy were not included in this review.

Studies that investigated the effect of exercise on anxiety and neurotic disorders were not included in the review.

We made a post-hoc decision to exclude trials of exercise for post-natal depression, because a separate Cochrane Review will address this particular question (Glyde, protocol in progress).

#### Types of interventions

Studies comparing any type of exercise (as defined by the trial authors) with no treatment/waitlist/placebo or to any other type of intervention (including pharmacotherapy, psychotherapy or alternative interventions).

Studies comparing exercise plus another intervention versus the other intervention alone were also included (e.g. exercise plus cognitive therapy versus cognitive therapy alone).

Studies comparing two different types of exercise with no non-exercising comparison group were not included.

Studies that measured outcomes immediately before and after a single exercise session were not included.

**Post-hoc decisions about intervention and comparisons**

When the protocol for this review was first published in the Cochrane Library, we did not expect to identify trials described as 'combination treatments' by the authors, where exercise was one component of the 'combination' . Hence we made a post-hoc decision to exclude such trials, because it would not have been possible to disentangle the effect of exercise from the effect of the other components of the intervention. Following editorial assessment of our review, we excluded a trial which provided an exercise intervention lasting only four days (Berlin 2003).

**Choice of comparisons for meta-analysis**

Where trials included a control arm, an exercise arm, and an 'established treatment' (e.g. CBT, antidepressants) arm, we extracted data on control versus exercise, and exercise versus established treatment (e.g CBT, antidepressants). This meant that data from the exercise arm were included in two separate comparisons.

Where trials compared an established treatment (e.g. CBT, antidepressants) versus exercise versus both the established treatment and exercise, we made two comparisons: established treatment (e.g. CBT, antidepressants) plus exercise versus established treatment (e.g. CBT, antidepressants) alone (and included this in the meta-analysis of treatment versus control); and we also compared exercise versus established treatment (e.g. CBT, antidepressants). This means that data from the 'established treatment alone' arm were used in two separate comparisons.

**Main comparisons**

Two main analyses were undertaken:

1. Exercise was compared to "no treatment". This included studies in which exercise was compared to no intervention; those in which it was compared to an intervention which the authors defined as a placebo; and those in which exercise was used as an adjunct to an established treatment which was received (in an identical way) by participants in both the exercising and non-exercising group e.g. exercise plus CBT versus CBT alone

2. Exercise was compared to other treatments for depression, including cognitive therapy, 'bright light' therapy and antidepressants.

## Types of outcome measures

**Primary outcome measures**

Studies had to include a measure of depression or mood at the outcome assessment, either as a continuous measure or as a dichotomous outcome.

Where trials used a number of different tools to assess depression we included the main outcome measure only in the meta-analysis. The main outcome measure was defined using a hierarchy of criterion as follows - identified by the trial authors as the main outcome measure, outcome reported in the abstract, first outcome reported in the results section.

Where trials used dichotomous outcomes as primary outcomes; and also provided data on continuous outcome measures, we used the data provided in the trial reports for the continuous outcome measure in our meta-analysis.

**Secondary outcome measures**

Following editorial review, we decided to extract data, when available, on the number of people who were screened for inclusion, the number recruited, attendance at the exercise interventions, and the number completing the interventions, in order to better understand the practical considerations of exercise trials for depression, and for the provision of exercise as a treatment for depression.

We recorded whether trials reported other clinically relevant endpoints (e.g quality of life), cost and adverse events.

## Search methods for identification of studies

1. Original search strategy (Lawlor 2001)

a) We searched Medline on Ovid, Embase on Ovid, Psycinfo on Silver Platter, Sports Discus on Silver Platter, the Cochrane Controlled Trials Register and the Cochrane Database of Systematic Reviews. Details of the search strategy used in Medline are provided below; this was modified as appropriate for other databases. Appropriate filters were applied to identify randomised controlled trials (Dickersin 1994, Lefebvre 1996).

b)We handsearched the following: BMJ, JAMA, Archives of Internal Medicine, New England Journal of Medicine, Journal of the Royal Society of Medicine, Comprehensive Psychiatry, British Journal of Psychiatry, Acta Psychiatrica Scandinavica and British Journal of Sports Medicine.

c) We searched the bibliographies of all retrieved articles for additional references.

d) We contacted experts - all authors of the studies included in the review and those with at least two publications amongst those that were excluded but that were related to the study area - to identify unpublished studies and ongoing studies where results may become available before the end of the review.

Medline Search Strategy:

1. exp EXERCISE/
2. exp Exercise Therapy/
3. exp Exertion/
4. exp Physical Fitness/
5. exp Walking/
6. exp Running/
7. exp Swimming/
8. exp Jogging/
9. exp "Physical Education and Training"/
10. exercise$ near aerobic$.tw.
11. train$ near aerobic$.tw.
12. exercise$ near strength$.tw.
13. train$ near strength$.tw.
14. bicycling$.tw.

15. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
16. exp DEPRESSION/
17. exp Depressive Disorder/
18. exp Dysthymic Disorder/
19. 16 or 17 or 18
20 15 and 19
2. To supplement and update the original searches, we undertook the following:
a) Electronic searches (performed on 26.3.07)
CCDANCTR-Studies were searched using the following terms: Diagnosis = Depression or Depressive Disorder or Dysthymic Disorder and Intervention = Exercise.
Cochrane Central Controlled Trials Register (CENTRAL) was searched using the following terms: Exercis*
Following editorial review, we also searched www.controlled-trials.com (on 20.5.08) to identify ongoing trials
All the selected studies and relevant review articles were sought as citations in the Scisearch on 25.5.07. Potentially relevent articles were obtained and scrutinised for relevance.
b) Handsearches
a/ The references of all selected trials, systematic reviews and non-systematic reviews were inspected for more published reports and citations of unpublished research. These handsearches were performed during May 2007.
c) Personal communication
a/ To ensure all RCTs were identified, the authors of significant papers and other experts in the field were contacted to enquire about published, unpublished or ongoing trials. This was done during May and June 2007.

## Data collection and analysis

### Selection of studies

For the first version of the review (Lawlor 2001), three reviewers examined titles and abstracts to remove obviously irrelevant reports. Studies needed to be identified by only one reviewer for the full text to be retrieved. Two reviewers then examined full text reports to determine compliance of studies with eligibility criteria and corresponded with investigators where appropriate to clarify study eligibility.
For the current updated version of the review, one reviewer (Gillian Mead) examined titles and abstracts from the electronic searches, retrieved full-texts of new, potentially relevant papers, and discussed eligibility with a second reviewer (Wendy Morley). Gillian Mead corresponded with investigators, where appropriate, to clarify study eligibility. Gillian Mead and Wendy Morley made final decisions on study inclusion and proceeded to data collection.

### Data collection and management

Two reviewers (Debbie Lawlor and Stephen Hopker) extracted data for the first review in 2001 (Lawlor 2001). Two reviewers (Gillian Mead and Wendy Morley) independently extracted data for each new trial identified for this review. Data extracted were: quality criteria, participants, interventions, outcome measures, results and main conclusions. All four reviewers used the same structured form that had been piloted on two studies. Any discrepancies were resolved by referring to the original papers and discussion.
Following editorial assessment of the updated review, one reviewer (Gillian Mead) scrutinised the publications again and extracted data (when available) on the number of patients screened, the number randomised, the number allocated exercise, the number who dropped out of the exercise arm (please see additonal table), secondary clinical outcomes, cost and adverse events.
We found current contact details of all authors through correspondence addresses on study reports and by searching websites. We contacted all authors by email or post (sending three reminders to non-responders), to establish missing details in the methods and results sections of the written reports and to determine authors' knowledge of, or involvement in, any current work in the area. On the envelopes we put return address details and a request to inform us if the addressee was no longer at that address.

### Assessment of study quality

Two reviewers (Debbie Lawlor and Stephen Hopker) assessed the quality of the trials included in the first review (Lawlor 2001). Two reviewers (Gillian Mead and Wendy Morley) assessed the quality of new trials identified for this update. We recorded whether allocation was concealed, whether intention to treat analysis was undertaken, and whether there was blinding of outcome assessor (Schulz 1995). For concealment of allocation we distinguished between trials that were adequately concealed (central randomisation at a site remote from the study; computerised allocation in which records are in a locked, unreadable file that can be assessed only after entering patient details; the drawing of non-opaque envelopes), inadequately concealed (open list or tables of random numbers; open computer systems; drawing of non-opaque envelopes) and unclear (no information in report, and the authors either did not respond to requests for information or were unable to provide information).
There are two separate aspects of 'intention to treat' analyses. First, there is the issue of whether participants were analysed according to original treatment assignment, regardless of whether they participated in the allocated treatment. The second issue concerns missing outcome data. If trials only included data from participants who completed the trial i.e. 'available cases' and did not attempt to deal with missing outcome data by using a recognised statistical method, e.g. imputing using last observation carried forward (LOCF), we also defined as 'not intention to treat'. Hence, trials could only be defined as 'intention to treat' if participants were analysed according to the allocated treatment AND if all participants either completed allocated treatments or if missing outcome data were replaced using a recognised statistical method e.g. LOCF. When information could not be obtained either from the publication or from the authors, we classifed the trial as 'not intention to treat'.

For blinding we distinguished between trials in which the main outcome was measured by an assessor who was blind to treatment allocation (blind) and those in which the main outcome was measured either by the participants themselves or by a non-blinded assessor (not blind).

**Measures of treatment effect**

We undertook a narrative review of all studies and a meta-analysis of those studies with appropriate data. To include data from as many trials as possible we calculated effect sizes for each trial using Cohen's method (Rosenthal 1994) and a standardised mean difference (SMD) for the overall pooled effect. Where trials used a number of different tools to assess depression we included the main outcome measure only in the meta-analysis. The main outcome measure was defined using a hierarchy of criterion as follows - identified by the authors as the main outcome measure, outcome reported in the abstract, first outcome reported in the results section.

We interpreted the SMDs using the following 'rule of thumb': 0.2 represents a small effect, 0.5 a moderate effect, and 0.8 a large effect (Cohen 1988).

We pooled long-term follow-up data from those trials that reassessed patients long after the interventions had been completed.

**Unit of analysis issues**

Where trials had more than two arms (e.g. exercise, other active treatment, control), we used data from the exercise arm for two separate comparisons: exercise versus other active treatment and exercise versus control.

If there were more than one intensity of exercise in a trial, we chose the exercise arm with the greatest clinical effect.

**Data synthesis**

We used a random effects model based on DerSimonian and Laird's method to calculate the pooled effect size (DerSimonian 1986).

**Assessment of heterogeneity**

We used the $Chi^2$ statistic, together with the $I^2$ statistic, to assess heterogeneity.

**Investigation of heterogeneity and subgroup analyses**

1. We explored the effect of different types of exercise (aerobic, resistance exercise or mixed aerobic and resistance) on outcome.
2. In future updates of the review we plan to explore the effect of the duration of the intervention by categorising studies in the main comparisons by length of intervention.

We will also consider performing additional subgroup analyses according to the following criteria: supervised vs unsupervised, indoor vs outdoor and individual vs group.

**Sensitivity analyses**

We undertook sensitivity analyses to explore how much of the variation between studies comparing exercise to no exercise is explained by between study differences in:

1. publication type (peer reviewed journal, conference abstract/ proceedings, doctoral dissertation)
2. allocation concealment
3. intention to treat analysis
4. blinding.

# RESULTS

## Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

**Results of the search**

Of the 144 potentially relevant papers retrieved for scrutinisation, we excluded 116 studies. Reasons for exclusion are given in Characteristics of Excluded studies. Amongst these 116 excluded studies, there were 67 papers describing clinical trials. Reasons for excluding these 67 papers are also summarised in more detail below.

**Included studies**

A total of 28 trials fulfilled our criteria, of which 14 had already been identified in 2001 (Lawlor 2001). Of the 28 trials, 17 were from US (Blumenthal 1999; Blumenthal 2007; DOSE 2002; Doyne 1987; Epstein 1986; Greist 1979; Hess-Homeier 1981; McCann 1984; Vickers 2005; Fremont 1987; Klein 1985; Reuter 1984; Setaro 1985; Orth 1979; Fetsch 1979; Bonnet 2005; Singh 1997). One was from Canada (McNeil 1991), three from the UK (Mather 2001; Mutrie 1988 Veale 1992), one from Australia ( Singh 2005), two from Hong Kong (Chou 2004; Tsang 2006), one from Norway (Martinsen 1985), one from Germany (Knuppen 2007), one from Russia (Pinchasov 2000) and one from Thailand (Nabkasorn 2005).

Of these 28 trials, 19 were peer reviewed papers (Blumenthal 1999; Blumenthal 2007; Chou 2004; DOSE 2002; Doyne 1987; Fremont 1987; Greist 1979; Klein 1985; Knuppen 2007; Martinsen 1985; Mather 2001; McCann 1984; McNeil 1991; Nabkasorn 2005; Pinchasov 2000; Singh 1997; Singh 2005; Tsang 2006; Veale 1992); six were doctoral dissertations (Bonnet 2005; Epstein 1986; Fetsch 1979; Hess-Homeier 1981; Setaro 1985; Orth 1979) and three were published in abstract form only (Mutrie 1988; Reuter 1984; Vickers 2005).

Of these 28 trials, data from two studies were unsuitable for statistical pooling (McCann 1984; Greist 1979). Preliminary information published in abstract form is also included in the systematic review but data are not currently available for meta-analysis, but may be available for future versions of the review (Vickers 2005). One trial (Nabkasorn 2005) provided data in graphical form only which we were able to include after manually converting the graph into mean and SD values. Hence, data from 25 trials were used in the meta-analyses.

Three trials (Blumenthal 1999, Blumenthal 2007; Mather 2001) provided data on whether patients fulfilled diagnostic criteria for depression at the end of the study, as well as depression scales. We used the scale results described in the paper (rather than using

formulae to convert the dichotomous outcomes to continuous outcomes) to allow inclusion of these trials in the meta-analysis.

