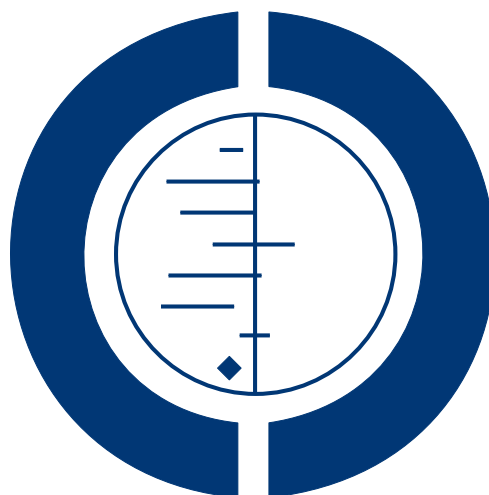


Exercise for treating fibromyalgia syndrome (Review)

Busch AJ, Barber KA, Overend TJ, Peloso PMJ, Schachter CL



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Exercise for treating fibromyalgia syndrome

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ABSTRACT

Background

Fibromyalgia (FM) is a syndrome expressed by chronic widespread body pain which leads to reduced physical function and frequent use of health care services. Exercise training is commonly recommended as a treatment. This is an update of a review published in Issue 2, 2002.

Objectives

The primary objective of this systematic review was to evaluate the effects of exercise training including cardiorespiratory (aerobic), muscle strengthening, and/or flexibility exercise on global well-being, selected signs and symptoms, and physical function in individuals with FM.

Search methods

We searched MEDLINE, EMBASE, CINAHL, SportDiscus, PubMed, PEDro, and the Cochrane Central Register for Controlled Trials (CENTRAL, Issue 3, 2005) up to and including July 2005. We also reviewed reference lists from reviews and meta-analyses of treatment studies.

Selection criteria

Randomized trials that were selected focused on cardiorespiratory endurance, muscle strength and/or flexibility as treatment for FM.

Data collection and analysis

Two of four reviewers independently extracted data for each study. All discrepancies were rechecked and consensus was achieved by discussion. Methodological quality was assessed by two instruments: the van Tulder and the Jadad methodological quality criteria. We used the American College of Sport Medicine (ACSM) guidelines to evaluate whether interventions had provided a training stimulus that would effect changes in physical fitness. Due to significant clinical heterogeneity among the studies we were only able to meta-analyze six aerobic-only studies and two strength-only studies.

Main results

There were a total of 2276 subjects across the 34 included studies; 1264 subjects were assigned to exercise interventions. The 34 studies comprised 47 interventions that included exercise. Effects of several disparate interventions on global well-being, selected FM signs and symptoms, and physical function in individuals with FM were summarized using standardized mean differences (SMD). There is moderate quality evidence that aerobic-only exercise training at recommended intensity levels has positive effects global well-being (SMD 0.49, 95% CI: 0.23 to 0.75) and physical function (SMD 0.66, 95% CI: 0.41 to 0.92) and possibly on pain (SMD 0.65, 95% CI: -0.09 to 1.39) and tender points (SMD 0.23, 95% CI: -0.18 to 0.65). Strength and flexibility remain under-evaluated.

Authors' conclusions

There is 'gold' level evidence (www.cochranemsk.org) that supervised aerobic exercise training has beneficial effects on physical capacity and FM symptoms. Strength training may also have benefits on some FM symptoms. Further studies on muscle strengthening and flexibility are needed. Research on the long-term benefit of exercise for FM is needed.

PLAIN LANGUAGE SUMMARY

Exercise for fibromyalgia

This summary of a Cochrane review presents what we know from research about the effect of exercise for fibromyalgia. The review shows that in people with fibromyalgia:

- moderate intensity aerobic training for 12 weeks may improve overall well-being and physical function; moderate intensity aerobic exercise probably leads to little or no difference in pain or tender points.
- strength training for 12 weeks may result in large reductions in pain, tender points and depression, and large improvement in overall well-being but may not lead to any difference in physical function.
- the exercise programs that were studied were safe for most. The intensity of aerobic exercise training should be increased slowly aiming for a moderate level. If exercisers experience increased symptoms, they should cut back until symptoms improve. If in doubt about adverse effects, they should check with a health care professional.
- it is not known whether exercise training for more than 12 weeks improves other symptoms such as fatigue, stiffness or poor sleep. Many people with FM do have difficulty staying on an exercise program. Strategies to help individuals exercise regularly were not measured in these studies.
- it is not known whether flexibility training, programs combining types of exercise, and programs combining exercise with non-exercise strategies improve the symptoms of fibromyalgia.

What is fibromyalgia and what are the different types of exercise?

Fibromyalgia is a syndrome of persistent widespread pain and tenderness. Individuals may also experience a wide range of other symptoms such as difficulty sleeping, fatigue, stiffness, and depression. Symptoms may put people off exercising but studies show that the majority are able to exercise. Exercise training can include aerobics such as stepping and walking; strengthening exercises such as lifting weights or using resistance machines; and stretching for flexibility. Although exercise is part of the overall management of fibromyalgia, this review examined the effects of exercise when used separately or combined with other strategies such as education programs, biofeedback and medications.

Best estimate of what happens to people with fibromyalgia who take part in aerobic exercise:

In the studies, aerobic exercises were done for at least 20 minutes once a day (or twice for at least 10 minutes), 2 to 3 days a week. Strength training was done 2 to 3 times a week and with at least 8 to 12 repetitions per exercise. The exercise programs lasted between 2 ½ to 24 weeks.

When compared to no exercising, aerobic exercise training may:

- improve overall well-being by 7 points on a scale of 0 to 100.
- improve ability to perform aerobic exercise; by using 2.8 ml/kg/minute more oxygen when walking on a treadmill.
- increase the amount of pressure that can be applied to a tender point by 0.23 kgs/cm² before the onset of pain.
- reduce pain by 1.3 on a scale of 0 to 10.
- have unknown effects on fatigue, depression or stiffness.

These results are based on moderate quality evidence.

Best estimate of what happens to people with fibromyalgia who take part in strength training:

When compared to no exercise, strength training may:

- reduce pain by 49 fewer points on scale of 0 to 100.
- improve overall well-being by 41 points on a scale of 0 to 100.
- lead to 2 fewer active tender points on a scale of 0-18.

These results are based on low quality evidence.

The numbers given are our best estimate. When possible, we have also presented a range because there is a 95 percent chance that the true effect of the treatment lies somewhere within that range.

