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The effectiveness of exercise as an intervention in the management of depression: systematic review and meta-regression analysis of randomised controlled trials

Debbie A Lawlor, Stephen W Hopker

Abstract

Objective To determine the effectiveness of exercise as an intervention in the management of depression.

Design Systematic review and meta-regression analysis of randomised controlled trials obtained from five electronic databases (Medline, Embase, Sports Discus, PsycLIT, Cochrane Library) and through contact with experts in the field, bibliographic searches, and hand searches of recent copies of relevant journals.

Main outcome measures Standardised mean difference in effect size and weighted mean difference in Beck depression inventory score between exercise and no treatment and between exercise and cognitive therapy.

Results All of the 14 studies analysed had important methodological weaknesses; randomisation was adequately concealed in only three studies, intention to treat analysis was undertaken in only two, and assessment of outcome was blinded in only one. The participants in most studies were community volunteers, and diagnosis was determined by their score on the Beck depression inventory. When compared with no treatment, exercise reduced symptoms of depression (standardised mean difference in effect size -1.1 (95% confidence interval -1.5 to -0.6); weighted mean difference in Beck depression inventory -7.3 (-10.0 to -4.6)). The effect size was significantly greater in those trials with shorter follow up and in two trials reported only as conference abstracts. The effect of exercise was similar to that of cognitive therapy (standardised mean difference -0.3 (95% confidence interval -0.7 to 0.1)).

Conclusions The effectiveness of exercise in reducing symptoms of depression cannot be determined because of a lack of good quality research on clinical populations with adequate follow up.

Introduction

Depression is a common and important cause of morbidity and mortality worldwide. The effect of exercise on depression has been the subject of research for several decades, and the literature on the subject is growing.¹ In the past decade "exercise on prescription" schemes have become popular in primary care in the United Kingdom,² many of which include depression as a referral criterion.

Several plausible mechanisms for how exercise affects depression have been proposed. In the developed world taking regular exercise is seen as a virtue; the depressed patient who takes regular exercise may, as a result, get positive feedback from other people and an increased sense of self worth. Exercise may act as a diversion from negative thoughts, and the mastery of a new skill may be important.^{3,4} Social contact may be an important mechanism, and physical activity may have physiological effects such as changes in endorphin and monoamine concentrations.^{5,6}

This review summarises the evidence from randomised controlled trials of the effectiveness of exercise as a treatment for depression.

Methods

Identification of the studies

We searched Medline (1966-99), Embase (1980-99), Sports Discus (1975-99), PsycLIT (1981-99), the Cochrane Controlled Trials Register, and the Cochrane Database of Systematic Reviews using the terms "exercise," "physical activity," "physical fitness," "walking," "jogging," "running," "cycling," "swimming," "depression," "depressive disorder," and "dysthymia." We also examined bibliographies, contacted experts, and hand searched copies published in the 12 months to December 1999 of selected journals (for details see the longer version of this paper on the *BMJ's* website).

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Inclusion criteria

Studies were included in the review if the participants were diagnosed as having depression (by any method of diagnosis and with any severity of depression) and were aged 18 or above. Only randomised controlled trials were included. Studies had to include depression as an outcome measure and could be in any language. We excluded studies that compared different types of exercise, those that measured outcomes immediately before and after a single exercise session, and those that looked at the effect of exercise on anxiety or other neurotic disorders. We included studies that compared exercise and other, established treatments for depression.

Study quality

We assessed the quality of studies by noting whether allocation was concealed and intention to treat analysis was undertaken, and whether there was blinding.^{7, 8}

Data extraction

The two authors independently extracted data, using a structured form. We resolved discrepancies by referring to the original papers and discussion.

Contact with authors

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.

Outcome measures

The studies used a number of psychometric instruments to assess depression, with several using more than one instrument. To include data from as many trials as possible we calculated effect sizes for each trial, using Cohen's method,⁹ and a standardised mean difference for the overall effect. As the main outcome measure in 10 of the 14 trials that were finally included was the Beck depression inventory, we also combined data from these trials to calculate the weighted mean difference in the Beck depression inventory score.