***Types of study design***

Thirteen trials had two arms (Bonnet 2005, Chou 2004, Fetsch 1979, Knuppen 2007, Martinsen 1985; Mather 2001; Nabkasorn 2005, Pinchasov 2000, Reuter 1984, Singh 1997, Tsang 2006, Veale 1992; Vickers 2005), 11 had three arms (Blumenthal 1999, Doyne 1987, Epstein 1986, Fremont 1987, Greist 1979, Hess-Homeier 1981, Klein 1985, McCann 1984, McNeil 1991; Mutrie 1988; Singh 2005), two had four arms (Orth 1979; Blumenthal 2007), one had five arms (four intensities of exercise and control) (DOSE 2002) and one had six arms (CBT plus aerobic exercise, aerobic exercise only, CBT only, CBT plus non-aerobic exercise, non-aerobic exercise only or no intervention (Setaro 1985).

Of the 13 trials with two arms, exercise was compared with wait-list or usual care in three trials (Chou 2004; Nabkasorn 2005, Veale 1992), exercise was compared with a placebo intervention (e.g. social activity) in six trials (Knuppen 2007; Martinsen 1985; Mather 2001; Singh 1997; Tsang 2006; Vickers 2005), exercise was compared with CBT in two trials (Fetsch 1979; Reuter 1984), two trials compared CBT plus exercise versus CBT alone (Bonnet 2005, Reuter 1984) and one trial compared exercise with bright light therapy (Pinchasov 2000).

Of the 11 trials with three arms, one trial compared exercise versus exercise plus sertraline versus sertraline (Blumenthal 1999), three compared exercise versus wait list versus a placebo intervention (e.g social activity) (McCann 1984; McNeil 1991; Mutrie 1988), two compared exercise versus usual care versus CBT (Epstein 1986; Hess-Homeier 1981), one compared exercise versus CBT versus both exercise and CBT (Fremont 1987), one compared exercise versus low intensity CBT versus high intensity CBT (Greist 1979), one compared exercise versus a placebo versus CBT, (Klein 1985), one compared high intensity resistance training versus low intensity resistance training versus usual care (Singh 2005) and one compared running versus weight-lifting versus wait-list (Doyne 1987). Of the trials with four arms, one compared exercise to three types of control (Orth 1979) and the other compared home-based exercise versus supervised exercise versus sertraline versus placebo (Blumenthal 2007).

***Types of participants***

21 trials recruited participants from non-clinical populations (Blumenthal 1999; Blumenthal 2007; McNeil 1991; Doyne 1987; Fremont 1987; Epstein 1986; Klein 1985; McCann 1984; Hess-Homeier 1981; DOSE 2002; Nabkasorn 2005; Pinchasov 2000; Setaro 1985; Singh 1997; Singh 2005; Tsang 2006; Vickers 2005; Greist 1979; Orth 1979; Fetsch 1979; Bonnet 2005) with most involving recruitment of participants through the media. Six trials recruited participants from clinical populations (i.e. hospital in-patients or out-patients) (Knuppen 2007; Chou 2004; Martinsen 1985; Mutrie 1988; Reuter 1984; Veale 1992). One recruited participants from both clinical and non-clinical populations (Mather 2001).

Of the 21 trials recruiting people from non-clinical populations, diagnosis of depression was by a clinical interview in nine studies (Blumenthal 1999; Blumenthal 2007; Bonnet 2005; DOSE 2002; Doyne 1987; Klein 1985; Pinchasov 2000; Singh 1997; Singh 2005). The other 12 studies used a cut-off point on one of several depression scales (Beck Depression Inventory: Epstein 1986; Fremont 1987; Fetsch 1979 Hess-Homeier 1981; McCann 1984; McNeil 1991), CES-D (Nabkasorn 2005; Vickers 2005), Geriatric Depression Scale (Tsang 2006), Depression Adjective Checklist (Orth 1979), Symptom Checklist Score (Greist 1979) or Minnesota Multiple Personality Inventory (Setaro 1985).

There were more women than men (see Characteristics of included studies table), and mean age ranged from 22 years (Orth 1979) to 82.7 years (Tsang 2006).

***Types of Interventions***

Twenty-one trials provided aerobic exercise, of which 13 trials provided running (Blumenthal 1999; Doyne 1987; Epstein 1986; Fetsch 1979; Fremont 1987; Greist 1979; Hess-Homeier 1981; Klein 1985; McCann 1984; Nabkasorn 2005; Orth 1979; Reuter 1984; Veale 1992), three provided treadmill walking (Bonnet 2005; Blumenthal 2007; DOSE 2002), two provided walking (Knuppen 2007; McNeil 1991), one provided aerobic training with an instructor (Martinsen 1985), one provided aerobic dance (Setaro 1985) and one which provided cycling on a stationary bike (Pinchasov 2000). Two provided mixed exercise i.e. endurance, muscle strengthening and stretching (Mather 2001; Mutrie 1988), one provided Tai-Chi (Chou 2004), two provided resistance training (Singh 1997; Singh 2005), one provided Qigong exercises (Tsang 2006) and one provided 'individually tailored' exercises (Vickers 2005). For the purposes of our meta-analyses, we classified Qigong and Tai-Chi as mixed exercises. Two provided resistance training alone (Singh 1997; Singh 2005).

Thirteen trials (Bonnet 2005; Blumenthal 2007; Chou 2004; DOSE 2002; Doyne 1987; Fremont 1987; Knuppen 2007; McCann 1984; Mather 2001; Mutrie 1988; Setaro 1985; Singh 1997; Singh 2005) provided indoor exercise, one trial provided outdoor exercise (McNeil 1991) and the remaining trials did not report whether the exercise was indoors or outdoors.

Only one trial stated that unsupervised exercise was provided (Orth 1979). One trial included both supervised and home-based exercise arms (Blumenthal 2007). The other trials provided supervised exercise or did not report this information. Seven (DOSE 2002; Blumenthal 2007; Doyne 1987; Greist 1979; Klein 1985; McNeil 1991; Mutrie 1988; Orth 1979) provided individual exercises, 11 provided group exercises (Blumenthal 1999; Chou 2004; Fetsch 1979; Fremont 1987; McCann 1984; Mather 2001; Nabkasorn 2005; Setaro 1985; Singh 1997; Singh 2005; Veale 1992) and the remaining trials did not report this information.

The duration of the intervention ranged from 10 days (Knuppen 2007) to 16 weeks (Blumenthal 1999; Blumenthal 2007; Tsang 2006).

***Types of outcomes***

Other clinical endpoints and adverse effects

Four trials recorded clinical endpoints as well as mood (Knuppen 2007: length of hospital stay), Mather 2001 (patient and clinical global impression), Singh 1997 (sickness impact profile) and Singh 2005: quality of life). Five trials systematically recorded and reported adverse events (DOSE 2002; Blumenthal 2007; Knuppen 2007; Singh 1997; Singh 2005). No trial provided data on costs.

**Excluded studies**

Of the 116 papers excluded, 67 papers described clinical trials. The reasons for excluding these 67 clinical trials are described in more detail below.

Twenty five studies were non-randomised trials (Auchus 1994; Blue 1979; Conroy 1982; D'Amato 1990; Dimeo 2001; Doyne 1983; Fetsch 1983; Giardinelli 1996; Hartz 1982; Hayward 2000; Johnson 1986; Kaplan 1983; Kurz 1998; Moreau 1981; Palleschi 1998; Pappas 1990; Stein 1989; Roth 1986; Margolis 1982; Stewart 1994; Sanstead 1983; Williams 1979; Williams 1986; Martinsen 1989b; Rief 1996).

In 22 trials, participants did not have to have depression (as defined by the authors of the trial) to be eligible for the trial (Carney 1987; Dalton 1980; Eby 1985; Hannaford 1988; Hembree 2000; Herrera 1994; Hughes 1986; Kim 2004; Kupecz 2001; Lai 2006; Leppamaki 2002; Morey 2003; Motl 2004; Neidig 1999; Nguyen 2001; Palenzuela 1998; Rhodes 1980; Salminen 2005; Stein 1992; Stern 1983; Tsang 2003; Tenorio 1986).

Seven trials provided a combination of treatments (which included exercise) (Buffone 1980; Brown 2001 d; D'Amato 1990; Herrera 1994; Nickel 2005; Ouyang 2001).

One trial was a retrospective subgroup analysis of depressed patients from a randomised trial of exercise for osteoarthritis (Penninx 2002).

Seven trials compared two types of exercise with no non-exercising control (Bosscher 1993; Passmore 2006; Sexton 1989; TREAD 2004; Veale 1992 b; Wieman 1980; Williams 1992).

Two trials included only a single bout of exercise (Bodin 2004; Bartholomew 2005) and one trial provided exercise for only 4 days (Berlin 2003).

Two trials that recruited patients with post-natal depression were excluded (Armstrong 2003, Armstrong 2004).

**Ongoing studies**

Five ongoing trials fulfilled our inclusion criteria (DEMO 2007; McClure 2008; OPERA 2008; Peacock 2006; UPBEAT 2006). These will be included in future updates of the review.

## Risk of bias in included studies

**Allocation concealment**

Allocation concealment was adequate in 8 trials (DOSE 2002; Blumenthal 2007; Mather 2001; Martinsen 1985; Singh 1997; Singh 2005; Veale 1992; Knuppen 2007).

**Incomplete outcome data**

Seven trials performed 'intention to treat' (ITT) analyses ( Blumenthal 1999; Blumenthal 2007; DOSE 2002; Mather 2001; Mutrie 1988; McNeil 1991; Singh 1997). Two trials reported data for individual patients (Orth 1979; Bonnet 2005), so by using last observation carried forward we replaced data from the patients who did not complete the trial and included these data in the meta-analysis of ITT trials. One trial reported that the analysis was ITT, because it used the 'worse case assumption' to replace data from patients who did not complete the trial, but only included 38 of the 39 randomised patients in the analyses, so we classified it as 'not ITT' (Knuppen 2007).

Long-term follow-up data beyond the end of the interventions are described for five trials (Klein 1985 (follow-up for 9 months), Blumenthal 1999 at 10 months); Singh 1997 at 26 months, Mather 2001 (follow-up at 34 weeks), and Fremont 1987 (follow-up at 4 months). The remaining trials assessed participants only at the end of the interventions.

**Blinding**

Seven trials included blinding of outcome assessor (Blumenthal 1999; Blumenthal 2007; DOSE 2002; Klein 1985; Mather 2001; Singh 2005, Knuppen 2007).

**Other sources of bias**

One trial (Tsang 2006) stopped recruiting when the main outcome measure became statistically significant, rather than stipulating in advance how many people to recruit. This approach means that the results were probably biased in favour of exercise.

## Effects of interventions

We included 25 trials in our meta-analyses. The remaining three trials could not be included for the reasons stated above (Greist 1979; McCann 1984; Vickers 2005).

**COMPARISON 1: EXERCISE VERSUS CONTROL**

23 trials (907 participants) included a comparison of exercise with either wait-list or placebo.

**Primary outcome measure**

***Reduction in symptom severity at post-treatment (Graph 1.1)***

The pooled standardised mean difference (SMD) calculated using the random effects model was -0.82 (95% CI -1.12 to -0.51), indicating a large clinical effect. There was significant heterogeneity ($I^2$=77%).

***Reduction in symptom severity at follow-up (Graph 1.2)***

The pooled SMD from the five trials (Klein 1985; Blumenthal 1999; Singh 1997; Mather 2001; Fremont 1987) (218 participants) that provided long-term follow-up data found only a moderate effect (SMD -0.44, 95% CI -0.71 to -0.18). No statistical heterogeneity was indicated.

**Secondary outcome measures**

Insufficient numbers of trials (see description of studies) reported other clinical endpoints or adverse events to perform meta-analyses of these outcomes. Four trials reported a lack of difference in

adverse events between groups (DOSE 2002; Singh 1997; Singh 2005; Knuppen 2007).

**COMPARISON 2: EXERCISE VERSUS COGNITIVE THERAPY**

**Primary outcome (Graph 2.1)**

Six trials (152 participants) provided data comparing exercise with cognitive therapy, the SMD was -0.17 (95% CI -0.51, 0.18), indicating no significant difference between the two interventions. No statistical heterogeneity was indicated.

**Secondary outcomes**

Insufficient numbers of trials reported other clinical endpoints or adverse events to perform meta-analyses of these outcomes.

**COMPARISON 3: EXERCISE VERSUS BRIGHT LIGHT THERAPY**

**Primary outcome (Graph 3.1)**

One trial found that exercise was superior to bright light therapy in reducing depression symptoms (Pinchasov 2000) (WMD -6.40, 95% CI -10.20, -2.60).

**Secondary outcomes**

Insufficient numbers of trials reported other clinical endpoints or adverse events to perform meta-analyses of these outcomes

**COMPARISON 4: EXERCISE VERSUS ANTIDEPRESSANTS**

**Primary outcome (Graph 4.1)**

For the two trials (201 participants) that compared exercise with antidepressants (Blumenthal 1999; Blumenthal 2007) the SMD was -0.04 (95% CI -0.31, 0.24), indicating no significant difference between the two interventions.

**Secondary outcomes**

One trial found significantly higher rates of diarrhoea and loose stool in the sertraline than the exercise group (Blumenthal 2007).

**Subgroup analyses**

***Type of exercise***

We explored the influence of the type of exercise on outcomes. The SMD for aerobic exercise indicated a moderate clinical effect (SMD -0.63, 95% CI -0.95, -0.30), whilst the SMDs for both mixed exercise (SMD -1.47, 95% CI -2.56, -0.37) and resistance exercise (SMD -1.34, 95% CI -2.07, -0.61) indicated large effect sizes, but confidence intervals were wide.

***Intensity of exercise***

We attempted to extract data on intensity of exercise but this was reported for only a few trials, and there was too much variation in other aspects of the trial methodologies to attribute differences in outcomes to differences exercise intensities. One of the included trials compared four different 'doses' of aerobic exercise (DOSE 2002) and found the public health dose was significantly more effective than the low dose and control in reducing weekly HRSD scores. One of the included trial provided two intensities of progressive resistance training (Singh 2005) and found that the high intensity training was more effective than the low intensity training.