BACKGROUND

Description of the condition

The 1990 American College of Rheumatology (ACR) criteria for classification of fibromyalgia (FM) syndrome define it as widespread pain for longer than three months duration, with pain on palpation of at least 11 of 18 specified tender points on the body (Wolfe 1990). While the ACR criteria are most frequently used in research studies, clinicians may also employ the American Pain Society criteria for a clinical diagnosis of FM (Burckhardt 2005), that include the presence of widespread pain (all four quadrants of the body and along the midline axial) for at least three consecutive months and pain on palpation of 9 of 11 bilateral sites on the body. A 1996 consensus report offers a broader picture of FM, describing it as a “syndrome of widespread pain, decreased pain threshold, and characteristic symptoms that include non-restorative sleep, fatigue, stiffness, mood disturbance, irritable bowel syndrome, headache, paresthesias, and other less common features” (Wolfe 1996, page 534). The American Pain Society Guideline for Management of Fibromyalgia Syndrome in Adults and Children (Burckhardt 2005) also acknowledge that other symptoms including fatigue, headache, poor sleep, psychological distress and cognitive dysfunction often are part of the syndrome and can have

a substantial impact on an individual’s physical and emotional function and overall health-related quality of life.

Wolfe 1995 reported the prevalence of FM (all ages) to be 2% (females 3.4%, males 0.5%). A recent large-scale Canadian study (McNalley 2006) describes self-reported prevalence of FM as 1.1% for all ages (1.83% in females, 0.33% in males) with a female to male ratio of six to one. Limitations in activities associated with daily living have been reported to be as high in FM patients as in patients with rheumatoid arthritis (Hawley 1991). In individuals who seek medical attention, the condition is chronic and non-remitting, with symptoms affecting every aspect of life, including work, family life and leisure (Henriksson 1994). Researchers have reported a substantial impact of FM on ability to work and productivity. Twenty to 50% of persons with FM could work few or no days (Ledingham 1993, Wolfe 1997), 36% had an average of two or more absences from work per month (Martinez 1995), and 26.5% to 55% had received disability or social security payments (Martinez 1995, Wolfe 1997).

Many individuals with FM have been shown to be sedentary (Clark 1993) and with levels of cardiorespiratory fitness well below average (Bennett 1989, Burckhardt 1989, Clark 1993, Clark 1994). While the underlying pain, fatigue and depression are likely to

contribute to sedentary lifestyles and therefore low levels of fitness, the studies being evaluated indicate that individuals with FM are able to perform maximal tests cardiorespiratory fitness, low and moderate intensity aerobic exercise, flexibility and muscle strengthening exercise.

Description of the intervention

Despite examination of a wide range of treatments, optimal management of FM is still unknown. Current reviews (Bellamy 1998, Berman 1999, Burckhardt 2002, Hadhazy 2000, Holdcraft 2003, Mannerkorpi 2003, Sim 2002) and evidence-based guidelines (Goldenberg 2004) have examined a range of treatment options divided into pharmacologic and non-pharmacologic. Non-pharmacologic strategies include interventions classified as mind-body cognitive/cognitive-behavioral, exercise, complementary and alternative therapies. Goldenberg 2004 concluded that “despite the chronicity and complexity of FM, there are pharmacological and non-pharmacological interventions available that have clinical benefit. Based on current evidence, a stepwise program emphasizing education, certain medications, exercise, cognitive therapy, or all 4 should be recommended” (page 2388). Goldenberg 2004 goes on to advise that optimal management is “best arrived at when patients and health care professionals work as a team” (page 2394). However, while exercise is recognized as one part of the management of FM, not all of the clinically relevant and practically important aspects of an exercise prescription have been elucidated.

How the intervention might work

While pain in individuals with FM may be related to central nervous system pain processing abnormalities that include central sensitization and inadequate pain inhibition, peripheral tissues including muscle may contribute to chronic pain through initiating and/or maintaining central sensitization (Staud 2005, Staud 2006). Exercise may thus contribute to pain through the process of muscle microtrauma, repair and adaptation associated with normal acute exercise and exercise training. Several studies have described metabolic findings in muscle tissue that are consistent with deconditioning (Bennett 1989, Elvin 2006, Lund 1986, Park 1998, Bengtsson 1986a, Bengtsson 1986b, Jubrias 1994). The metabolic adaptations induced by aerobic and by strength training may normalize some of these findings, thus contributing to improvements in pain (Costill 1979, Deschenes 2002, Holloszy 1984).

Exercise training has been used successfully to address a number of conditions that are also commonly experienced by individuals with FM. Aerobic and strength training have been shown to improve depression in individuals with clinical depression (Brosse 2002, Dunn 2001). Moderate exercise can improve sleep in individuals with sleep complaints (King 1997, Singh 1997). One can also reflect on training-induced improvements in cardiorespiratory fitness to suggest that fatigue may also improve because as one's maximal aerobic capacity improves, the individual will be

performing activities of daily living at lower absolute percentages of maximal capacity.

Why it is important to do this review?

Incorporating exercise into one's weekly routine is not a small endeavour. It is the responsibility of clinicians and researchers to identify for clients with FM both the effects that they can expect in terms of FM signs and symptoms and the most efficacious methods of achieving those effects. This review is necessary to determine the effectiveness of various types and training volumes of exercise for improvement of FM signs and symptoms. The review should also examine what outcomes are most impacted by exercise in this population. The review is also needed to guide clinicians and individuals with FM through the maze of studies towards the currently known best prescriptions for, and ways to perform exercise by individuals with FM.

OBJECTIVES

The primary objective of this systematic review was to evaluate the effects of exercise training including cardiorespiratory (aerobic), muscle strengthening, and/or flexibility exercise on global well-being, selected signs and symptoms, and physical function in individuals with FM.

METHODS

Criteria for considering studies for this review

Types of studies

We selected randomized clinical trials (RCT) that compared an intervention that included an exercise component with an untreated control or a non-exercise intervention. Studies were included if the authors used words such as randomly, random or randomization, to describe the method of assignment of subjects to groups.

Types of participants

The studies used a variety of published criteria for the diagnosis of FM: Smythe 1981, Wolfe 1990, Yunus 1981, Yunus 1982, Yunus 1984. Although some differences exist between the diagnostic criteria, for the purpose of this review all were considered to be acceptable and comparable. While exclusion criteria varied among studies, all allowed for exclusion of individuals with medical conditions for which exercise could be either contraindicated or unsafe under unmonitored conditions.

Types of interventions

Exercise was defined as the “planned, structured and repetitive bodily movement done to improve or maintain one or more components of physical fitness” (ACSM 2001). In classifying exercise interventions, we recognized two types of interventions. Composite interventions included both an exercise and non-exercise component(s) delivered simultaneously. Exercise-only interventions did not include a non-exercise component and were classified by the predominant type exercise. In classifying the type of exercise, the exercise performed in warm-up and cool-down were not considered. Exercise-only interventions included aerobic-only training, strength-only training, flexibility-only training, or mixed exercise-only interventions. No restrictions on frequency, intensity or duration were made beyond requiring that the exercise component of composite interventions be a substantial part of that treatment.