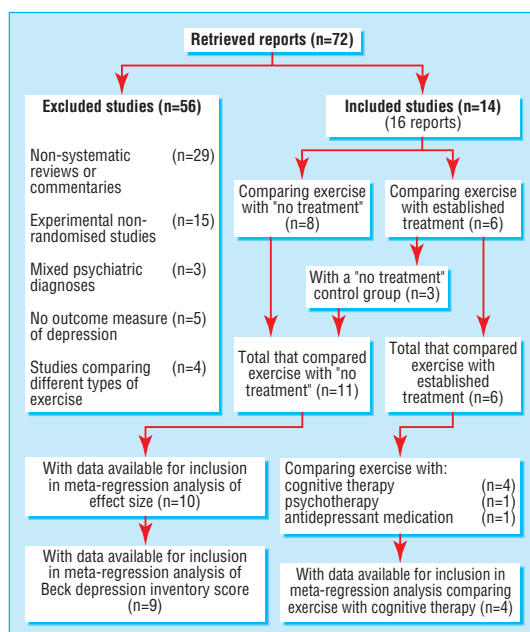


Fig 1 Process of inclusion of studies for review and analysis

Statistical analysis

We undertook a narrative review of all studies and a meta-regression analysis of those studies with appropriate data. The effect of exercise compared with "no treatment" was considered separately from the effect of exercise compared with an established treatment for depression. Some studies were included in both analyses as they contained exercise, established treatment, and control groups.

We anticipated that systematic differences between studies (heterogeneity) would be likely. This was the case for the meta-analysis of studies comparing exercise with no treatment; for these we used a random effects model.¹⁰ The results of studies comparing exercise with cognitive therapy were homogeneous; for meta-analysis of these we used the fixed effects inverse variance method.¹¹ We also undertook a meta-regression analysis to assess the effects of allocation concealment, intention to treat analysis, blinding, the setting, baseline severity of depression, type of exercise, type of publication, and length of follow up.

Results

Study inclusion and characteristics

Figure 1 summarises the process of inclusion of the studies for review and analysis. Of 72 potentially relevant studies, we excluded 56. Sixteen articles reporting 14 studies fulfilled the inclusion criteria¹²⁻²⁷; 11 studies compared exercise with no treatment and six compared it with an established treatment.

Missing data and contact with authors

Authors of 11 of the 14 studies responded to our request to provide missing data,^{12-19 21-25 27} but three were unable to provide all the information.^{24 25 27} Only seven of the 14 written reports provided adequate data for statistical pooling and confirmation of study conclusions. Through contact with authors we were able to obtain adequate data for a further five.

Quality assessment

Most studies were of poor quality. In no study was treatment allocation described, and contact with authors established that allocation might have been adequately concealed in only three studies.^{13 14 21} Intention to treat analysis was undertaken in two studies.^{12 13} Assessment of outcome was blind in only one of the 14 studies.

Study populations

Nine of the studies involved non-clinical populations,^{12 13 16 18-20 23 24 26} and most participants were recruited through the media.

Only four of the nine studies with non-clinical participants used clinical interview to confirm the presence of depression,^{12 13 18 23} the remainder using a cut-off point on the self reported Beck depression inventory score (each study using a different value).

Exercise compared with placebo intervention or as an adjunct to standard treatment

Of the studies that compared exercise with no treatment, 10 had data available for analysis (for more details see the *BMJ's* website). Figure 2 shows the standardised mean differences in effect size of these studies. The pooled standardised mean difference in effect size was -1.1 (95% confidence interval -1.5 to -0.6). Significant heterogeneity between studies ($Q = 35.0, P < 0.001$) was

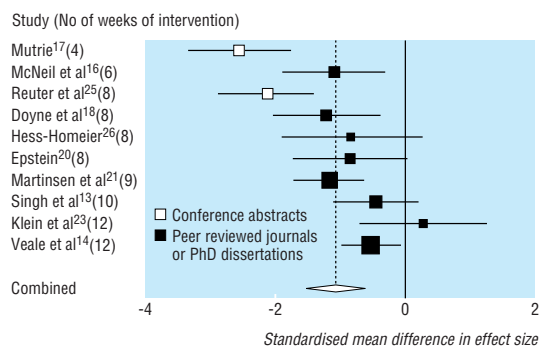


Fig 2 Standardised mean difference in size of effect of exercise compared with “no treatment” for depression

not associated with allocation concealment, intention to treat analysis, blinding, setting, baseline severity of depression, or exercise type but was associated with type of publication and length of follow up. When the variables “abstract” and “follow up” were combined in the model, the estimated variance between the studies was reduced to zero. The effect of treatment was significantly higher in conference abstracts than in peer reviewed journals and doctoral dissertations (pooled standardised mean differences in effect size -2.3 (-2.9 to -1.8 ; $n=2$) and -0.7 (-1.0 to -0.5 ; $n=8$), respectively). The pooled standardised mean difference in effect size of the four studies in which the duration of intervention was >8 weeks was -0.6 (-0.9 to -0.3).

Pooling the nine studies that used the Beck depression inventory as a measure of depression gave a weighted mean difference in the score of -7.3 (-10.0 to -4.6). Again there was significant heterogeneity, associated with type of publication and length of follow up.