Eight trials measured indices of fitness and correlated these with study bias (Beggs test p = 0.13, Egger test p = 0.09).

mood (Blumenthal 1999; Doyne 1987; Fremont 1987; Knuppen 2007; Martinsen 1985; Pinchasov 2000; Singh 2005; Veale 1992). Of these, four trials found that mood correlated with fitness ( Blumenthal 1999; Pinchasov 2000; Martinsen 1985; Singh 2005) whilst the other four trials found no relationship.

We considered whether to perform additional subgroup analyses according to the following criteria: supervised vs unsupervised, indoor vs outdoor and individual vs group, but this information was not reported for a substantial number of studies (see description of studies above) and so any analysis might have been biased. One trial found no difference between supervised and home-based exercise (Blumenthal 2007).

**Sensitivity analyses**

Sensitivity analyses were conducted for the first comparison of exercise versus waiting list or placebo.

***Peer reviewed journal publications (Graph 6.1)***

For the 21 trials (867 participants) that were reported in peer reviewed journal publications, the SMD was -0.66 (95% CI -0.95, -0.37), showing a moderate clinical effect of borderline statistical significance in favour of exercise

***Published as abstracts/conference proceedings only (Graph 6.2)***

The pooled SMD for the two studies published as conference abstracts only was -2.17 (95% CI -3.06, -1.27), showing a large, statistically significant effect size in favour of exercise.

***Allocation concealment (Graph 6.3)***

For the eight trials (430 participants) with adequate allocation concealment, the SMD was -0.77 (95% CI -1.12, -0.42), showing a large clinical effect in favour of exercise.

***Use of intention to treat analysis (Graph 6.4)***

For the nine trials (403 participants) with intention to treat analyses, the SMD was -0.63 (95% CI -1.16, -0.10), showing a moderate clinical effect of borderline statistical significance in favour of exercise.

***Blinded outcome assessment (Graph 6.5)***

For the seven trials (411 participants) with blinded outcome assessments, the SMD was -0.39 (95% CI -0.75, -0.03), showing a moderate clinical effect of borderline statistical significance in favour of exercise.

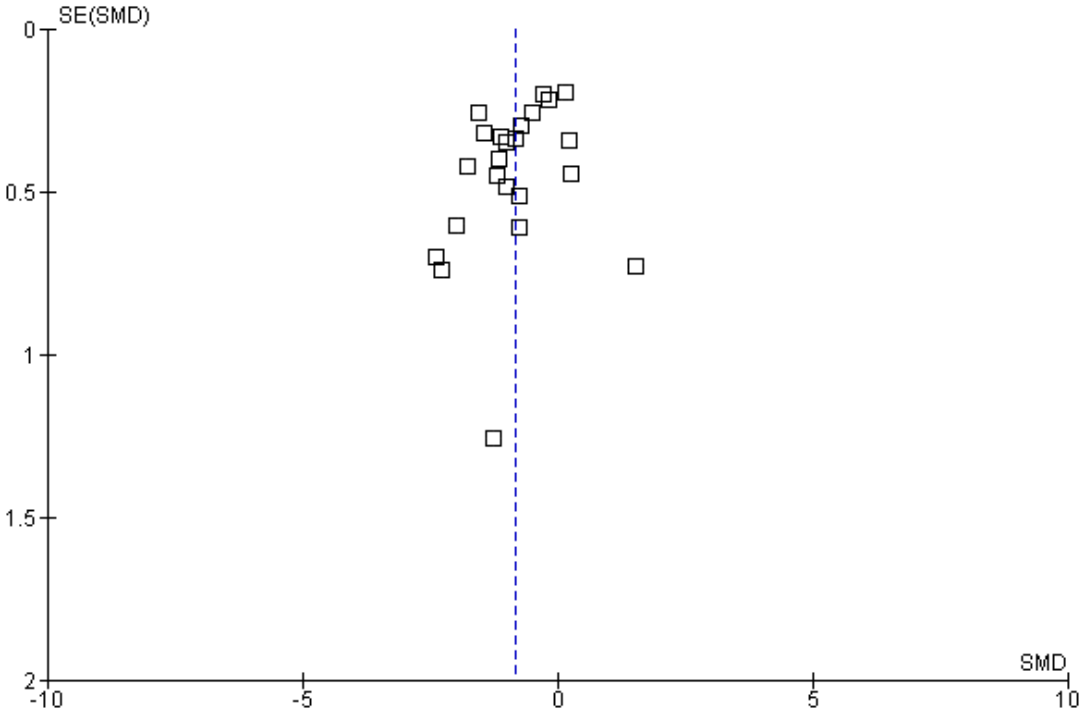
***Allocation concealment, intention to treat analysis and blinded outcome assessment (Graph 6.6)***

For the three trials (Blumenthal 2007, DOSE 2002, Mather 2001) (216 participants) with adequate allocation concealment and intention to treat analyses and blinded outcome assessment, the SMD was -0.42 (95% CI -0.88, 0.03) i.e. a moderate clinical effect, which was not statistically significant.

**Publication bias**

We explored publication bias for Comparison 1.1, exercise versus control, using a Funnel plot (Figure 1). Visual inspection suggested asymmetry, indicating a relationship between intervention effect and study size, suggesting either publication bias or a systematic difference between small and larger studies (small study effects). However, there was no conclusive statistical evidence for small

**Figure 1. Funnel plot of comparison: 1 Exercise versus control, outcome: 1.1 Reduction in depression symptoms post treatment.**




**Recruitment and retention of participants**

Additional Table 1 presents data about the feasibility of recruiting and retaining patients both in the trial as a whole and in the exercise intervention in particular. We extracted data, when available, about the number of patients who were considered for inclusion in each trial, although this information was not available for all trials. The trials that did provide these data used different recruitment techniques (ranging from screening of people responding to advertisements to inclusion of those patients who were considered eligible by a referring doctor). Hence, we decided not to pool these data.

We extracted data on the number randomised and completing each trial (see Additional Table 1) . This ranged from 100% completion (Mather 2001; McNeil 1991; Mutrie 1988; Singh 1997; Tsang 2006) to 42% completion (Doyne 1987). For the exercise intervention, this ranged from 100% completion (Mather 2001; McNeil 1991; Mutrie 1988; Singh 1997), to 55% completion (Klein 1985).

Nine trials reported attendance rates for exercise; these were 59% (Mather 2001), 70% (Doyne 1987), 72% (DOSE 2002), 78% (Nabkasorn 2005), 92% (Blumenthal 1999, Blumenthal 2007), 93% (Singh 1997), 95% (Chou 2004), 95% to 100% (Singh 2005). One trial rescheduled missed visits (McNeil 1991) so participants attended the full course of exercise. As with intensity of exercise, it is difficult to attribute any differences in outcome to differences in attendance rates, because there were other sources of variation in the type of interventions (e.g. duration of intervention, type of exercise) and differences in the methodological quality between trials which might account for differences in outcome.

## DISCUSSION

**Summary of main results**

This review found that exercise has a large effect (SMD -0.82, 95% CI -1.12, -0.51) on depressive symptoms in people with a diagnosis of depression when compared with no treatment (waiting list/placebo). However, it is likely that this result is biased in favour of exercise for methodological reasons. When only those trials with blinded outcome assessments were included in the analysis, the effect size was only moderate, though of borderline statistical significance. When only those trials with intention to treat analyses were included, the effect size was similarly moderate but only of borderline statistical significance. When only those tri-

als fulfilling all three methodological criteria, including allocation concealment, were included, the effect size was moderate and not statistically significant. Effect sizes were higher for mixed exercise and resistance exercise than aerobic exercise alone, but confidence intervals were wide and other methodological aspects of the trials may have confounded these analyses. We excluded trials which compared two types of exercise intervention without a non-exercising control group, as these were not relevant to our particular research question. When compared with other established treatments (CBT and antidepressants), there was no difference between exercise and the established intervention. The effect of exercise on depressive symptoms in those trials which included long-term follow-up was only moderate, suggesting that the benefits of exercise may gradually be lost after the intervention is completed, implying that exercise may need to be continued long-term in order to maintain the initial benefits. The need for long-term treatments is sometimes also true for other interventions such as antidepressants for depression. One challenge is how best to ensure that people continue to exercise in the longer term.

Outstanding uncertainties remain about how effective exercise is for depression, mainly because of methodological considerations. Furthermore, if exercise is of benefit for depression, we cannot determine the optimum type, frequency and duration of exercise, whether it should be performed supervised or unsupervised, indoors or outdoors, or in a group or alone. Only five trials reported adverse events (DOSE 2002, Knuppen 2007, Singh 1997, Singh 2005; Blumenthal 2007); adverse events were generally uncommon. One trial found that loose stools were more common in the sertraline than exercise group (Blumenthal 2007). Ideally both the risks and benefits of exercise for depression should be evaluated in future trials. There were no data on costs, so we cannot comment on the cost-effectiveness of exercise for depression.

The mechanisms by which exercise may improve depression remain uncertain. There was no clear relationship between the duration of the exercise intervention and outcomes. If exercise improves mood via improvements in fitness, we would have expected the trials which were longer in duration to demonstrate the bigger effect sizes. Only half of the trials which related mood to indices of physical fitness found significant correlations. If exercise mediated changes in mood by improving fitness, we might have expected significant correlations in all trials. One trial found that more intense exercise led to larger improvements in mood (Singh 2005). Another trial, DOSE 2002, found that the public health dose of exercise was significantly more effective than the low dose and control in reducing weekly HRSD scores. All the trials except one provided supervised exercise, so we cannot determine whether the improvements in mood may have been mediated by social contact with the person supervising the exercise. One trial found no difference between supervised and home-based exercise (Blumenthal 2007).

The data we extracted on aspects of feasibility (see additional Table 1) suggest that a large number of people need to be screened to identify suitable participants, unless recruiting from a clinical population e.g. in-patients with depression. A substantial number of people dropped out from both the exercise and control interventions, and even those who remained in the trial until the outcome assessments were not able to attend all exercise sessions. These data demonstrate some of the challenges of performing exercise trials for depression, and should be considered when designing future trials.

**Overall completeness and applicability of evidence**

The literature was systematically searched in 2001 (Lawlor 2001). The extensive search strategy in 2001 included electronic searches, hand-searching, and contact with authors to identify unpublished studies. The search performed in 2007 was also extensive: the electronic searches were provided by the Cochrane CCDN Review Group (note that the review group regularly searches the literature for relevant trials). The reviewers also checked reference lists and review articles, performed citation searches to identify further studies, and made contact with the authors of the studies published since the initial review in 2001 (Lawlor 2001) in order to identify any other trials (published, unpublished or ongoing). As a final check for ongoing studies, we searched www.controlled-trials.com. Altogether, 144 full references were obtained and carefully scrutinised, of which 28 trials fulfilled our criteria. However, it is possible that we have missed unpublished trials.

The results of this review are applicable to patients with a diagnosis of depression who participated in a programme of regular physical exercise within the context of a clinical trial, and the trials we identified are relevant to the review question. There were more women than men, and there was a wide range in mean ages (22 years to 87.5 years). Whether the same effect sizes (on mood) would be found in other types of exercise programmes outside the context of a clinical trial, is uncertain. This review cannot make any recommendations of the effectiveness of exercise referral schemes for depression (DOH 2001) as none of the trials specifically evaluated these programmes. Nor can we draw any conclusions about the effect of exercise on other relevant outcomes such as quality of life, activities of daily living, or its cost-effectiveness because the majority of trials did not systematically report this information. We cannot comment about the effect of exercise in people with dysthymia (or sub-clinical depression) and those without mood disorders, as we explicitly excluded these trials from the review. Future systematic reviews and meta-analyses might include these people, though new reviews would need to ensure that the search strategy was sufficiently comprehensive to identify all relevant trials. We made a post-hoc decision to exclude two trials of exercise for post-natal depression, as another Cochrane review will address this question.

**Quality of the evidence**

We included 28 trials in our review, which ranged in size from

11 participants to 202 participants. The number of comparison groups ranged from two to six, and there was wide variation in the type and duration of the exercise intervention. The majority of the trials had methodological weaknesses. We explicitly aimed to determine the influence of study quality, in particular allocation concealment, blinding and intention to treat analyses on effect sizes. When only those trials with adequate allocation concealment, intention to treat analysis and blinded outcome assessors were included, the effect size was moderate and not statistically significant.

**Potential biases in the review process**

We attempted to avoid bias by ensuring that we had identified all relevant studies through comprehensive systematic searching of the literature and contact with authors of the trials to identify other trials, both published and unpublished. However, we accept that some publication bias is inevitable. This is likely to lead to an overestimate of effect sizes, because positive trials are more likely to be published than negative trials. We attempted to obtain further information from authors, particularly to clarify methodological aspects of the trials but for some trials this information could not be obtained. We used the same protocol as had been used in 2001 (Lawlor 2001) but had to make a number of post-hoc decisions in relation to inclusion or exclusion of trials. For example, several trials were described as a 'combination' intervention; we decided to exclude these as we would not have been able to determine the effect of exercise on its own. We also made post-hoc decisions, on the advice of the editorial team, to exclude a trial which provided an exercise intervention which lasted only FOUR days (Berlin 2003) and also to exclude trials in post-natal depression (Armstrong 2003; Armstrong 2004). Exclusion of these trials did not influence the overall result of the review.

**Agreements and disagreements with other studies or reviews**

Previous systematic reviews which found that exercise improved depression included uncontrolled trials (North 1990; Craft 1998; Carlson 1991, so the results of these reviews are probably biased in favour of exercise. A more recent systematic review (Stathopoulou 2006) which identified trials in peer-reviewed journals only included only nine of the trials which we identified for our review (Klein 1985; Doyne 1987; McNeil 1991; Veale 1992; Singh 1997; Singh 2005; Pinchasov 2000; DOSE 2002), and also included two trials which we had excluded (Bosscher 1993; Sexton 1989). This review (Stathopoulou 2006) found a larger effect size than we did. A further review included only older people (Sjosten 2006), whereas we included all ages of participants.