Types of outcome measures

Outcome measures did not form part of the inclusion criteria for this review. We grouped the outcome measures into six constructs representing global well-being, commonly experienced signs and symptoms of FM and observer-measured physical function.

Primary outcomes

Primary outcomes represented four constructs.

1. Pain (e.g., visual analogue scale (VAS) or 10 point ordinal scale)
2. Global well-being (overall feeling of well-being) or perceived improvement in FM symptoms (outcomes such as the Fibromyalgia Impact Questionnaire (FIQ) total score, study participant-rated change in FM symptoms, observer-rated change in FM symptoms). (Note: The FIQ is a self-report questionnaire developed to evaluate overall impact of FM. The individual with FM rates commonly experienced FM symptoms, including (but not restricted to) pain, fatigue, depression, anxiety, level of restedness after sleep, and effect of FM on work. The scores for each item can be reported individually or summed to report the FIQ total score. In this review we have used the FIQ total score to represent overall or global well being.)
3. Physical function
 - a. Physical performance -aerobic (e.g., submaximal or maximal treadmill or cycle ergometer tests, 6 minute walk)
 - b. Physical performance -musculoskeletal (e.g., grip strength, hip and knee extension strength)
 - c. Physical performance- flexibility (e.g., sit and reach test)
4. Tender points (e.g., pain threshold of tender points using dolorimetry or tenderness to thumb pressure)

Secondary outcomes

Secondary outcomes represented two constructs.

5. Depression (e.g., Beck Depression Inventory, FIQ subscale for depression).
6. Fatigue and sleep (e.g., FIQ fatigue subscale, sleep VAS)

Search methods for identification of studies

In the original review we searched MEDLINE (1966-12/2000), CINAHL (1982-12/2000), HealthSTAR (1990-12/2000), SportDiscus (1975 - 12/2000), EMBASE (1974 to 12/2000), and the Cochrane Controlled Trials Register (CCTR, Issue 4, 2000).

Electronic searches

The search terms and parameter of our earlier review are provided in Table 1. For this update, we searched the following databases from 1/2000 to 5/2005: MEDLINE (Ovid), EMBASE (Ovid), CINAHL (Ovid), SportDiscus (Ovid), PubMed, PEDro, and the Cochrane Central Register of Controlled Trials Register (CENTRAL, Issue 3, 2005). The primary search terms were:

1. exp FIBROMYALGIA/
2. fibromyalgia.tw.
3. fibrositis.tw.
4. or/1-3
5. exp exercise/
6. exp EXERTION/
7. exp Physical Fitness/
8. exp Exercise Test/
9. exp Exercise Tolerance/
10. exp SPORTS/
11. exp PLIABILITY/
12. exp Physical Endurance/
13. exertion\$.tw.
14. exercis\$.tw.
15. sport\$.tw.
16. ((physical or motion) adj5 (fitness or therapy or therapies)).tw.
17. (physical\$ adj2 endur\$).tw.
18. manipulat\$.tw.
19. (skate\$ or skating).tw.
20. jog\$.tw.
21. swim\$.tw.
22. bicycl\$.tw.
23. (cycle\$ or cycling).tw.
24. walk\$.tw.
25. (row or rows or rowing).tw.
26. weight train\$.tw.
27. muscle strength\$.tw.
28. or/5-27
29. 4 and 28
30. limit 29 to yr=2000 - 2005

Other sources

Reference lists from identified articles, meta-analyses and reviews of all types of treatment for FM were reviewed independently by two reviewers and all promising references were scrutinized.

Data collection and analysis

Selection of studies

Two reviewers (AJB, CLS) independently scanned the titles and

reviewed abstracts of studies generated from searches. The reference lists from bibliographies of review articles were also examined and abstracts were retrieved for all promising titles. We retrieved all complete publications for the promising abstracts. The full text articles were then examined independently by two reviewers to determine if they met the selection criteria. Disagreements between the two reviewers were resolved in consensus meetings of the full team. Foreign language studies were translated and included in the review. In our opinion, no important papers were missed.

Data extraction and management

For the preparation of the first review (16 studies, [Busch 2002](#)), two reviewers (AJB, CLS) independently extracted data (study characteristics, study results). Point estimates for selected variables were extracted by one of the reviewers and a research assistant, and checked by a pair of reviewers. For the preparation of this major update, two of four reviewers (AJB, CLS, KARB, TJO) independently extracted data for each study. All discrepancies were rechecked and consensus achieved by discussion.

Assessment of methodological quality of included studies

Two instruments for assessing methodological quality were applied in this review: the van Tulder Methodological Quality Criteria ([van Tulder 1997](#), [van Tulder 2003](#)) and the Jadad Methodological Quality Criteria ([Jadad 1996](#)). The van Tulder Methodological Quality Criteria were applied with two deviations from those of [van Tulder 1997](#). We interpreted 'patient blinding' to mean rigorous information control because it is not possible to blind subjects to an exercise intervention (item h). We used a withdrawal rate of 20% (item l) as acceptable and awarded positive scores if data from at least 80% of subjects were analysed at completion of the primary short-term end point of the study, or if all subjects who entered the study were analysed at completion (i.e., intention-to-treat analysis). The Jadad Methodological Quality Criteria were applied exactly as described by [Jadad 1996](#).

Before beginning the methodological evaluation for the 2002 review, three reviewers (AJB, CLS, PMP) independently evaluated a sample of two studies and subsequently agreed upon a consistent interpretation of criteria for each of the two instruments. The three reviewers then independently applied the two instruments, using standardized forms for each. Differences in ratings were resolved by consensus. For the current update, reviewers (AJB, CLS, KARB, TJO) worked in pairs, independently evaluating a sample of two studies and then reviewing the established interpretation of criteria for the instruments. Consensus on further clarification of the interpretation was achieved in a meeting of the four reviewers. Reviewers then worked in pairs, independently applying the two instruments, using standardized forms for each. Differences in ratings were resolved by consensus. To avoid bias, one of the included studies ([Schachter 2003](#)) which was authored by three of the current reviewers was examined by the two reviewers not involved in that study. Inter-rater reliability calculated for the updated assessment using Kappa was very good ($K = 0.914$, "almost perfect" according to [Landis 1977](#)).

In this update we consider the 11 items of the van Tulder methodological criteria that reflect internal validity ([van Tulder 2003](#)). We arbitrarily classified studies into high, moderate and low quality studies based on scores on these eleven items. Studies achieving a score of 8-11 were classified as being of high quality; studies scoring 5-7 were classified as being of moderate quality and those scoring 1-4 were classified as low quality studies. In this review, we place greater weight on moderate to high quality studies (i.e., those with a score of 5 or greater). In actuality, this represented a score of 50% or greater because one of the 11 items (the blinding of the care provider) is seldom achieved in exercise studies.