Exercise compared with standard treatments for depression

Six studies compared exercise and standard interventions, four of which compared exercise and cognitive therapy (for details see the *BMJ*'s website). Figure 3, which shows the standardised mean differences of these four studies, shows that the difference in effect size between exercise and cognitive therapy was not significant (standardised mean difference -0.3 (95% confidence interval -0.7 to 0.1)). These studies were homogeneous ($Q=2.9$, $P=0.4$).

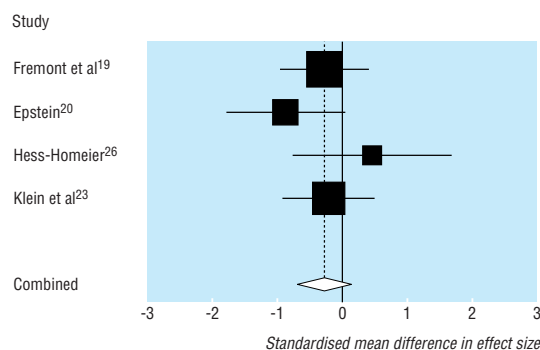


Fig 3 Standardised mean difference in size of effect of exercise compared with cognitive therapy

Only one study compared exercise and standard antidepressant treatment.¹² Its main outcome measure—the Hamilton rating scale of depression—did not differ significantly between the groups of patients receiving the exercise intervention, medication, or both; and at the end of the 16 week intervention period the proportion of patients diagnosed as no longer depressed was similar in each group.

Discussion

Quality of the studies

Exercise may be efficacious in reducing depressive symptoms, but the poor quality of much of the evidence is of concern. The fact that none of the measures of study quality explained the variation among the studies is likely to be due to the low quality of most of the studies. The evidence does not support a sustained effect of exercise beyond the intervention period. Participants from one study are being followed up for two years (N Singh, personal communication, 1999),¹³ and the results of this follow up will provide important information.

The size of the effect of exercise compared with no treatment in the studies we analysed is similar to those found by three previous meta-analyses.^{28–30} We aimed to provide a better quality analysis by including only trials that were described as randomised controlled trials. That our results did not differ might be because the effect of randomisation was mitigated by the lack of adequate concealment, intention to treat analysis, and blinding, making the trials in our analysis no better than non-randomised trials.

Type of exercise

There was no association between type of exercise and the variation in results between studies, indicating that aerobic and non-aerobic exercise have a similar effect. Studies directly comparing different exercise types support such a finding.^{31–34} However, this may be because the effect is due to psychosocial factors, such as learning a new skill or socialising, rather than to the exercise itself. None of the participants in the studies we reviewed exercised alone: they were either with other participants or with a coach. McNeil et al included a social contact control group and found no significant difference in the effect on depressive symptoms between this group and the exercise group.¹⁶

Implications

Our aim was to assess clinical effectiveness—that is, the likely effect of exercise on clinical patients in everyday practice. Although no trial can exactly replicate everyday practice, the screening out of individuals who were not motivated to exercise, the use of non-clinical volunteers, and the lack of intention to treat analysis in most of the studies suggest that our results overestimate what would be likely in real life. In the United Kingdom rates of compliance with “exercise on prescription” schemes among patients with any referral criteria vary from 20% to 50%.^{2, 35} It is reasonable to assume that compliance among patients with depression would be similar or worse. Salmon has pointed out that the allocation of depressed patients in these studies to activities such as running or aerobics “must puzzle clinicians, who in treating depressed people, often have to contend with an absence of

What is already known on this topic

Depression is common

Management is often inadequate and many patients do not comply with antidepressant medication

The effect of exercise on depression has been a subject of interest for many years

What this study adds

Most studies of the effect of exercise on depression are of poor quality, have brief follow up, and are undertaken on non-clinical volunteers

Exercise may be efficacious in reducing symptoms of depression in the short term but its effectiveness in clinical populations is unknown

A well designed, randomised controlled trial with long term follow up is needed

motivation to tackle much less strenuous features of life's routine.³⁶ Furthermore, the fact that most studies used non-clinical participants means that the results may be less generalisable.

To use as much of the available data as possible we calculated the standardised mean difference using effect sizes. The result is therefore expressed as a standard deviation. That is to say, our results show that people who exercise are "1.1 standard deviations less depressed than non-exercisers"; in clinical terms such a result is difficult to understand. We also calculated pooled differences in the mean score on the Beck depression inventory, statistics that likewise will probably have little meaning for most doctors and patients. A more useful outcome measure would be the likelihood of being depressed after the intervention—only two studies included a dichotomous outcome, and these found no significant difference between the exercise and control groups in the numbers of participants with depression after the intervention.^{12 20} A dichotomous result is a more understandable and perhaps a more important outcome measure in clinical terms, and such measures should be included in future research in this area.