# AUTHORS' CONCLUSIONS

## Implications for practice

It is reasonable to recommend exercise to people with depressive symptoms and to those who fulfil diagnostic criteria for depression. However, we cannot give people accurate information about how effective exercise might be, nor can recommendations be made about the relative benefits of aerobic exercise, resistance exercise or mixed exercise, whether group or individual exercises are better, nor about the optimum duration of exercise. Given that the drop-out rates from exercise can be substantial, a pragmatic approach would be to recommend that patients choose a form of exercise which they will enjoy; this may improve adherence and increase the likelihood that people will continue exercise long-term.

## Implications for research

Future systematic reviews and meta-analyses could be performed to investigate the effect of exercise on people with dysthymia. Trials comparing two types of exercise could also be systematically reviewed, to provide more insights into the possible mechanisms by which exercise may improve depression. A future update of the current review, including results from ongoing trials, will increase the accuracy of estimates of effect sizes.

This review found that methodological factors, in particular intention to treat analyses and blinding of outcome assessors, influenced effect sizes and the significance of these effects. Hence, further trials that are methodologically robust are required to determine more accurately the effect of exercise on depression. The ongoing trials we identified will provide further data in the next few years. Additional trials that formally evaluate whether Exercise on Referral Schemes are effective for depression would also be useful (NICE 2006). Future trials need to report adverse events and costs. Researchers must consider how to optimise recruitment and how to motivate participants to attend prescribed exercise sessions. If participants do not actually attend exercise sessions, trial results are more likely to be negative.

# ACKNOWLEDGEMENTS

An initial review of the effects of exercise in the treatment of depression, in which Professor Debbie Lawlor was the principal investigator, began as part of a training course at the NHS Centre for Reviews and Dissemination, University of York. Dr Stephen Hopker, consultant psychiatrist at Bradford Community Trust, was an investigator in the earlier review and Mr Alan Lui, audit nurse Airedale General Hospital, helped with the protocol development and retrieval of articles. Dr Domenico Scala, Senior House Officer in psychiatry and Lynfield Mount Hospital, Bradford, translated one Italian paper that was excluded from the review.

The updated version of the review was led by Dr Mead; co-reviewers are Dr Morley, Professor Lawlor and Professor McMurdo. Subsequently Dr Carolyn Greig, Senior Research Fellow, joined the review team to provide expertise in physical activity, and Mr Paul Campbell, also joined the team to provide expertise in depression. Ms Maureen Harding, Geriatric Medicine, University of

Edinburgh, retrieved articles and provided administrative support. We are also grateful to the CCDAN editorial base for performing searches and editorial assistance.

The views expressed in this review are those of the authors.

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Stathopoulou G, Powers MB, Berry AC, Smits JAJ, Otto MW. Exercise interventions for mental health: a quantitative and qualitative review. *Clinical Psychology: Science and Practice* 2006;**13**:179–193.

* *Indicates the major publication for the study*

## CHARACTERISTICS OF STUDIES

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

**Blumenthal 1999**

| | |
|---|---|
| Methods | RCT |
| Participants | Community volunteers recruited via media. Eligible if had DSM IV major depressive disorder<br>Mean age 70 (range 61-88)<br>63% female<br>N = 156 |
| Interventions | 1. Group walking or jogging 3 times per week<br>2. Sertraline (SSRI) at standard dose<br>3. Combined walking or jogging and sertraline<br>Duration of interventions: 16 weeks.<br>Exercise intensity was 70% to 85% of target heart rate |
| Outcomes | 1. Clinical diagnosis of depression using DSM-IV<br>2. Hamilton Rating Scale for Depression<br>3. Beck Depression Inventory |
| Notes | Analysis intention to treat, using last observation carried forward for missing data.<br>Reviewers used group 2 and group 3 in the meta-analysis<br>Outcome assessor blind |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | No | C - Inadequate |

**Blumenthal 2007**

| | |
|---|---|
| Methods | RCT |
| Participants | People with major depression recruited through television, radio and newspaper. mean age 52 SD 8, 76% women. N=202 |
| Interventions | 1. Home based aerobic exercise<br>2. Supervised aerobic exercise<br>3. Sertraline<br>4. Placebo<br>Intervention 16 weeks |
| Outcomes | Primary endpoint was remission (no MDD) and a HAM score of <8, and also a continuous severity score on the HAM-D |

**Blumenthal 2007** (*Continued*)

| | |
|---|---|
| Notes | Analysis intention to treat using last observation carried forward<br>Blinded outcome assessment |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Yes | A - Adequate |

**Bonnet 2005**

| | |
|---|---|
| Methods | RCT |
| Participants | University counselling service<br>Mean age 23.3 years<br>82% women<br>N=11 |
| Interventions | 1. CBT plus exercise<br>2. CBT alone<br>Exercise was walking on a treadmill for 20 minutes, twice a week for 6 weeks<br>Cognitive therapy: met counsellors once a week for 9 weeks |
| Outcomes | 1. DSM IV MDD, dysthymia or depressive disorder<br>2. Above cut-off depression on BDI and CES-D |
| Notes | Self report<br>Randomisation method not stated<br>7/11 randomised patients completed the interventions.<br>Data provided for each patient. Mean and SD calculated by us carrying foward baseline data for patients who dropped out |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | B - Unclear |

**Chou 2004**

| | |
|---|---|
| Methods | RCT |
| Participants | Patients attending a psychogeriatric outpatient department with unipolar major depression or dysthymia<br>Mean age 72.6<br>50% female |

**Chou 2004** (*Continued*)

| | |
|---|---|
| | N=14 |
| Interventions | 1. Tai Chi exercise<br>2. Wait list control<br>Tai-chi led by a Tai chi practitioner, 45 minutes, 3 times a week for 3 months. Not stated if in a group or alone |
| Outcomes | CES-D (total score and subscales) |
| Notes | Randomisation method not stated, unclear if intention to treat, unclear if outcome assessor blind to treatment allocation |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | B - Unclear |

**DOSE 2002**

| | |
|---|---|
| Methods | RCT |
| Participants | Community volunteers recruited via media. Men or women aged 20-45 with mild to moderate depression<br>Mean age 35.9<br>75% women<br>N=80 |
| Interventions | 4 different doses of exercise<br>1. Public health dose 3/week<br>2. Public health dose 5/week<br>3. Low dose 3/week.<br>4. High dose 3/week<br>5. Control<br>Exercise was on a treadmill or stationary bike, individually and monitored by laboratory staff<br>Duration 12 weeks |
| Outcomes | Change in HRSD from baseline to 12 weeks . Note that public health dose 3/ week had greatest effect and was included in the meta-analysis |
| Notes | Intention to treat (though data from the last available exercise session rather than data collected at 12 weeks were used in the analysis)<br>Outcome assessors blind |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Yes | A - Adequate |

**Doyne 1987**

| | |
|---|---|
| Methods | RCT |
| Participants | Community volunteers recruited via media<br>Mean age 28.5 (SD 4.36)<br>100% female<br>N = 40 |
| Interventions | 1. Supervised running or walking 4 times a week for 8 weeks<br>2. Supervised strength training 4 times a week<br>3. Waiting list control |
| Outcomes | 1. Beck Depression Inventory<br>2. Lubin's Depression Adjective List<br>3. Hamilton Rating Scale for Depression |
| Notes | Outcome assessment not blind<br>Analysis not intention to treat |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | No | C - Inadequate |

**Epstein 1986**

| | |
|---|---|
| Methods | RCT |
| Participants | Community volunteers recruited via media<br>Mean age 39.4<br>(range 24-60)<br>92% female |
| Interventions | 1. Group walking or jogging for 30 minutes 3-5 times a week for 8 weeks<br>2. Cognitive therapy 1 session of 1.5 hours per week<br>3. Waiting list control |
| Outcomes | 1. Beck Depression Inventory<br>2. Zung Self-Rating Depression Scale |
| Notes | Outcome assessment not blind<br>Analysis not intention to treat |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|

**Epstein 1986** (*Continued*)

| | | |
|---|---|---|
| Allocation concealment? | No | C - Inadequate |

**Fetsch 1979**

| | |
|---|---|
| Methods | RCT |
| Participants | Depressed people referred from a University counselling service and recruited via advertisements |
| Interventions | 1. Running 4 session over 4 weeks<br>2. Stroking therapy (a type of 'talking' therapy). 4 sessions over 4 weeks) |
| Outcomes | 1. Beck depression inventory |
| Notes | Outcome assessment not blind (self report)<br>analysis not intention to treat (only 16/21 randomised patients completed trial and were included in the analysis) |

***Risk of bias***

| **Item** | **Authors' judgement** | **Description** |
|---|---|---|
| Allocation concealment? | Unclear | B - Unclear |

**Fremont 1987**

| | |
|---|---|
| Methods | RCT |
| Participants | Community volunteers recruited via media<br>Data on age and gender not available<br>N = 61 |
| Interventions | 1. Group running<br>2. Cognitive therapy<br>3. Combined running and cognitive therapy<br>10 weeks |
| Outcomes | Beck depression Inventory |
| Notes | Outcome assessment not blind<br>Analysis not intention to treat |

***Risk of bias***

| **Item** | **Authors' judgement** | **Description** |
|---|---|---|
| Allocation concealment? | No | C - Inadequate |

**Greist 1979**

| | |
|---|---|
| Methods | RCT |
| Participants | Community volunteers<br>Age range 18-30<br>53.4% female<br>N = 28 |
| Interventions | 1. Supervised running<br>2. Time limited psychotherapy<br>3. Time unlimited psychotherapy |
| Outcomes | Symptom checklist score |
| Notes | Outcome assessment not blind<br>Analysis not intention to treat |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | No | C - Inadequate |

**Hess-Homeier 1981**

| | |
|---|---|
| Methods | RCT |
| Participants | Community voluteers recruited via media<br>Data on age and gender distribution not available<br>N = 20 |
| Interventions | 1. Running or walking with the instructor for 30 minutes 4 times a week for 8 weeks<br>2. Cognitive therapy: 1 session of 1 hour and 2 of half an hour per week<br>3. Waiting list control |
| Outcomes | Beck depression inventory |
| Notes | Outcome assessment not blind<br>Analysis not intention to treat |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | No | C - Inadequate |

**Klein 1985**

| | |
|---|---|
| Methods | RCT |
| Participants | Community voluteers recruited via media<br>Mean age 30.1 (SD 6.72)<br>72% female<br>N = 74 |
| Interventions | 1. Supervised running twice a week for 12 weeks<br>2. Group cognitive therapy for 2 hours once a week<br>3. Control group: meditation for 1 hour twice weekly |
| Outcomes | 1. Symptom Checklist<br>2. Target symptoms<br>3. Structural Analysis of Social Behaviour<br>4. Social Adjustment Self-reported Questionnaire<br>5. Cornell Medical Index<br>6. Role Rating Questionnaire<br>7. Hamilton Rating Scale<br>8. Global Assessment Scale |
| Notes | Main outcome assessment not blind. Hamilton Rating Scale administered by interviewer blind to allocation.<br>Analysis not intention to treat |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | No | C - Inadequate |

**Knuppen 2007**

| | |
|---|---|
| Methods | RCT |
| Participants | Inpatients with major depression<br>Mean age 49<br>55% women<br>N=38 |
| Interventions | 1. Walking training for 10 days<br>2. placebo (low intensity stretching and relaxation) |
| Outcomes | 1. Bech-Rafaelsen Scale (BRMS)<br>2. Center for Epidemiologic Studies Depression Scale (CES-D) |
| Notes | Authors state intention to treat. but of the 39 recruited, only 38 were used in the analysis. Outcome assessor for BRMS blinded to treatment allocation |

***Risk of bias***

**Knuppen 2007** (*Continued*)

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Yes | A - Adequate |

**Martinsen 1985**

| | |
|---|---|
| Methods | RCT |
| Participants | Psychiatric hospital inpatients<br>Mean age 40<br>(range 17-60)<br>Data on sex distribution not available<br>N = 49 |
| Interventions | 1. Aerobic exercise with instructor for 1 hour three times a week for 9 weeks<br>2. Control group attended occupational therapy whilst intervention group exercised |
| Outcomes | Beck Depression Inventory |
| Notes | Outcome assessment not blind<br>Analysis not intention to treat |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Yes | A - Adequate |

**Mather 2001**

| | |
|---|---|
| Methods | RCT |
| Participants | Primary care, psychiatric services, advertisement in paper and radio. N=86 (59 female and 27 male) Mean age 63.7 (range 53-78) in exercise and 66.2 (56-91) in control group |
| Interventions | 1. endurance, muscle strengthening and stretching<br>2. health education classes<br>10 weeks |
| Outcomes | 1. Hamilton rating scale for depression<br>2. Geriatric Depression Scale<br>3. Clinical gobal impression<br>4. Patient global ipression |
| Notes | Outcome assessor blind<br>Intention to treat |

**Mather 2001** (*Continued*)

| *Risk of bias* | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | Yes | A - Adequate |

**McCann 1984**

| | |
|---|---|
| Methods | RCT |
| Participants | Undergraduate psychology students with a requirement to participate in a research project<br>No details of age<br>100% female<br>N = 47 |
| Interventions | 1. Aerobic exercise: group running, jogging or dancing for 1 hour twice weekly for 10 weeks<br>2. Placebo control group - muscle relaxation for 15-20 minutes 4 times a week<br>3. Waiting list control |
| Outcomes | Beck Depression Inventory |
| Notes | Outcome assessment not blind<br>Analysis not intention to treat |

| *Risk of bias* | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | No | C - Inadequate |

**McNeil 1991**

| | |
|---|---|
| Methods | RCT |
| Participants | Community volunteers from religious and community organisations<br>Mean age 72.5<br>Details of gender distribution not provided<br>N = 30 |
| Interventions | 1. Walking accompanied by investigator for 20 minutes 3 times a week for 6 weeks<br>2. Social contact control group (visit by investigator for a "chat" avoiding any discussion of depression or health, twice a week)<br>3. Waiting list control group |
| Outcomes | Beck Depression Inventory |