Evaluation of congruence of exercise/physical activity with recognized guidelines

We used the American College of Sport Medicine (ACSM) guidelines ([ACSM 2001](#); [ACSM 2006](#)), to evaluate whether interventions had provided a training stimulus that would effect changes in physical fitness. The ACSM recommendations for achieving improvements in physical fitness represent widely accepted criteria. Since exercise guidelines have not been developed for those with FM, the ACSM guidelines (developed for healthy individuals) were used.

ACSM guidelines: ([ACSM 2006](#))

1. Cardiorespiratory Endurance (Aerobic Training) The dosage required is as follows: a) frequency of exercise at least three days per week, b) intensity of exercise sufficient to achieve equal to or greater than 40% of heart rate reserve (min-max: 40-85%) or 64% of predicted maximum heart rate (min-max: 64-94%), c) sessions of at least 20 minutes duration (min-max: 20-60 minutes), either as continuous exercise or spread intermittently throughout the day in blocks of 10 minutes or more, and using any mode of aerobic exercise involving use of major muscle groups in rhythmic activities, d) for a total time period of at least six weeks. While ACSM recommends an exercise frequency of 3-5 days per week, it acknowledges that "deconditioned persons may improve CR fitness with only twice-weekly exercise, greater improvement is achieved with a frequency of 3-5 sessions per week." ([ACSM 2006](#))
2. Muscle Strengthening: The dosage requirements for strength training interventions are: a) frequency of 2-3 days per week, b) a minimum of one set of 8-12 repetitions at an intensity of the 8 to 12 Repetition Maximum of each exercise, using any type of strengthening exercise that can be progressed over time.
3. Flexibility Training: Flexibility prescription refers to controlled static stretching in which a subject assumes a position and holds it for a given duration. Dosage requirements are: a) frequency of exercise equal to or greater than two days per week, b) intensity to a position of mild discomfort, c) 3 to 4 repetitions for each stretch held for a duration of 10-30 seconds.

The Physical Activity Guideline of the Centres for Disease Control and Prevention (CDC) ([CDC 2001](#)) represents a recommendation supported by epidemiological studies about minimum intensities and duration of physical activity that can improve health-related variables (such as blood pressure and lipid profile). The

recommendation that most adults should perform at least 30 minutes of moderate intensity physical activity (in blocks of at least 10 minutes) on five or more days of the week or at least 20 minutes of vigorous intensity exercise at least three days per week, represents a public health statement to the general population. We used the CDC Guideline to evaluate whether interventions had provided an exercise or physical activity stimulus that could improve health. Two reviewers independently classified studies either as meeting, or not meeting, the ACSM and CDC training guidelines, and then reached a consensus by discussion.

Measures of treatment effect

We planned a priori to consider several variables for outcome measures: pain, tenderness or tender points, global assessments by either patient or physician, the Fibromyalgia Impact Questionnaire (FIQ), anxiety and depression measures, and measures of physical performance and self-efficacy. The outcome measures of interest were most often presented as continuous data with means and standard deviations. Thus, we used a standardized mean difference (SMD), which converts scales to a common metric. To calculate SMD, we used means and standardized deviations of change scores for each intervention. When not available, standard deviations of change scores were derived directly from confidence intervals of change scores, or estimated from the pretest and posttest standard deviations (or standard errors) where these were provided. SMDs were calculated using RevMan Analyses, a statistical analysis tool incorporated in RevMan.

Evaluation of clinically important differences

Recent literature suggests use of relative difference in change scores or percent change as a guide for determining clinically important difference. The *Philadelphia Panel*, 2001 regards a 15% difference between groups as clinically important and the American College of Rheumatology (ACR) established a definition of improvement in rheumatoid arthritis clinical trials that is 20% in selected measures (Felson 1995). A reduction of approximately 30% in the 11-point pain intensity numerical rating scale (PI-NRS) was found to represent a clinically important difference in clinical trials of chronic pain therapies (Farrar 2001). The PI-NRS study reviewed data from 10 placebo-controlled clinical trials including 2724 subjects, 529 of which had (FM). An additional placebo-controlled study with 99 subjects (Dunkl 2000) found the 11-point PI-NRS, FM Impact Questionnaire (FIQ) and tender point counts were all able to distinguish among groups of patients with FM who reported improved clinical status from those who did not.

Percent change results must be interpreted with caution since estimates of important change have been found to vary by magnitude of baseline measurement on a given scale (Stratford 1998). Disease status or activity level at baseline affects relative improvement when using percent change as a marker for improvement (vanRiel 2000). The scale's sensitivity to change is also dependent on the construct that is used as a comparison for determining clinical importance (Riddle 1998).

We used a conservative estimate of 30% relative percentage im-

provement as a benchmark for clinical importance based on work by Farrar 2001. Farrar 2001 determined that a reduction of approximately 30% on the pain intensity numerical rating scale represents a clinically important difference for patients with chronic pain (Farrar 2001). This is also consistent with the findings of Dunkl 2000 who examined responsiveness of measures of clinical improvement in FM. Relative percentage improvement was calculated as the mean change in the treatment group minus the mean change in the control group divided by the pooled mean for the baseline scores for the variable.

The Cochrane Musculoskeletal Group has recently adopted new guidelines for describing and interpreting clinical relevance (Tugwell 2004). In this review, in addition to using a criterion of 30%, we have applied the new guidelines. The guidelines were used to develop the plain language summary.

Randomized clinical trials (RCT)

We included RCTs that compared the effects of exercise to the effects of other treatments (e.g., relaxation, Cognitive Behaviour Training) or to control conditions that did not involve any form of activity or treatment (e.g., treatment as usual, attention only, wait list controls). When multiple interventions were compared in a single study, we analysed the comparisons that arose from each exercise intervention separately. In the meta-analysis, we included only the studies which compared exercise to an untreated control. We preferentially analysed intention to treat (ITT) data whenever available. To create a more complete data set for analysis, we contacted authors of studies with missing data requesting data required for analysis. Several authors generously provided estimates of central tendency or variability (means, standard deviations of pretest and posttest data or standard deviations of change scores) (Buckelew 1998; Burckhardt 1994; DaCosta 2005; Gowans 1999; Richards 2002) and information needed for the qualitative analysis (Altan 2004; Cedraschi 2004; Hakkinen 2001; Mengshoel 1992; Redondo 2004). Studies that only provided categorical data and those for which we were not able to obtain missing data were excluded from meta-analysis (Genc 2002).