We conclude that it is not possible to determine from the available evidence the effectiveness of exercise in the management of depression. However, exercise may be efficacious in reducing the symptoms of depression in some volunteers in the short term. Doctors could recommend more physical activity to their motivated patients, but this should not replace standard treatment, particularly for those with severe disease. Other health benefits could accrue to patients who do become more active.^{37 38} There is a need for well designed, randomised controlled trials on a clinical population that measure both continuous and dichotomous outcomes and that follow up participants for at least 12 months.

This work began as part of a training course at the NHS Centre for Reviews and Dissemination, University of York, and we thank Jos Kleinan and other staff at the centre for their help. Alan Lui (audit nurse, Airedale General Hospital, West Yorkshire) helped with the protocol development and retrieval of articles. Domenico Scala (senior house officer, psychiatry, Lynfield Mount Hospital, Bradford) translated one Italian paper. Matthias Egger and David Gunnell (department of social medicine, University of Bristol) gave useful comments on an earlier draft.

Contributors: Both authors developed the idea for the review, the protocol, and the search strategy, applied the search strategy, and independently extracted data from retrieved articles. DAL undertook all statistical analyses and wrote the original draft of the paper. Both authors contributed to the final version of the paper, and both act as guarantors.

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Medically unexplained symptoms in frequent attenders of secondary health care: retrospective cohort study

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Abstract

Objective To estimate the prevalence of medically unexplained symptoms in patients who most frequently attend outpatient services.

Design Retrospective cohort study over three years with review of case notes.

Setting Secondary care services in the South Thames (West) NHS region.

Participants Outpatient attenders with new appointments in 1993.

Main outcome measures Number of outpatient appointments, and number of consultation episodes for medically unexplained conditions.

Results Medical records of 361 of 400 sampled frequent attenders were examined, and 971 consultation episodes were recorded. Ninety seven (27%) had one or more consultation episodes in which the condition was medically unexplained; 208 (21%) of the 971 consultation episodes were medically unexplained. Abdominal pain, chest pain, headache, and back pain were commonly found to be medically unexplained.

Conclusions Medically unexplained symptoms present in most hospital specialties and account for a considerable proportion of consultations by frequent attenders in secondary care.

Introduction

A small proportion of patients attending outpatient clinics in secondary care attend frequently and are responsible for a high proportion of healthcare costs.^{1,2} Early studies showed that many such patients consult for physical symptoms which, after extensive investigation, remain medically unexplained.³ These symptoms occur commonly in all medical settings, yet they remain poorly understood and are often persistent and disabling.⁴ There have been few studies of frequent attenders in secondary care. Previous work has been limited to single specialties and teaching hospitals⁵ or has focused on inpatient admissions.⁶

We examined the outpatient consultations of frequent attenders in all the general hospitals across one regional health authority and included both medical and surgical specialties. We estimated the prevalence of

medically unexplained symptoms in those patients who most frequently attend outpatient services.

Methods

South Thames (West) NHS region has recorded outpatient hospital activity in computerised form since 1991. To identify frequent attenders we defined a population in which potential subjects were all patients in the region aged 18-65 years who had a new appointment to secondary medical or surgical care in 1993 (index appointments). We excluded specialties for specific conditions, such as obstetrics (but not gynaecology), oncology, and psychiatry.

We followed patients with index appointments over a three year period to assess their overall service use within the region by counting all outpatient appointments. The population was stratified by two age groups (18-45 years and 46-65 years). Frequent attenders were then defined as the top 5% of outpatient users in each age group.

We randomly selected 200 patients from the total in each age group (24 489 aged 18-45 years; 36 743 aged 46-65 years) for inclusion in the study. The study was approved by the local research ethics committee.

A consultation episode was defined as all appointments after referral and was completed after discharge, death, or referral elsewhere. We recorded details of the reason(s) for referral and identified investigations and treatment received at each appointment. Finally, we noted the diagnosis (if given) for each consultation episode and determined whether the episode was medically unexplained, mixed (evidence of both physical and psychological disorder), or factitious. Criteria for a medically unexplained episode were that the patient presented with physical symptoms, the patient received investigations for these symptoms, and the investigations and clinical examination revealed no abnormality or only abnormalities that were thought to be trivial or incidental.^{7,8}

Results

Of the 12 NHS trusts we contacted in the region, only one refused examination of its medical records. A total of 361 (90%) sets of case notes were traced and obtained for examination: 189 (95%) for patients aged

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