**McNeil 1991** (*Continued*)

| | |
|---|---|
| Notes | Outcome assessment not blind<br>All completed intervention so classified as intention to treat |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | No | C - Inadequate |

**Mutrie 1988**

| | |
|---|---|
| Methods | RCT |
| Participants | Depressed patients referred to study by general practitioner (primary care physician)<br>Mean age 42.1<br>83% female<br>N = 36 |
| Interventions | 1. Aerobic exercise - conducted on an individual basis and without group contact, 29 minutes 3 times a week for 4 weeks<br>2. Strength and stretching exercise completed on an individual basis and without group contact, 20 minutes 3 times a week<br>3. Waiting list control |
| Outcomes | 1. Beck Depression Inventory<br>2. Profile of Mood States |
| Notes | Outcome assessment not blind<br>All completed intervention so analysis intention to treat |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | No | C - Inadequate |

**Nabkasorn 2005**

| | |
|---|---|
| Methods | RCT |
| Participants | Student nurses with mild to moderate depressive symptoms<br>aged 18-20<br>All female<br>N=59 |
| Interventions | 1. group jogging 50 minutes a day 5 days a week for 8 weeks<br>2. usual care |

**Nabkasorn 2005** (*Continued*)

| | |
|---|---|
| Outcomes | 1. CES-D scores (data from means and SD at end of treatment not available so obtained from published graph) |
| Notes | Outcome assessment not blind<br>Analysis not intention to treat |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | B - Unclear |

**Orth 1979**

| | |
|---|---|
| Methods | RCT |
| Participants | College students with dysphoria or depression<br>mean age 22<br>27% female<br>N=11 |
| Interventions | 1. Jogging 5 times a week for 30 minutes over 4 weeks<br>2. Meditation<br>3. Self-chosen activity<br>4. Self monitoring (control) |
| Outcomes | 1. Depression adjective checklist<br>2. Minnesota Multiphasic Personality Inventory |
| Notes | Randomisation method not stated.<br>Self-report outcomes.<br>Not stated whether intention to treat though all patients allocated control and running provided data at baseline and post-intervention |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | B - Unclear |

**Pinchasov 2000**

| | |
|---|---|
| Methods | RCT |
| Participants | Several groups including one with depression in the absence of seasonal affective disorder Also one group of depressed people fulfilling criteria for seasonal affective disorder mean age 35.2<br>100% female |

**Pinchasov 2000** (*Continued*)

| | |
|---|---|
| | N=63 |
| Interventions | 1. 54 minutes per day of cycling on stationary bicycle for 1 week<br>2. bright light therapy |
| Outcomes | 1. HDRS score<br>2. Body weight<br>3. Oxygen consumption |
| Notes | Randomisation method unclear.<br>Unclear if outcome assessment was blind |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | B - Unclear |

**Reuter 1984**

| | |
|---|---|
| Methods | RCT |
| Participants | University students presenting to mental health clinic with depression<br>Details of age and gender distribution not provided<br>N = 18 |
| Interventions | 1. Supervised running for at least 20 minutes 3 times a week for 10 weeks plus counselling<br>2. Counselling only |
| Outcomes | Beck Depression Inventory |
| Notes | Outcome assessment not blind<br>Analysis not intention to treat |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | D - Not used |

**Setaro 1985**

| | |
|---|---|
| Methods | RCT |
| Participants | Community volunteers recruited via the media<br>Age range 18 to 35 (mean age not stated)<br>26% female<br>185 men and women aged 18 to 35 participated |

**Setaro 1985** (*Continued*)

| | |
|---|---|
| Interventions | 1. Cognitive therapy and aerobic dance classes<br>2. Aerobic dance classes only<br>3. Cognitive therapy only<br>4. Cognitive therapy and non-aerobic exercise classes<br>5. Non-aerobic exercise only<br>6. No intervention<br>Duration of interventions was 10 weeks |
| Outcomes | Minnesota Multiphasic Personality Inventory |
| Notes | Outcome assessment not blind<br>Analysis not intention to treat |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Unclear | B - Unclear |

**Singh 1997**

| | |
|---|---|
| Methods | RCT |
| Participants | Community volunteers from two registers of individuals interested in participation in research<br>Mean age 70<br>(range 61-88)<br>63% female<br>N=32 |
| Interventions | 1. Supervised non-aerobic progressive resistance training 3 times a week for 10 weeks<br>2. Control group received health seminars twice a week in which depression and mental health were not discussed |
| Outcomes | 1. Beck Depression Inventory<br>2. Hamilton Rating Scale of Depression |
| Notes | Outcome assessment not blind<br>Intention to treat analysis |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Yes | A - Adequate |

**Singh 2005**

| | |
|---|---|
| Methods | RCT |
| Participants | People responding to a postal questionnaire who had DSM IV depression or dysthymia<br>Mean age 69<br>55% women<br>N=60 |
| Interventions | 1. progressive resistance training at 80% of one repetition max<br>2. Resistance training at 20% of one repetition max<br>3. Usual care<br>Each intervention group held three times a week for 8 weeks |
| Outcomes | 1. Hamilton Rating Scale for depression<br>2. Geriatric Depression score |
| Notes | Not intention to treat (50/60 completed the study and were available for assessment) outcome.<br>Outcome assessment blind |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Allocation concealment? | Yes | A - Adequate |

**Tsang 2006**

| | |
|---|---|
| Methods | RCT |
| Participants | People over 65 with either diagnosis of depression or features of depression in care homes.<br>Of those finishing the study, mean age 82.8 in control group and 82.1 in the intervention group<br>68% female<br>N=82 |
| Interventions | 1. Qigong (meditation, breathing exercise and body movement)<br>2. Newspaper reading group<br>16 weeks |
| Outcomes | 1. Geriatric depression score (chinese version)<br>2. Chinese general self-efficacy scale<br>3. Personal well-being index<br>4. General health questionnaire<br>5. Self concept scale |
| Notes | Not intention to treat<br>Not blinded outcome assessor stopped recruitment when results of the main outcome measure was significant |

**Tsang 2006** (*Continued*)

| ***Risk of bias*** | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | Unclear | B - Unclear |

**Veale 1992**

| | |
|---|---|
| Methods | RCT |
| Participants | Psychiatric hospital outpatients and day hospital patients<br>Mean age 35.5<br>(range 19-58)<br>64% female<br>N=41 |
| Interventions | 1. Group running 3 times a week for 12 weeks, plus routine care<br>2. Control group - routine care only |
| Outcomes | 1. Beck Depression Inventory<br>2. State-trait anxiety inventory |
| Notes | Outcome assessment not blind<br>Analysis not intention to treat |

| ***Risk of bias*** | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | Yes | A - Adequate |

**Vickers 2005**

| | |
|---|---|
| Methods | RCT |
| Participants | Depressed smoking women<br>mean age 41<br>100% female<br>N=60 |
| Interventions | 1. individually tailored exercises<br>2. health education |
| Outcomes | 1. depressive symptom severity |
| Notes | Results published in abstract form and further details are not yet available |

**Vickers 2005** (*Continued*)

| *Risk of bias* | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Allocation concealment? | Unclear | B - Unclear |

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

| Study | Reason for exclusion |
|---|---|
| Antonelli 1982 | non systematic review |
| Armstrong 2003 | Post-natal depression |
| Armstrong 2004 | Post-natal depression |
| Auchus 1994 | non-randomised controlled trial |
| Bartholomew 2005 | single bout of exercise |
| Berlin 2003 | Duration of exercise was only 4 days |
| Biddle 1989 | non systematic review |
| Blue 1979 | non-randomised controlled trial |
| Bodin 2004 | single bout of either martial arts or stationary bike |
| Bosscher 1993 | comparing different types of exercise with no non-exercising control group |
| Boyll 1986 | college students |
| Broocks 1997 | non systematic review |
| Brown 2001 d | the intervention was multimodal, consisting of light exposure, exercise instructions and vitamins. control group took vitamins only |
| Buffone 1980 | combination of exercise and cognitive behavioural therapy. No control group |
| Burbach 1997 | non systematic review |
| Byrne 1993 | non systematic review |
| Carney 1987 | patients were those undergoing haemodialysis. Did not have to have depression to be included |

(*Continued*)

| | |
|---|---|
| Conroy 1982 | non-randomised controlled trial |
| Coverley 1987 | non systematic review |
| D'Amato 1990 | non-randomised controlled trial. All subjects received both flexibility exercise and structured reminiscence |
| Dalton 1980 | trial in a 'wheelchair bound population' with diverse aetiologies |
| DeVaney 1991 | a trial of reducing exercise in those exercising more than 6 hours per week |
| DiLorenzo 1999 | no outcome measure of depression |
| Dimeo 2001 | non-randomised study of exercise for depression |
| Dishman 1995 | non systematic review |
| Doyne 1983 | non-randomised controlled trial |
| Eby 1985 | Trial of exercise in students who did not have to have depression to enter trial |
| Emery 1990a | no outcome measure of depression |
| Emery 1990b | no outcome measure of depression |
| Fetsch 1983 | non-randomised controlled trial |
| Fitzsimmons 2001 | Not exercise (the participant was placed in wheelchair adapted for connection to the front of a bicycle, the carer pedalled and steered the bicycle) |
| Giardinelli 1996 | non-randomised controlled trial |
| Glenister 1996 | non systematic review |
| Hales 1987 | non systematic review |
| Hannaford 1988 | general mental health patients with no separation of those with depression |
| Hartz 1982 | non-randomised controlled trial |
| Hayward 2000 | non-randomised controlled trial |
| Hembree 2000 | subjects were ageing female population residing in a retirement home environment |
| Herrera 1994 | combination of psychological therapy and exercise in patients with chronic renal failure |
| Hughes 1986 | effect of exercise on mood in people free from psychopathology |

(*Continued*)

| | |
|---|---|
| Kaplan 1983 | non-randomised controlled trial |
| Khatri 2001 | subgroup analysis of Blumenthal 1999 |
| Kim 2004 | effect of exercise on mental distress in healthy subjects |
| Knapen 2003 | Non-psychotic psychiatric patients with no separation of those with depression |
| Kubesh 2003 | outcome was executive function, no measurement of mood as an outcome |
| Kupecz 2001 | subjects were veterans |
| Kurz 1998 | not described as randomised |
| Labbe 1988 | comparison of exercise with exercise and instructions about how to improve compliance to exercise |
| Lacombe 1988 | Three types of exercise, no non-exercising control |
| LaFontaine 1992 | non systematic review |
| Lai 2006 | trial in stroke patients. Did not have to have depression to be eligible |
| Leppamaki 2002 | effects of exercise on symptoms of mental distress in subjects who are healthy |
| Margolis 1982 | not desribed as randomised |
| Martinsen 1987 | non systematic review |
| Martinsen 1988a | non systematic review |
| Martinsen 1988b | non systematic review |
| Martinsen 1989b | non-randomised controlled trial |
| Martinsen 1989c | non systematic review |
| Martinsen 1993 | non systematic review |
| Martinsen 1994 | non systematic review |
| Moore 1998 | non systematic review |
| Moreau 1981 | not described as randomised |
| Morey 2003 | older sedentary adults |
| Motl 2004 | older adults, did not have to be depressed to be included in the trial |

(*Continued*)

| | |
|---|---|
| Munro 1997 | Cost effectiveness analysis of the likely public health benefits of purchasing exercise for over 65s |
| Neidig 1999 | subjects had HIV infection |
| Netz 1994 | general mental health patients with no separation of those with depression |
| Nguyen 2001 | trial in patients with chronic obstructive pulmonary disease |
| Ouyang 2001 | Combination of sports training and cognitive therapy. Control was waiting list |
| Palleschi 1998 | non-randomised controlled trial |
| Palmer 2005 | Subjects were recovering from substance abuse |
| Pappas 1990 | non-randomised controlled trial |
| Passmore 2006 | aerobic exercise versus aerobic and resistance exercise, no non-exercising control |
| Pelham 1993 | general mental health patients with no separation of those with depression |
| Penninx 2002 | retrospective subgroup analysis of patients who participated in a randomised trial of exercise for knee osteoarthritis who also had depression |
| Perri 1984 | no outcome measure of depression |
| Pezzarossa 1991 | non systematic review |
| Plante 1996 | non systematic review |
| Raglin 1990 | non systematic review |
| Rhodes 1980 | not randomised, subjects not depressed |
| Rief 1996 | non-randomised controlled trial |
| Roth 1986 | subjects had a high number of life events, not depression |
| Roth 1987 | no outcome measure of depression |
| Sachs 1981 | non systematic review |
| Sachs 1982 | non systematic review |
| Salminen 2005 | Coronary heart disease patients with no separation of those with depressive symptoms.<br>Intervention described by authors as health advocacy, counselling and activation programme |
| Salmon 1990 | non systematic review |

(*Continued*)

| | |
|---|---|
| Salmon 2001 | non systematic review |
| Sanstead 1983 | not randomised |
| Scully 1998 | non systematic review |
| Sexton 1989 | comparing different types of exercise with no non-exercising group |
| Simons 1985 | non systematic review |
| Skrinar 2005 | DSM IV or psychotic disorders. no separation |
| Sonstroem 1997 | non systematic review |
| Stein 1989 | no non-exercising control |
| Stein 1992 | not described as randomised. Did not have to be depressed to participate |
| Stern 1983 | trial in patients with myocardial infarction |
| Stewart 1994 | non-randomised controlled trial |
| Taylor 1986 | trial in patients with myocardial infarction |
| Tenorio 1986 | trial in subclinical depression |
| TREAD 2004 | ongoing trial comparing two intensities of exercise |
| Tsang 2003 | Subjects had chronic physical disease not depression |
| Van Coppenolle 1993 | non systematic review |
| Van De Vliet 2003 | single study design |
| van der Merwe 2004 | intervention was a manual based therapy programme not exercise |
| Veale 1992 b | Comparison of two different types of exercise |
| Weinstein 1983 | non systematic review |
| Weiss 1989 | not randomised |
| Weyerer 1994 | non systematic review |
| Wieman 1980 | jogging versus racket ball so no non-exercising control |
| Williams 1979 | Non randomised study |