Assessment of heterogeneity

We created the data extraction tables and then discussed as a team what issues of clinical heterogeneity should be examined. Important sources of heterogeneity were considered to be: variations in interventions (aerobic training, flexibility training, strength training or mixed/composite training) and dosage of exercise intervention (meeting ASCM training criteria), disparate comparators (e.g., intervention versus a control group or intervention versus a second intervention), and timing of measurement of outcome measures and methodological quality.

Heterogeneity among the trials was next assessed using the heterogeneity statistics (chi squared, I^2). We considered values of $P = 0.1$, or smaller, to be indicative of significant heterogeneity. Where $P < .1$ and or $I^2 > 50\%$, the results were examined for sources of clinical heterogeneity and methodological differences. If no methodological or clinical reasons could be found to explain the statisti-

cal heterogeneity, we proceeded with the meta-analysis using the random effects model.

Assessment of reporting biases

When appropriate, publication bias was assessed using a visual assessment of the funnel plot (RevMan Analyses).

Data synthesis (meta-analysis)

Using RevMan Analyses software, mean change scores were compared and weighted and combined using a random effects model. Where meta-analysis was inappropriate, we used RevMan Analyses to produce effect sizes (SMD) and effect size confidence intervals. We used Cohen's categories for effect size (Cohen 1988) to evaluate the magnitude of the effect (.2 = small effect, .5 = medium effect, .8 = large effect). We used the following levels of evidence descriptors of van Tulder 2003 to classify the results of the meta-analysis:

- Strong - consistent findings among multiple high quality (HQ) RCTs
- Moderate - consistent findings among multiple low quality (LQ) RCTs and/or controlled clinical trials (CCTs) and/or one HQ RCT
- Limited - one LQ RCT and/or CCT
- Conflicting - inconsistent findings among findings among multiple trials (RCTs and/or CCT)
- No evidence from trials - no RCTs or CCTs

We defined inconsistent as:

1. In the absence of high quality studies, at least one RCT clearly favors control while at least one RCT(s) clearly favors treatment
2. If more than one high quality studies is available, and at least one HQ RCT clearly favors control while at least one HQ RCT clearly favors treatment

We defined consistent as:

1. All studies clearly favor treatment
2. All studies clearly favor control
3. Some studies clearly favor treatment, the remainder are inconclusive (do not exclude the null)

We defined "clearly favor" as: the confidence interval excludes zero. Outcome Measures: When researchers reported more than one measure for a dependent variable, we used the following order of preference for entry into the meta-analysis:

1. Pain: VAS, VAS FIQ, Ordinal Scale
2. Tender Points: dolorimetry, total myalgic score, tender point count
3. Global: FIQ Total, subject-rated VAS or ordinal scale, QOL scale, SIP Total.
4. Depression: Beck Cognitive, Beck Total, CES, FIQ-depression, AIMS Depression
5. Objective Measures of Physical Function: selected on a case-by-case basis depending on the researchers' stated objectives

Subgroup analysis

Subgroup analyses were limited to aerobic-only interventions (from moderate to high quality studies) and strength-only interventions (from poor quality studies). Future updates may include

refinements to meta-analysis as new trials come available; for example, we hope to also examine the effects of moderate to high quality strength training and flexibility training as such studies are published.

Sensitivity analysis

Except for the aerobic-only exercise studies, there were too few studies in any other grouping to perform sensitivity analysis. We assessed the bias related to low methodological quality using visual inspection of the forest plots of poor quality studies versus the moderate to high quality aerobic-only studies.

RESULTS

Description of studies

See: [Characteristics of included studies](#); [Characteristics of excluded studies](#).

Results of the search

We inspected 2226 titles generated from the searches conducted in 2002 and 2005 and found 64 citations of full-length articles describing experimental trials which examined the effects of interventions that included an exercise component in subjects with FM.

Included studies

Thirty-four reports (Altan 2004; Buckelew 1998; Burckhardt 1994; Cedraschi 2004; DaCosta 2005; Genc 2002; Meyer 2000; Gowans 1999; Hakkinen 2001; Hakkinen 2002; Isomeri 1993; Jentoft 2001; Jones 2002; Keel 1998; King 2002; Mannerkorpi 2000; Martin 1996; McCain 1988; Mengshoel 1992; Meyer 2000; Nichols 1994; Norregaard 1997; Ramsay 2000; Redondo 2004; Richards 2002; Schachter 2003; Sencan 2004; Valim 2003; Valkeinen 2004; vanSanten 2002a; vanSanten 2002b; Verstappen 1997; Wigers 1996; Zijlstra 2005) met our selection criteria and were included for analysis. Three publications were accompanied by subsequent reports dealing with the same subjects. Hakkinen 2002 reported on additional variables from the Hakkinen 2001 study and thus was counted as one study for analysis. Two publications presented information on long term uncontrolled follow-up of included RCTs: Gowans 2004 was a follow-up to Gowans 2001; Mannerkorpi 2002 was a follow-up to Mannerkorpi 2000; data were not analysed in this review and the reports were treated as secondary studies. The basic characteristics of the included studies are summarized in the 'Characteristics of Included Studies' Table.

Participants

There were a total of 2276 subjects with the confirmed diagnosis of FM across the studies; 1264 subjects were assigned to exercise interventions. The average sample size for the smallest experimental group was 24.7 (SD=16.4, min-max: 5-80) for the 34 original studies. Mean age in the studies ranged from 27.5 to 60.2 years in 34 studies (unspecified in Ramsay 2000). For the 2197 subjects for

whom gender was reported, 96.4% were female. Nineteen studies involved only females; twelve examined both males and females, with females in the majority; and the remaining three studies did not specify the gender of participants. Few studies used participation in regular physical activity prior to study entry as an exclusion criterion.

Interventions

The 34 studies in the review comprised 47 interventions that included exercise. Subjects were randomized to at least one aerobic-only intervention in 15 studies, to strength-only interventions in three studies, to flexibility-only interventions in 3 studies, to mixed exercise only intervention in 11 studies, and to a composite aerobic exercise plus education interventions in four studies. Other composite interventions were explored in only one study each: mixed exercise plus medication; flexibility exercise plus medication; mixed exercise plus self management strategies and group discussion; aerobic exercise plus biofeedback; aerobic exercise within a multidisciplinary program; and aerobic exercise as part of a spa treatment. Twelve studies had more than one intervention that included exercise. The details regarding the interventions are provided in [Table 2](#).

Evaluation of Training Stimulus

Twenty studies described exercise interventions that met ACSM recommendations: 17 for aerobic training, three for strength training ([Hakkinen 2001](#); [Jentoft 2001](#); [Valkeinen 2004](#)) and two for flexibility ([Jones 2002](#); [Mannerkorpi 2000](#)). Eleven of 14 studies that did not meet the ACSM recommendations did not provide sufficient detail about the aerobic, strengthening or flexibility exercises to accurately determine the adequacy of the training stimulus or flexibility intervention. In one study ([Norregaard 1997](#)) it was determined that ACSM guidelines for intensity of aerobic training stimulus had not been met because the majority of subjects could not achieve the target heart rate levels (i.e., 40%-50% VO_2 max). In [Mannerkorpi 2000](#), exercise was performed at subject-selected paces that were below pain and fatigue thresholds, and was not designed to elicit a training effect. In [Zijlstra 2005](#), the duration of the exercise program was too short (15 days).