(*Continued*)

| | |
|---|---|
| Williams 1986 | non-randomised controlled trial |
| Williams 1992 | aerobic versus low intensity exercise. No control |

## Characteristics of ongoing studies *[ordered by study ID]*

**DEMO 2007**

| | |
|---|---|
| Trial name or title | A Randomised parallel-group observer-blinded clinical trial of aerobic versus non-aerobic versus relaxation training for patients with light to moderate depression |
| Methods | |
| Participants | Diagnosis of depression, aged 18-55 years, 135 expected |
| Interventions | Progressive resistance training vs aerobic training vs relaxation training (control), all twice a week for 4 months |
| Outcomes | Hamilton Depression scale (primary outcome), secondary outcomes include other measures of mood, cognitive testing, biochemistry (cortisol and prolactin) and quality of life |
| Starting date | 2005 |
| Contact information | Dr J Krogh Psychiatric department, Bispebjerg Hospital, Copenhagen Denmark jk27@bbh.hosp.dk |
| Notes | due to complete in September 2008 |

**McClure 2008**

| | |
|---|---|
| Trial name or title | Step Up Wellness Program for Depression, physical Inactivity and Smoking |
| Methods | |
| Participants | Moderate depressive symptoms and current smoker |
| Interventions | Walking group 3 times a week for 3 months plus weekly phone calls vs usual care |
| Outcomes | depressive symptoms, physical activity and smoking quit attempts |
| Starting date | November 2008 |
| Contact information | Jennifer McLure Group Health Center for Health studies, Seattle, Washington 98101 |
| Notes | |

**OPERA 2008**

| | |
|---|---|
| Trial name or title | Older poeple's exercise intervention in residential and nursing accommodation |
| Methods | |
| Participants | Residents of nursing and residential homes |
| Interventions | Active intervention (group based exercise run biweekly and promotion of physical activity) vs depression awareness programme for 12 months |
| Outcomes | Primary outcome: geriatric depression scale<br>Secondary outcomes include quality of life, mobility, cognitive function, pain falls, hospital admission and medication use |
| Starting date | January 2008 |
| Contact information | Professor Martin Underwood, Centre for Health Sciences, Abernethy Building, Barts and the London NHS Trust, Whitechapel, London |
| Notes | Cluster RCT (approximately 1000 residents of 80 residential and nursing homes) |

**Peacock 2006**

| | |
|---|---|
| Trial name or title | A feasibility study to analyse the psychological benefits of green exercise in comparison to cognitive behavioural therapy with patients with mild to moderate depression |
| Methods | |
| Participants | Reactive, mild to moderate depression |
| Interventions | Green exercise (a series of short countryside walks over a 6 week period) vs CBT |
| Outcomes | Beck Depression Inventory |
| Starting date | March 2006 |
| Contact information | Ms J Peacock, University of Essex, Centre for Environment and Society, Colchester, UK jlpeac@essex.ac.uk |
| Notes | |

**UPBEAT 2006**

| | |
|---|---|
| Trial name or title | Understanding the prognostic benefits of exercise and antidepressant therapy (UPBEAT) |
| Methods | |
| Participants | Coronary heart disease and persistent depressive symptoms |

**UPBEAT 2006** (*Continued*)

| | |
|---|---|
| Interventions | Supervised exercise vs antidepressant vs placebo for 16 weeks |
| Outcomes | Mood, heart function |
| Starting date | July 2006 |
| Contact information | James A Blumenthal blume003@mc.duke.edu |
| Notes | |

## DATA AND ANALYSES

### Comparison 1. Exercise versus control

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Reduction in depression symptoms post treatment | 23 | 907 | Std. Mean Difference (IV, Random, 95% CI) | -0.82 [-1.12, -0.51] |
| 2 Reduction in depression symptoms follow-up | 5 | 218 | Std. Mean Difference (IV, Random, 95% CI) | -0.44 [-0.71, -0.18] |

### Comparison 2. Exercise versus cognitive therapy

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Reduction in depression symptoms post-treatment | 6 | 152 | Std. Mean Difference (IV, Random, 95% CI) | -0.17 [-0.51, 0.18] |

### Comparison 3. Exercise versus bright light therapy

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Reduction in depression symptoms post-treatment | 1 | 18 | Mean Difference (IV, Random, 95% CI) | -6.4 [-10.20, -2.60] |

### Comparison 4. Exercise versus antidepressants

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Reduction in depression symptoms post-treatment | 2 | 201 | Std. Mean Difference (IV, Random, 95% CI) | -0.04 [-0.31, 0.24] |

**Comparison 5. Exercise versus control: subgroup analysis - type of exercise**

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Reduction in depression symptoms post-treatment | 23 | | Std. Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 1.1 Aerobic exercise | 17 | 640 | Std. Mean Difference (IV, Random, 95% CI) | -0.63 [-0.95, -0.30] |
| 1.2 Mixed exercise | 4 | 198 | Std. Mean Difference (IV, Random, 95% CI) | -1.47 [-2.56, -0.37] |
| 1.3 Resistance exercise | 2 | 69 | Std. Mean Difference (IV, Random, 95% CI) | -1.34 [-2.07, -0.61] |

**Comparison 6. Exercise versus control: sensitivity analyses**

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Reduction in depression symptoms post-treatment: peer reviewed journal publications and doctoral theses only | 21 | 867 | Std. Mean Difference (IV, Random, 95% CI) | -0.66 [-0.95, -0.37] |
| 2 Reduction in depression symptoms post-treatment: studies published as abstracts or conference proceedings only | 2 | 34 | Std. Mean Difference (IV, Random, 95% CI) | -2.17 [-3.06, -1.27] |
| 3 Reduction in depression symptoms post-treatment: studies with adequate allocation concealment | 8 | 430 | Std. Mean Difference (IV, Random, 95% CI) | -0.77 [-1.12, -0.42] |
| 4 Reduction in depression symptoms post-treatment: studies using intention to treat analysis | 9 | 403 | Std. Mean Difference (IV, Random, 95% CI) | -0.63 [-1.16, -0.10] |
| 5 Reduction in depression symptoms post-treatment: studies with blinded outcome assessment | 7 | 418 | Std. Mean Difference (IV, Random, 95% CI) | -0.39 [-0.75, -0.03] |
| 6 Reduction in depression symptoms post-treatment: allocation concealment, ITT, blinded outcome | 3 | 216 | Std. Mean Difference (IV, Random, 95% CI) | -0.42 [-0.88, 0.03] |

## Analysis 1.1. Comparison 1 Exercise versus control, Outcome 1 Reduction in depression symptoms post treatment.

Review: Exercise for depression

Comparison: 1 Exercise versus control

Outcome: 1 Reduction in depression symptoms post treatment

| Study or subgroup | Treatment N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Knuppen 2007 | 20 | 11.2 (4) | 18 | 15.5 (6.1) | | 5.0 % | -0.83 [ -1.49, -0.16 ] |
| Orth 1979 | 3 | 7 (6.6) | 2 | 16.5 (2.12) | | 1.3 % | -1.25 [ -3.71, 1.21 ] |
| McNeil 1991 | 10 | 11.1 (3) | 10 | 14.7 (3.7) | | 4.0 % | -1.02 [ -1.97, -0.08 ] |
| Bonnet 2005 | 5 | 24.46 (10.9) | 6 | 10.5 (5.8) | | 2.7 % | 1.51 [ 0.09, 2.93 ] |
| Mutrie 1988 | 9 | 9.46 (4.28) | 7 | 21.4 (5.26) | | 2.8 % | -2.39 [ -3.76, -1.02 ] |
| Epstein 1986 | 7 | 9 (10.94) | 10 | 16.3 (7.44) | | 3.8 % | -0.77 [ -1.78, 0.24 ] |
| Hess-Homeier 1981 | 6 | 9.8 (6.93) | 6 | 16.2 (8.42) | | 3.3 % | -0.77 [ -1.96, 0.43 ] |
| Singh 2005 | 18 | 8.5 (5.5) | 19 | 14.4 (6) | | 4.9 % | -1.00 [ -1.69, -0.31 ] |
| Nabkasorn 2005 | 21 | 14.4 (4.12) | 28 | 17.5 (4.23) | | 5.2 % | -0.73 [ -1.31, -0.14 ] |
| Doyne 1987 | 13 | 5.93 (8.44) | 11 | 15.25 (6.3) | | 4.2 % | -1.19 [ -2.08, -0.31 ] |
| Fremont 1987 | 18 | 10 (9.8) | 16 | 8 (7.1) | | 4.9 % | 0.23 [ -0.45, 0.90 ] |
| Mather 2001 | 43 | 12.6 (7.02) | 43 | 13.7 (6.02) | | 5.8 % | -0.17 [ -0.59, 0.26 ] |
| Reuter 1984 | 9 | 5.1 (4.75) | 9 | 18.56 (7.7) | | 3.3 % | -2.00 [ -3.19, -0.82 ] |
| Setaro 1985 | 25 | 62 (6.51) | 25 | 69.88 (3.96) | | 5.1 % | -1.44 [ -2.07, -0.81 ] |
| Singh 1997 | 17 | 9.8 (2.4) | 15 | 13.8 (2) | | 4.4 % | -1.75 [ -2.59, -0.92 ] |
| DOSE 2002 | 17 | 9 (3.6) | 13 | 14 (4.9) | | 4.5 % | -1.16 [ -1.94, -0.37 ] |
| Chou 2004 | 7 | 15.3 (9.8) | 7 | 39.1 (9.7) | | 2.7 % | -2.29 [ -3.73, -0.84 ] |
| Veale 1992 | 36 | 13.94 (6.6) | 28 | 17.79 (8.04) | | 5.5 % | -0.52 [ -1.03, -0.02 ] |
| Klein 1985 | 14 | 1.03 (0.94) | 8 | 0.83 (0.51) | | 4.3 % | 0.24 [ -0.64, 1.11 ] |
| Blumenthal 2007 | 51 | 9.2 (6.1) | 49 | 11.1 (7) | | 5.8 % | -0.29 [ -0.68, 0.11 ] |
| Blumenthal 1999 | 55 | 8.73 (6.86) | 48 | 7.81 (6.49) | | 5.9 % | 0.14 [ -0.25, 0.52 ] |
| Tsang 2006 | 48 | 3.19 (2.12) | 34 | 6.15 (1.46) | | 5.5 % | -1.56 [ -2.07, -1.06 ] |
| Martinsen 1985 | 24 | 12.1 (7.1) | 19 | 22.8 (11.4) | | 5.0 % | -1.14 [ -1.79, -0.48 ] |
| **Total (95% CI)** | **476** | | **431** | | | **100.0 %** | **-0.82 [ -1.12, -0.51 ]** |

Heterogeneity: $Tau^2 = 0.38$; $Chi^2 = 92.58$, df = 22 ($P<0.00001$); $I^2 = 76\%$

Test for overall effect: $Z = 5.19$ ($P < 0.00001$)

## Analysis 1.2. Comparison 1 Exercise versus control, Outcome 2 Reduction in depression symptoms follow-up.

Review: Exercise for depression

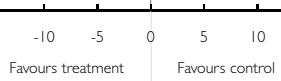
Comparison: 1 Exercise versus control

Outcome: 2 Reduction in depression symptoms follow-up

| Study or subgroup | Exercise N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Blumenthal 1999 | 29 | 10.6 (0.75) | 29 | 11 (0.81) | | 26.5 % | -0.51 [ -1.03, 0.02 ] |
| Fremont 1987 | 13 | 7.5 (5.4) | 13 | 9.9 (7.7) | | 12.1 % | -0.35 [ -1.13, 0.43 ] |
| Klein 1985 | 8 | 1.02 (0.67) | 10 | 1.47 (0.8) | | 8.0 % | -0.57 [ -1.53, 0.38 ] |
| Mather 2001 | 43 | 11.4 (6.69) | 43 | 13.7 (6.36) | | 40.0 % | -0.35 [ -0.78, 0.08 ] |
| Singh 1997 | 15 | 13 (2.2) | 15 | 14.4 (2.2) | | 13.4 % | -0.62 [ -1.35, 0.12 ] |
| **Total (95% CI)** | **108** | | **110** | | | **100.0 %** | **-0.44 [ -0.71, -0.18 ]** |

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.59$, df = 4 (P = 0.96); $I^2 = 0.0\%$

Test for overall effect: Z = 3.24 (P = 0.0012)



### Analysis 2.1. Comparison 2 Exercise versus cognitive therapy, Outcome 1 Reduction in depression symptoms post-treatment.

Review: Exercise for depression

Comparison: 2 Exercise versus cognitive therapy

Outcome: 1 Reduction in depression symptoms post-treatment

| Study or subgroup | Treatment N | Mean(SD) | Talking therapy N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Fremont 1987 | 15 | 6.1 (6.6) | 16 | 8 (7.1) | | 20.8 % | -0.27 [ -0.98, 0.44 ] |
| Epstein 1986 | 7 | 9 (10.94) | 9 | 17.22 (8.45) | | 10.3 % | -0.81 [ -1.85, 0.23 ] |
| Hess-Homeier 1981 | 5 | 9.8 (6.93) | 6 | 7.2 (5.03) | | 7.8 % | 0.40 [ -0.81, 1.60 ] |
| Klein 1985 | 14 | 1.03 (0.94) | 14 | 1.23 (0.84) | | 19.1 % | -0.22 [ -0.96, 0.53 ] |
| Setaro 1985 | 25 | 62 (6.51) | 25 | 60.68 (6.2) | | 31.5 % | 0.20 [ -0.35, 0.76 ] |
| Fetsch 1979 | 8 | 13.63 (7.95) | 8 | 19 (4.6) | | 10.5 % | -0.78 [ -1.81, 0.25 ] |
| **Total (95% CI)** | **74** | | **78** | | | **100.0 %** | **-0.17 [ -0.51, 0.18 ]** |

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 5.50$, df = 5 (P = 0.36); $I^2 = 9\%$

Test for overall effect: Z = 0.96 (P = 0.34)


### Analysis 3.1. Comparison 3 Exercise versus bright light therapy, Outcome 1 Reduction in depression symptoms post-treatment.

Review: Exercise for depression

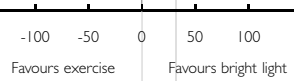
Comparison: 3 Exercise versus bright light therapy

Outcome: 1 Reduction in depression symptoms post-treatment

| Study or subgroup | Exercise N | Mean(SD) | Bright light N | Mean(SD) | Mean Difference IV,Random,95% CI | Weight | Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Pinchasov 2000 | 9 | 8.6 (2.8) | 9 | 15 (5.1) | | 100.0 % | -6.40 [ -10.20, -2.60 ] |
| **Total (95% CI)** | **9** | | **9** | | | **100.0 %** | **-6.40 [ -10.20, -2.60 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 3.30 (P = 0.00097)



**Analysis 4.1. Comparison 4 Exercise versus antidepressants, Outcome 1 Reduction in depression symptoms post-treatment.**

Review: Exercise for depression

Comparison: 4 Exercise versus antidepressants

Outcome: 1 Reduction in depression symptoms post-treatment

| Study or subgroup | exercise | | antidepressants | | Std. Mean Difference | Weight | Std. Mean Difference |
|---|---|---|---|---|---|---|---|
| | N | Mean(SD) | N | Mean(SD) | IV,Random,95% CI | | IV,Random,95% CI |
| Blumenthal 1999 | 53 | 8.19 (5.97) | 48 | 7.81 (6.49) | | 50.2 % | 0.06 [ -0.33, 0.45 ] |
| Blumenthal 2007 | 51 | 9.2 (6.1) | 49 | 10.1 (6.9) | | 49.8 % | -0.14 [ -0.53, 0.26 ] |
| **Total (95% CI)** | **104** | | **97** | | | **100.0 %** | **-0.04 [ -0.31, 0.24 ]** |

Heterogeneity: Tau² = 0.0; Chi² = 0.49, df = 1 (P = 0.48); I² =0.0%

Test for overall effect: Z = 0.27 (P = 0.79)

## Analysis 5.1. Comparison 5 Exercise versus control: subgroup analysis - type of exercise, Outcome 1 Reduction in depression symptoms post-treatment.

Review: Exercise for depression

Comparison: 5 Exercise versus control: subgroup analysis - type of exercise

Outcome: 1 Reduction in depression symptoms post-treatment

| Study or subgroup | aerobic exercise N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Aerobic exercise | | | | | | | |
| Blumenthal 1999 | 55 | 8.73 (6.86) | 48 | 7.81 (6.49) | | 7.9 % | 0.14 [ -0.25, 0.52 ] |
| Blumenthal 2007 | 51 | 9.2 (6.1) | 49 | 11.1 (7) | | 7.9 % | -0.29 [ -0.68, 0.11 ] |
| Bonnet 2005 | 5 | 24.46 (10.9) | 6 | 10.5 (5.8) | | 3.7 % | 1.51 [ 0.09, 2.93 ] |
| DOSE 2002 | 17 | 9 (3.6) | 13 | 14 (4.9) | | 6.2 % | -1.16 [ -1.94, -0.37 ] |
| Doyne 1987 | 13 | 5.93 (8.44) | 11 | 15.25 (6.3) | | 5.7 % | -1.19 [ -2.08, -0.31 ] |
| Epstein 1986 | 7 | 9 (10.94) | 10 | 16.3 (7.44) | | 5.2 % | -0.77 [ -1.78, 0.24 ] |
| Fremont 1987 | 18 | 10 (9.8) | 16 | 8 (7.1) | | 6.7 % | 0.23 [ -0.45, 0.90 ] |
| Hess-Homeier 1981 | 6 | 9.8 (6.93) | 6 | 16.2 (8.42) | | 4.4 % | -0.77 [ -1.96, 0.43 ] |
| Klein 1985 | 14 | 1.03 (0.94) | 8 | 0.83 (0.51) | | 5.8 % | 0.24 [ -0.64, 1.11 ] |
| Knuppen 2007 | 20 | 11.2 (4) | 18 | 15.5 (6.1) | | 6.7 % | -0.83 [ -1.49, -0.16 ] |
| Martinsen 1985 | 24 | 12.1 (7.1) | 19 | 22.8 (11.4) | | 6.8 % | -1.14 [ -1.79, -0.48 ] |
| McNeil 1991 | 10 | 11.1 (3) | 10 | 14.7 (3.7) | | 5.4 % | -1.02 [ -1.97, -0.08 ] |
| Nabkasorn 2005 | 21 | 14.4 (4.12) | 28 | 17.5 (4.23) | | 7.1 % | -0.73 [ -1.31, -0.14 ] |
| Orth 1979 | 3 | 7 (6.6) | 2 | 16.5 (2.12) | | 1.7 % | -1.25 [ -3.71, 1.21 ] |
| Reuter 1984 | 9 | 5.1 (4.75) | 9 | 18.56 (7.7) | | 4.5 % | -2.00 [ -3.19, -0.82 ] |
| Setaro 1985 | 25 | 62 (6.51) | 25 | 69.88 (3.96) | | 6.9 % | -1.44 [ -2.07, -0.81 ] |
| Veale 1992 | 36 | 13.94 (6.6) | 28 | 17.79 (8.04) | | 7.5 % | -0.52 [ -1.03, -0.02 ] |
| **Subtotal (95% CI)** | **334** | | **306** | | | **100.0 %** | **-0.63 [ -0.95, -0.30 ]** |
| Heterogeneity: Tau² = 0.29; Chi² = 53.29, df = 16 (P<0.00001); I² =70% | | | | | | | |
| Test for overall effect: Z = 3.79 (P = 0.00015) | | | | | | | |
| 2 Mixed exercise | | | | | | | |
| Chou 2004 | 7 | 15.3 (9.8) | 7 | 39.1 (9.7) | | 15.9 % | -2.29 [ -3.73, -0.84 ] |
| Mather 2001 | 43 | 12.6 (7.02) | 43 | 13.7 (6.02) | | 34.3 % | -0.17 [ -0.59, 0.26 ] |
| Mutrie 1988 | 9 | 9.46 (4.28) | 7 | 21.4 (5.26) | | 16.9 % | -2.39 [ -3.76, -1.02 ] |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| Study or subgroup | aerobic exercise N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Tsang 2006 | 48 | 3.19 (2.12) | 34 | 6.15 (1.46) | | 32.9 % | -1.56 [ -2.07, -1.06 ] |
| **Subtotal (95% CI)** | **107** | | **91** | | | **100.0 %** | **-1.47 [ -2.56, -0.37 ]** |
| Heterogeneity: $Tau^2$ = 1.00; $Chi^2$ = 26.23, df = 3 (P<0.00001); $I^2$ =89% | | | | | | | |
| Test for overall effect: Z = 2.63 (P = 0.0086) | | | | | | | |
| 3 Resistance exercise | | | | | | | |
| Singh 1997 | 17 | 9.8 (2.4) | 15 | 13.8 (2) | | 47.3 % | -1.75 [ -2.59, -0.92 ] |
| Singh 2005 | 18 | 8.5 (5.5) | 19 | 14.4 (6) | | 52.7 % | -1.00 [ -1.69, -0.31 ] |
| **Subtotal (95% CI)** | **35** | | **34** | | | **100.0 %** | **-1.34 [ -2.07, -0.61 ]** |
| Heterogeneity: $Tau^2$ = 0.13; $Chi^2$ = 1.87, df = 1 (P = 0.17); $I^2$ =46% | | | | | | | |
| Test for overall effect: Z = 3.58 (P = 0.00034) | | | | | | | |

### Analysis 6.1. Comparison 6 Exercise versus control: sensitivity analyses, Outcome 1 Reduction in depression symptoms post-treatment: peer reviewed journal publications and doctoral theses only.

Review: Exercise for depression

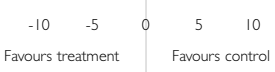
Comparison: 6 Exercise versus control: sensitivity analyses

Outcome: 1 Reduction in depression symptoms post-treatment: peer reviewed journal publications and doctoral theses only

| Study or subgroup | Treatment N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Blumenthal 1999 | 55 | 8.73 (6.86) | 48 | 7.81 (6.49) | | 6.6 % | 0.14 [ -0.25, 0.52 ] |
| Blumenthal 2007 | 51 | 9.2 (6.1) | 49 | 11.1 (7) | | 6.5 % | -0.29 [ -0.68, 0.11 ] |
| Bonnet 2005 | 5 | 24.46 (10.9) | 6 | 10.5 (5.8) | | 2.7 % | 1.51 [ 0.09, 2.93 ] |
| Chou 2004 | 7 | 15.3 (9.8) | 7 | 39.1 (9.7) | | 2.6 % | -2.29 [ -3.73, -0.84 ] |
| DOSE 2002 | 17 | 9 (3.6) | 13 | 14 (4.9) | | 4.8 % | -1.16 [ -1.94, -0.37 ] |
| Doyne 1987 | 8 | 8.18 (5.27) | 11 | 15.25 (6.3) | | 3.9 % | -1.15 [ -2.14, -0.15 ] |
| Epstein 1986 | 7 | 9 (10.24) | 10 | 16.3 (7.4) | | 3.9 % | -0.80 [ -1.81, 0.21 ] |
| Fremont 1987 | 18 | 10 (9.8) | 16 | 8 (7.1) | | 5.3 % | 0.23 [ -0.45, 0.90 ] |
| Hess-Homeier 1981 | 5 | 9.8 (6.93) | 6 | 16.2 (7.4) | | 3.1 % | -0.81 [ -2.07, 0.45 ] |
| Klein 1985 | 14 | 1.03 (0.94) | 8 | 0.83 (0.51) | | 4.4 % | 0.24 [ -0.64, 1.11 ] |
| Knuppen 2007 | 20 | 11.2 (4) | 18 | 15.5 (6.1) | | 5.3 % | -0.83 [ -1.49, -0.16 ] |
| Martinsen 1985 | 24 | 12.1 (7.1) | 19 | 22.8 (11.4) | | 5.4 % | -1.14 [ -1.79, -0.48 ] |
| Mather 2001 | 43 | 12.6 (7.02) | 43 | 13.7 (6.02) | | 6.4 % | -0.17 [ -0.59, 0.26 ] |
| McNeil 1991 | 10 | 11.1 (3) | 10 | 14.7 (3.7) | | 4.1 % | -1.02 [ -1.97, -0.08 ] |
| Nabkasorn 2005 | 21 | 14.4 (4.12) | 28 | 17.5 (4.23) | | 5.7 % | -0.73 [ -1.31, -0.14 ] |
| Orth 1979 | 3 | 7 (6.6) | 2 | 16.5 (2.12) | | 1.2 % | -1.25 [ -3.71, 1.21 ] |
| Setaro 1985 | 25 | 62 (6.51) | 25 | 69.88 (3.96) | | 5.5 % | -1.44 [ -2.07, -0.81 ] |
| Singh 1997 | 17 | 9.8 (9.8) | 15 | 13.8 (7.7) | | 5.2 % | -0.44 [ -1.14, 0.26 ] |
| Singh 2005 | 18 | 8.5 (5.5) | 19 | 14.4 (6) | | 5.2 % | -1.00 [ -1.69, -0.31 ] |
| Tsang 2006 | 48 | 3.19 (2.12) | 34 | 6.15 (1.46) | | 6.1 % | -1.56 [ -2.07, -1.06 ] |
| Veale 1992 | 36 | 13.94 (6.6) | 28 | 17.79 (8.04) | | 6.1 % | -0.52 [ -1.03, -0.02 ] |
| **Total (95% CI)** | **452** | | **415** | | | **100.0 %** | **-0.66 [ -0.95, -0.37 ]** |

Heterogeneity: $Tau^2 = 0.29$; $Chi^2 = 73.10$, df = 20 ($P<0.00001$); $I^2 = 73\%$

Test for overall effect: $Z = 4.46$ ($P < 0.00001$)



### Analysis 6.2. Comparison 6 Exercise versus control: sensitivity analyses, Outcome 2 Reduction in depression symptoms post-treatment: studies published as abstracts or conference proceedings only.

Review: Exercise for depression

Comparison: 6 Exercise versus control: sensitivity analyses

Outcome: 2 Reduction in depression symptoms post-treatment: studies published as abstracts or conference proceedings only

| Study or subgroup | Treatment N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Mutrie 1988 | 9 | 9.46 (4.28) | 7 | 21.4 (5.26) | | 42.7 % | -2.39 [ -3.76, -1.02 ] |
| Reuter 1984 | 9 | 5.1 (4.75) | 9 | 18.56 (7.7) | | 57.3 % | -2.00 [ -3.19, -0.82 ] |
| **Total (95% CI)** | **18** | | **16** | | | **100.0 %** | **-2.17 [ -3.06, -1.27 ]** |

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.17$, df = 1 (P = 0.68); $I^2 = 0.0\%$

Test for overall effect: Z = 4.74 (P < 0.00001)

### Analysis 6.3. Comparison 6 Exercise versus control: sensitivity analyses, Outcome 3 Reduction in depression symptoms post-treatment: studies with adequate allocation concealment.