Only three studies described exercise interventions that met CDC recommendations for aerobic training ([McCain 1988](#); [Meyer 2000](#); [Redondo 2004](#)). Seven of 32 interventions that did not meet the CDC recommendations did not provide sufficient detail about the aerobic exercise to accurately determine the adequacy of the training stimulus ([Buckelew 1998](#); [Burckhardt 1994](#); [Genc 2002](#); [Isomeri 1993](#); [Keel 1998](#); [Ramsay 2000](#); [Sencan 2004](#)). The remaining 25 studies were insufficient with respect to frequency and/or duration of exercise to satisfy the CDC standards for either moderate (30 min, 5 times/week) or vigorous (20 min, 3 times/week) exercise.

Outcomes

A variety of tests and measures (n=166) were used to evaluate the effects of the six outcomes in the 34 included studies. For example, pain was measured in 28 studies using 9 instruments. Most studies

(n = 22) used a 10 cm visual analogue scale to measure pain. The FIQ was the most commonly used test to measure for global well-being (n=13). The most commonly used test to measure physical performance (aerobic) was the 6-minute walk test (n = 6), however seven studies measured maximum oxygen uptake with staged treadmill or cycle ergometer tests. Although several studies used dolorimetry, the most common measure of tender points was the tender point count (12 studies). Depression was measured using the Beck Depression Inventory in five studies and the depression visual analogue in five studies. The most common measure of fatigue was the FIQ fatigue visual analogue scale which was reported in 10 studies.

Adverse Effects

[Norregaard 1997](#) noted that “many patients in the training group actually reported a deterioration of symptoms and did not want to complete the study”. [Verstappen 1997](#) commented that, “17% (of completers) reported that their complaints got worse during the intervention period, that the exercise aggravated the feelings of soreness and tiredness afterwards, or that the pain exceeded their tolerance level during the exercises”. [Mannerkorpi 2000](#) reported a reduction of planned intensity of exercise because “many patients reported increased pain for 3-4 days after the training sessions”. In contrast, [Mengshoel 1992](#) noted that “fibromyalgia patients may perform a low-intensity dynamic endurance exercise ... without exacerbating their general pain and fatigue symptoms”. While [Richards 2002](#) reported no adverse effects, they cited increased pain and stiffness as a reason for attrition (for unknown numbers of participants). [Schachter 2003](#) also reported that some participants reported increased pain, stiffness and fatigue (unknown numbers of participants). [Wigers 1996](#) reported that nine subjects experienced increased stress. Aside from these general comments, only five of the 1264 subjects assigned to exercise interventions were designated as having had an adverse effect possibly related to exercise. These included one metatarsal stress fracture ([Schachter 2003](#)), one case of ischialgia ([Wigers 1996](#)), and two cases of transient knee pain ([McCain 1988](#)).

With regards to strength training, [Jones 2002](#) reported a worsening of pain (n=3). Conversely, [Hakkinen 2001](#) did not report any adverse effects and stated “even heavy resistance training can be safely used in the treatment of fibromyalgia” and [Valkeinen 2004](#) reported no adverse effects and commented that “it is noteworthy that, after the initial phase of training, the patients did not complain of any unusual exercise induced pain or muscular soreness during the experimental period, and even intensive strength training did not worsen the symptoms.”

Among studies with flexibility exercise interventions, [Jones 2002](#) reported increased pain for some participants while no other researchers reported adverse effects with flexibility training.

In mixed exercise intervention studies, both [vanSanten 2002a](#) and [vanSanten 2002b](#) describe post exercise soreness as an important barrier to a compliance with mixed exercise training. They noted that despite continuous encouragement, about 50% of the partic-

ipants in both the high intensity and self-selected intensity mixed exercise training groups were not able to comply with the training sessions and patients in the high intensity group “felt completely ‘broken down’ for more than 24 hours after the training sessions.” Among studies with composite interventions, [Cedraschi 2004](#) speculated that increased pain may have contributed to high attrition rates in the exercise group, but this was not quantified.

Excluded studies

Twenty-seven studies which at first appeared to be appropriate were excluded from this systematic review. Of the 27 studies that were excluded, 4/27 did not adequately characterize the population, 19/27 were not randomized trials, and 4/27 did not include an intervention we would characterize as exercise. (see the ‘Characteristics of Excluded Studies’ Table).

Studies awaiting assessment

At present there are three new studies are awaiting review: [Assis 2006](#); [Gusi 2006](#); [Salek 2005](#).

Risk of bias in included studies

Methodological Analysis

Ten studies scored 3 out of 5 on the Jadad Scale; 21 scored 2, and two scored 1. The mean of van Tulder quality scores for internal validity was 5.06 (out of a total possible of 11); the mode was 4. The total quality scores for individual studies ranged from 1 to 9. Four studies were classified as high quality ratings, 15 as moderate quality, and 14 as low quality. More than half the studies were deficient in six or more internal validity criteria (concealment of treatment allocation, compliance with treatment, patient blinding, care provider blinding, control of co-intervention, valid randomization). Results of the methodological assessment including the van Tulder item by item analysis and the Jadad scores are provided in [Table 3](#). [Table 4](#) shows the quality assessments for studies that met ACSM dosage guidelines for the aerobic interventions training in the included studies.

Allocation

A method of allocation was specified in 17 studies and treatment allocation was concealed in 10 studies. Allocation methods ranged from computer generated random numbers to simple “by lot” procedures. Treatment allocation was generally concealed by use of an independent researcher who was not aware of the eligibility of the subjects and who had no knowledge of the assignment procedures. There was insufficient information in many studies to determine methods of allocation or any concealment of treatment allocation. With respect to quality of allocation concealment, 10 studies were judged as adequate, there was some uncertainty about adequate concealment in 20 studies and allocation was definitely not concealed in 4 studies.

Blinding

The care provider was blinded to the intervention in only two studies ([Richards 2002](#), [Wigers 1996](#)). The subjects were blinded to the intervention in six studies ([Buckelew 1998](#); [Keel 1998](#); [McCain](#)

[1988](#); [Sencan 2004](#); [vanSanten 2002a](#); [Zijlstra 2005](#)) while the outcome assessors for the main outcomes were blinded in 20 studies. Blinding of the care provider and subjects is difficult during training studies, but blinding of the outcome assessor should be standard practice to reduce the chance of bias in reporting outcomes.