Review: Exercise for depression

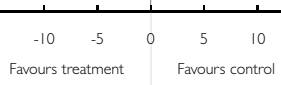
Comparison: 6 Exercise versus control: sensitivity analyses

Outcome: 3 Reduction in depression symptoms post-treatment: studies with adequate allocation concealment

| Study or subgroup | Exercise N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Blumenthal 2007 | 51 | 9.2 (6.1) | 49 | 11.1 (7) | | 16.0 % | -0.29 [ -0.68, 0.11 ] |
| DOSE 2002 | 17 | 9 (3.6) | 13 | 14 (4.9) | | 10.0 % | -1.16 [ -1.94, -0.37 ] |
| Knuppen 2007 | 20 | 11.2 (4) | 18 | 15.5 (6.1) | | 11.6 % | -0.83 [ -1.49, -0.16 ] |
| Martinsen 1985 | 24 | 12.1 (7.1) | 19 | 22.8 (11.4) | | 11.8 % | -1.14 [ -1.79, -0.48 ] |
| Mather 2001 | 43 | 12.6 (7.02) | 43 | 13.7 (6.02) | | 15.5 % | -0.17 [ -0.59, 0.26 ] |
| Singh 1997 | 17 | 9.8 (2.4) | 15 | 13.8 (2) | | 9.4 % | -1.75 [ -2.59, -0.92 ] |
| Singh 2005 | 18 | 8.5 (5.5) | 19 | 14.4 (6) | | 11.3 % | -1.00 [ -1.69, -0.31 ] |
| Veale 1992 | 36 | 13.94 (6.6) | 28 | 17.79 (8.04) | | 14.2 % | -0.52 [ -1.03, -0.02 ] |
| **Total (95% CI)** | **226** | | **204** | | | **100.0 %** | **-0.77 [ -1.12, -0.42 ]** |

Heterogeneity: $Tau^2 = 0.16$; $Chi^2 = 20.15$, df = 7 (P = 0.01); $I^2 = 65\%$

Test for overall effect: Z = 4.31 (P = 0.000016)



### Analysis 6.4. Comparison 6 Exercise versus control: sensitivity analyses, Outcome 4 Reduction in depression symptoms post-treatment: studies using intention to treat analysis.

Review: Exercise for depression

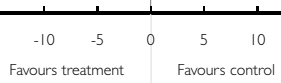
Comparison: 6 Exercise versus control: sensitivity analyses

Outcome: 4 Reduction in depression symptoms post-treatment: studies using intention to treat analysis

| Study or subgroup | Exercise N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Blumenthal 1999 | 55 | 8.73 (6.86) | 48 | 7.81 (6.49) | | 15.4 % | 0.14 [ -0.25, 0.52 ] |
| Blumenthal 2007 | 51 | 9.2 (6.1) | 49 | 11.1 (7) | | 15.4 % | -0.29 [ -0.68, 0.11 ] |
| Bonnet 2005 | 5 | 24.46 (10.9) | 6 | 10.5 (5.8) | | 7.6 % | 1.51 [ 0.09, 2.93 ] |
| DOSE 2002 | 17 | 9 (3.6) | 13 | 14 (4.9) | | 12.2 % | -1.16 [ -1.94, -0.37 ] |
| Mather 2001 | 43 | 12.6 (7.02) | 43 | 13.7 (6.02) | | 15.2 % | -0.17 [ -0.59, 0.26 ] |
| McNeil 1991 | 10 | 11.1 (3) | 10 | 14.7 (3.7) | | 10.9 % | -1.02 [ -1.97, -0.08 ] |
| Mutrie 1988 | 9 | 9.46 (4.28) | 7 | 21.4 (5.26) | | 7.9 % | -2.39 [ -3.76, -1.02 ] |
| Orth 1979 | 3 | 7 (6.6) | 2 | 16.5 (2.12) | | 3.6 % | -1.25 [ -3.71, 1.21 ] |
| Singh 1997 | 17 | 9.8 (2.4) | 15 | 13.8 (2) | | 11.9 % | -1.75 [ -2.59, -0.92 ] |
| **Total (95% CI)** | **210** | | **193** | | | **100.0 %** | **-0.63 [ -1.16, -0.10 ]** |

Heterogeneity: $Tau^2 = 0.43$; $Chi^2 = 39.32$, df = 8 (P<0.00001); $I^2 = 80\%$

Test for overall effect: Z = 2.34 (P = 0.020)



### Analysis 6.5. Comparison 6 Exercise versus control: sensitivity analyses, Outcome 5 Reduction in depression symptoms post-treatment: studies with blinded outcome assessment.

Review: Exercise for depression

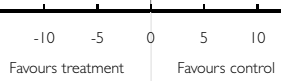
Comparison: 6 Exercise versus control: sensitivity analyses

Outcome: 5 Reduction in depression symptoms post-treatment: studies with blinded outcome assessment

| Study or subgroup | Exercise N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Blumenthal 1999 | 55 | 8.73 (6.86) | 48 | 7.81 (6.49) | | 18.2 % | 0.14 [ -0.25, 0.52 ] |
| Blumenthal 2007 | 53 | 9.2 (6.1) | 49 | 11.1 (7) | | 18.2 % | -0.29 [ -0.68, 0.10 ] |
| DOSE 2002 | 17 | 9 (3.6) | 13 | 14 (4.9) | | 10.9 % | -1.16 [ -1.94, -0.37 ] |
| Klein 1985 | 14 | 1.03 (0.94) | 8 | 0.83 (0.51) | | 9.8 % | 0.24 [ -0.64, 1.11 ] |
| Knuppen 2007 | 20 | 11.2 (4) | 18 | 15.5 (6.1) | | 12.9 % | -0.83 [ -1.49, -0.16 ] |
| Mather 2001 | 43 | 12.6 (7.02) | 43 | 13.7 (6.02) | | 17.5 % | -0.17 [ -0.59, 0.26 ] |
| Singh 2005 | 18 | 8.5 (5.5) | 19 | 14.4 (6) | | 12.5 % | -1.00 [ -1.69, -0.31 ] |
| **Total (95% CI)** | **220** | | **198** | | | **100.0 %** | **-0.39 [ -0.75, -0.03 ]** |

Heterogeneity: $Tau^2 = 0.14$; $Chi^2 = 17.61$, df = 6 (P = 0.01); $I^2 = 66\%$

Test for overall effect: Z = 2.14 (P = 0.032)

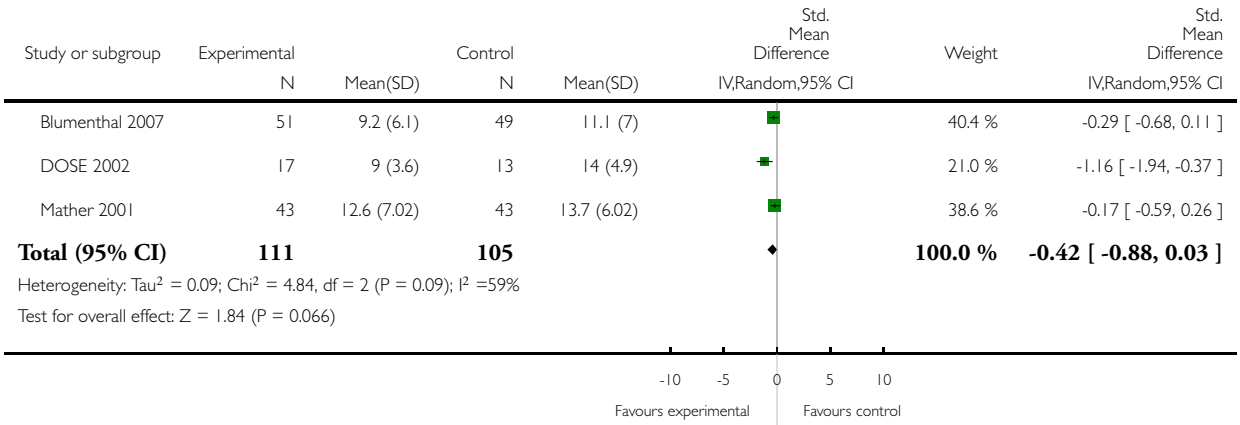


**Analysis 6.6. Comparison 6 Exercise versus control: sensitivity analyses, Outcome 6 Reduction in depression symptoms post-treatment: allocation concealment, ITT, blinded outcome.**

Review: Exercise for depression

Comparison: 6 Exercise versus control: sensitivity analyses

Outcome: 6 Reduction in depression symptoms post-treatment: allocation concealment, ITT, blinded outcome




## ADDITIONAL TABLES

**Table 1. Number screened, number still in trial and exercise intervention at end of trial**

| Trial ID | screened | randomised | allocated exercise | completed trial | completed exercise |
|---|---|---|---|---|---|
| Blumenthal 1999 | 604 underwent telephone screening | 156 | 55 | 133 | 46 |
| Bonnet 2005 | not reported | 11 | 5 | 7 | 3 |
| Chou 2004 | 30 | 14 | 7 | not reported | not reported |
| DOSE 2002 | 1664 assessed for eligibility | 80 | 17 | 45 | 11 |
| Doyne 1987 | 285 responded to adverts | 57 | not reported | 24 | 13 |
| Epstein 1986 | 250 telephone inquiries received | 33 | 7 | not reported | 7 |
| Fetsch 1979 | not reported | 21 | 10 | 16 | 8 |

**Table 1. Number screened, number still in trial and exercise intervention at end of trial** (*Continued*)

| | | | | | |
|---|---|---|---|---|---|
| Fremont 1987 | 72 initially expressed an interest | 61 | 21 | 49 | 18 |
| Greist 1979 | not reported | 28 | 10 | 22 | 8 |
| Hess-Homeier 1981 | not reported | 17 | 5 | not reported | not reported |
| Klein 1985 | 209 responded to an advertisement | 74 | 27 | 42 | 15 |
| Knuppen 2007 | not reported | 39 | 20 | 35 | 19 |
| Martinsen 1985 | not reported | 43 | 24 | 37 | 20 |
| Mather 2001 | 1185 referred or screened | 86 | 43 | 86 | 43 |
| McCann 1984 | 250 completed BDI, 60 contacted | 47 | 16 | 43 | 15 |
| McNeil 1991 | 82 | 30 | 10 | 30 | 10 |
| Mutrie 1988 | 24 | 24 | 9 | 24 | 9 |
| Nabkasorn 2005 | 266 volunteers screened | 59 | 28 | 49 | 21 |
| Orth 1979 | 17 | 11 | 3 | 7 | 3 |
| Pinchasov 2000 | not reported | 18 | 9 | not reported | not reported |
| Reuter 1984 | not reported | not reported | 9 | not reported | 9 |
| Setaro 1985 | 211 responses to advertisement | 180 | 30 | 150 | 25 |
| Singh 1997 | letters sent to 2953 people, 884 replied | 32 | 17 | 32 | 17 |
| Singh 2005 | 451 | 60 | 20 | 54 | 18 |
| Tsang 2006 | not reported | 82 | 56 | 82 | 48 |
| Veale 1998 | not reported | 83 | 48 | 57 | 36 |
| Blumenthal 2007 | 457 | 202 | 51 (supervised), 53 home based | 183 | 45 (supervised), 51 home-based |

## FEEDBACK

### Concerning the DOSE 2002 trial, 3 November 2009

#### Summary

I recently read [the] review entitled "Exercise for Depression" and would like to point out some errors in your review. First, you stated the following in your review,

"We attempted to extract data on intensity of exercise but this was reported for only a few trials, and there was too much variation in other aspects of the trial methodologies to attribute differences in outcomes to differences exercise intensities. One of the included trials compared four different 'doses' of aerobic exercise (DOSE 2002) and found that high intensity exercise was more effective than low intensity exercise."
In actuality, participants were allowed to self-select intensity and the two factors that were manipulated were frequency of exercise and total energy expenditure. It was the total energy expenditure that seemed to have a great effect on reduction of symptoms when the low dose was compared with the higher dose.

Second, the study is not cited correctly throughout the article and finally I am not sure why the main results paper was not included in this review because it was published in 2005. What was included was our baseline design paper that had no results.
I would like to see this error corrected in the review.
Andrea L. Dunn, PhD

#### Reply

Reply of Dr Gillian Mead, 10 November 2009
The 2005 paper is now cited as well as the 2002 paper.
The purpose of our review was to determine the effectiveness of exercise for depression. Thus we included trials which compared exercise with 'no treatment' and trials which compared exercise to other treatments for depression e.g. CBT. Our conclusions were that
'It is reasonable to recommend exercise to people with depressive symptoms and to those who fulfil diagnostic criteria for depression....'

I agree... that it would be misleading if people with depression and researchers were given the impression that exercise had to be intense to bring about benefits. Based on our subgroup analyses, we have stated that 'we cannot give people accurate information about how
effective exercise might be, nor can recommendations be made about the relative benefits of aerobic exercise, resistance exercise or mixed
exercise, whether group or individual exercises are better, nor about the optimum duration of exercise'. We then go on to say that further research is required.
[Concerning intensity within the DOSE study] - text has been added for clarification in both the 'Description of studies' and the 'Discussion'.

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## WHAT'S NEW

Last assessed as up-to-date: 25 March 2007.

| Date | Event | Description |
|---|---|---|
| 12 November 2009 | Feedback has been incorporated | Feedback received from a triallist received 3 November 2009 concerning the DOSE 2002 study was addressed on 10 November 2009 |

## HISTORY

Protocol first published: Issue 3, 2003

Review first published: Issue 4, 2008

| Date | Event | Description |
|---|---|---|
| 13 May 2009 | New citation required but conclusions have not changed | Incorrect 'date assessed as up to date' changed from February 2000 to March 2007 (date of last electronic searches). Abstract corrected to reflect true history of searches |
| 13 August 2008 | New search has been performed | This is an updated version of a previous review published in the BMJ in 2001 and includes several new trials |
| 30 July 2008 | Amended | Converted to new review format |
| 21 February 2000 | New citation required and conclusions have changed | Substantive amendment |

## CONTRIBUTIONS OF AUTHORS

This review is based on a previously published BMJ review by Debbie Lawlor and Stephen Hopker. The review was updated and modified by Dr Mead, with contributions from Dr Morley, Dr Greig, Dr Campbell and Professor McMurdo

## DECLARATIONS OF INTEREST

Professor McMurdo is co-director of D.D. Developments, a University of Dundee not-for-profit organisation which provides exercise classes for older people.

## SOURCES OF SUPPORT

### Internal sources


- NHS Lothian, University of Edinburgh, UK.


### External sources


- No sources of support supplied


## INDEX TERMS

### Medical Subject Headings (MeSH)

*Exercise; Depression [*therapy]; Randomized Controlled Trials as Topic; Treatment Outcome

### MeSH check words

Adult; Humans; Middle Aged; Young Adult