Follow-up and exclusions

Attrition rates for the 17 aerobic exercise intervention groups averaged 27.0% (SD=18.9%, min-max: 0 to 67%); attrition for the two strength training interventions was 0% (SD=0%). In the two flexibility interventions for which attrition data was provided, attrition was 12.5% (SD= 4.9%, min-max: 9 -16%). The 13 mixed exercise interventions had attrition rates of 14.6% (SD=11.8%, min-max: 0-40%). The 11 composite interventions had dropout rates of 14.8% (SD= 9.6%, min-max: 0-27%). Mean attrition in the 20 non-treatment control groups was 12.3% (SD=11.8%, min-max: 0-47%) and in the comparator groups was 18.0% (SD= 14.1%, min-max: 0-49%).

Selective reporting

Review authors did not have concerns over selective reporting of time points (i.e., only 2 of the 34 did not have comparability of timing of outcome assessment in across groups). Few studies measured the complete cluster of variables chosen by reviewers for major comparisons. A limited number of studies did not include point estimates and estimates of variability for major outcome measures.

Other potential sources of bias:

Sample size

Small sample size is a methodological weakness of most included studies; only five studies of the 34 included studies meet the standard of 50 subjects per group. In general, there is a trend over time toward larger sample sizes. Mean sample sizes for included studies across 5 year intervals are 18.0, 16.0, 24.0, and 34.9 for 1985-90, 1991-95, 1996-00, 2000-05, respectively.

Adherence

Fundamental to application of exercise as an intervention for FM is the requirement that exercise must be tolerated by individuals with FM. [Norregaard 1997](#) noted “many patients in the training group actually reported a deterioration of symptoms and did not want to complete the study”. [Verstappen 1997](#) commented that, “17% (of completers) reported that their complaints got worse during the intervention period, that the exercise aggravated the feelings of soreness and tiredness afterwards, or that the pain exceeded their tolerance level during the exercises”. [Mannerkorpi 2000](#) reported a reduction of planned intensity of exercise because “many patients reported increased pain for 3-4 days after the training sessions”. Where [McCain 1988](#) reported participants did not have difficulty performing high intensity cycling, [vanSanten 2002a](#) reported that 50% of participants both in a similar high intensity program as well as those in a lower intensity program consistent with ACSM guidelines were unable to fully comply with the training sessions and that participant in the high intensity group reported feel-

ing “broken-down”. Such difficulties with exercise combined with high attrition rates in exercise studies suggest the importance of identifying the dose-response curves for FM signs and symptoms for different types (and to a lesser extent, modes) of exercise. One important tool used in the examination of these questions is exercise adherence. To accurately describe the dose-response relationship for exercise training, detailed data on the frequency, intensity and duration of performed exercise are required.

A common tool used to represent exercise adherence in included studies is the reporting of exercise frequency, as measured by total attendance at sessions (in the case of organized exercise sessions) or participant-reported performance of exercise sessions (in the case of independent exercise programs such as home exercise programs). Focusing on studies that used aerobic training or included an aerobic training component within a mixed exercise or composite intervention, eighteen studies monitored attendance at organized exercise sessions or performance of independent exercise sessions. In using frequency as a measure of exercise adherence, authors operate under the assumption that participants performed all of the prescribed exercise (duration) at the prescribed intensity. Yet difficulties cited in the preceding paragraph suggest that this assumption may be inaccurate, that the intensity and duration of performed exercise may differ greatly from the prescribed exercise. Taking further steps to identify the dose-response curves for exercise requires employment of techniques to monitor exercise duration and intensity. Focusing on studies that used aerobic training or incorporated an aerobic training component within a mixed or composite intervention, fourteen measured intensity using rating of perceived exertion or heart rate (via measurement of pulse by participant, heart rate or pulse monitors). No studies reported whether participants completed the prescribed duration of exercise in each session. No studies reported detailed results of systematic data collection and analysis of participant adherence to exercise performance in a way that would allow readers to understand the exact training volume achieved by participants.

In studies of strength training, adherence can be assessed through a combination of attendance/performance of independent sessions and the monitoring of sets and repetitions of exercises. Focusing on studies that evaluated strength training, one study reported on attendance at organized exercise sessions. No studies reported on performed sets and repetitions of exercises.

Effects of interventions

The results will be presented beginning with the meta-analysis, followed by the analyses of standardized mean differences (effect sizes), and description of relative percentage change (clinically significant difference).

1. Meta-analysis

After preliminary meta-analyses in which we examined sources of statistical heterogeneity, clinical heterogeneity and methodological quality, we meta-analyzed the data for effects of exercise on pain,

global wellbeing, and objective measures of physical function for aerobic-only interventions and strength-only interventions when compared to untreated control groups. We further restricted our meta-analysis to moderate and high quality studies for evaluation of treatment effects of aerobic-only interventions. The results are displayed with significance level, standardized mean difference (SMD) with confidence intervals and forest plots.

Meta-analyses of Aerobic-Only Exercise Interventions compared to Untreated Control Groups

There is moderate evidence that short term (6 to 23 weeks) aerobic-only exercise training prescribed at ACSM levels results in:

- Moderately large positive (but statistically insignificant) effects on pain: SMD = 0.65 (95%CI: -0.09 to 1.39) pooled from 183 subjects in one high quality (Wigers 1996) and two moderate quality studies (Buckelew 1998; Schachter 2003)
- Medium-size positive effects on global well-being: SMD = 0.49 (95%CI: 0.23 to 0.75) pooled from 269 subjects from four moderate quality studies (Buckelew 1998; Gowans 2001; King 2002; Schachter 2003)
- Moderately large positive effects on objective measures of physical function: SMD = 0.66 (95%CI: 0.41 to 0.92) pooled from 253 subjects in one high quality (Wigers 1996) and three moderate quality studies (Gowans 2001; King 2002; Schachter 2003)
- Small, statistically insignificant effect for tender points: Although the pooling of data from 309 subjects is non-significant: SMD = 0.23 (95%CI: -0.18 to 0.65), one high quality, Wigers 1996 reported significant large effects, while three moderate quality studies (Buckelew 1998; Gowans 2001; Schachter 2003) found a small non-significant positive effect and another moderate quality study (King 2002) found a small non-significant negative effect.

There is conflicting evidence that the effect of short-term (6 to 23 weeks) aerobic-only exercise training prescribed at ACSM levels results in:

- Small to medium improvement in depression: SMD = 0.40 (95%CI: 0.04 to 0.76) pooled from 233 subjects from one high quality (Wigers 1996) and one medium quality study (Schachter 2003) which showed no evidence of effect, and two moderate quality studies (Buckelew 1998; Gowans 2001) which demonstrated medium to large effects.

There is limited evidence (one medium quality study, Schachter 2003, 87 subjects) that 16 weeks of Aerobic Only prescribed at ACSM levels has no effect in individuals with FM on stiffness: SMD = -0.17 (95%CI: -0.59 to 0.25) or fatigue: SMD = 0.00 (95%CI: -0.52 to 0.52).

There is limited evidence from one moderate quality study (Sencan 2004, 40 subjects) that short term (6 weeks) aerobic-only exercise training prescribed at an unspecified intensity compared to an untreated control produces large improvements in pain: SMD = 1.34 (95% CI: 0.65 to 2.04), tender points: SMD = 3.90 (95%

CI: 2.80 to 4.99), and depression: SMD = 1.22 (95% CI: 0.54 to 1.90).

Meta-analyses of Strength-Only Exercise Interventions compared to Untreated Control Groups

There is limited evidence from two low quality studies (Hakkinen 2001; Valkeinen 2004) that 21 weeks of Strengthening Exercise Only prescribed at ACSM levels versus Untreated Control for individuals with FM results in:

- a large effect on pain (Hakkinen 2001, 21 subjects, SMD = 3.00, 95%CI: 1.68 to 4.32)
 - a large effect on global wellbeing (Hakkinen 2001; Valkeinen 2004, 47 subjects, SMD = 1.43, 95%CI: 0.76 to 2.10)
 - a medium (non-significant) effect on objective measures of physical function (Hakkinen 2001; Valkeinen 2004, 47 subjects, SMD = 0.52, 95%CI: -0.07 to 1.10).
 - a large effect on tender points (Valkeinen 2004, 26 subjects, SMD = 1.52, 95%CI: 0.63 to 2.41)
 - a large effect on depression (Hakkinen 2001, 21 subjects, SMD = 1.14, 95%CI: 0.20 to 2.08)
 - no differences in magnitude and time course of adaptations of the neuromuscular system to strength training in 11 women with FM (Hakkinen 2002) as compared to 10 healthy women.
- The authors also found a similar response in systematic in growth hormone levels during an acute bout of exercise in participants with FM and healthy controls.

2. Effectiveness of all other interventions in included studies

Several interventions were excluded from the meta-analyses because of inadequate replication or clinical heterogeneity. The standardized mean differences (effect sizes) and confidence intervals for the effects of these exercise-only interventions and the composite interventions on global well-being, pain, tender points, observer-measured physical function and depression are summarized in Table 5 and Table 6. Several statistically significant medium to large effect sizes (equal to or greater than .5 with 95% confidence interval excluding zero) were identified favouring several exercise-only and composite interventions. In terms of frequency, global well-being was the most commonly identified as having a statistically significant medium to large effect size; six interventions produced significant effect sizes of this magnitude for variables addressing global change.

3. Relative Percentage Change

The calculation of relative percentage change revealed several sporadic clinically significant improvements in a variety of outcomes.

- Aerobics Only Interventions: Clinically significant improvement (>30% greater change at post-test) in five aerobics-only interventions as compared to an untreated control in depression (Buckelew 1998, Wigers 1996), tender points (Sencan 2004, Wigers 1996), in FIQ Total (Schachter 2003), dynamic endurance (Mengshoel 1992), FIQ rested and self-efficacy for function (Schachter 2003).
- Strength Only Interventions: Greater than 30% improvement was seen in the strength training group as

compared to an untreated control group in pain (Hakkinen 2001), global well-being (Hakkinen 2001, Valkeinen 2004), and depression (Hakkinen 2001).

- Other Interventions: Mannerkorpi 2000 found clinically significant improvement in anxiety, SF-36 general health, SF-36 role physical, and SF-36 vitality. Clinically significant improvement was observed in anxiety and depression from composite program of aerobics exercise and education when compared to an untreated control group in two studies (Cedraschi 2004, Zijlstra 2005). Altan 2004 and Buckelew 1998 found clinically significant improvement in depression resulting from mixed exercise and composite aerobics and biofeedback (respectively) compared to an untreated control group. Cedraschi 2004 and Zijlstra 2005 found clinically significant improvement in FIQ worked missed resulting from composite interventions of aerobic and spa and aerobics and education as compared to untreated control groups.

In addition to these findings, the results of the detailed analysis of clinical relevance using the 2006 Cochrane Musculoskeletal Group guidelines are presented in Table 7 and Table 8.

4. Long-term effects

Most studies examined the effects of short-term interventions - interventions varied between 2.5 weeks to 24 weeks (quartiles of 8, 12, and 20 weeks). Seven aerobic only studies reported follow-up assessment varying from 12 weeks to 4 years. At 12 weeks, King 2002 found no between group differences between the aerobics only group and the control. At 24 weeks post intervention, improvements in pain pressure threshold, depression, and pain were maintained (Sencan 2004). Richards 2002 reported improved FIQ scores at 24 weeks, and fewer active tender points in the aerobic group compared to the relaxation group at 1 year. At one year follow-up, DaCosta 2005 reported improved upper body pain and FIQ scores. Gowans 1999 conducted a program review of participants 3 to 6 months after completion of the intervention (no control group was used in the follow up) and reported significant improvements in 6 minute walk, fatigue, self-efficacy for pain and symptoms. Gowans 2004 noted in an uncontrolled follow-up of Gowans 2001, that improvements in physical function (6 min walk test) mood (Beck Depression Inventory - total, Beck Depression Inventory - somatic), self-efficacy (function), and symptom severity (FIQ total) were maintained at 6 and 12 month (ITT analysis). Buckelew 1998 included a two year maintenance phase in which interventions were monitored on a monthly basis and exercise was performed as a home program, and which lost very few participants to follow up. Improvements in self-reported physical function and self-efficacy for function were seen at one year follow up. Wigers 1996 evaluated participants 4.5 years after the intervention and found that improvements were not retained in the exercise group, and that most of the group was not still exercising. In an uncontrolled follow-up to Mannerkorpi 2000, Mannerkorpi 2002 noted that participants in the exercise group had maintained

improvements in FIQ total, FIQ physical function, SF-36 physical function, SF-36 general health, and grip strength to six months, and FIQ pain, FIQ fatigue, physical function (6 min walk test) and SF-36 bodily pain, social function, vitality to 24 months. Zijlstra 2005 noted that at 3 months follow-up, the spa group were significantly better than controls in the physical component of health status measure RAND-36, pain, fatigue, subject evaluated general health, number of tender points, graded tender point score, and FIQ total. Cedraschi 2004 noted that at 24 months follow-up, significantly more patients in the treatment group than in the control group had engaged in a new physical activity. At 12 week follow-up, Altan 2004 found improvements in depression inventory were retained; there were no between group differences in symptoms (FIQ, pain, fatigue, stiffness, sleep), tender points, patient- or physician-rated global health status, or in chair test either immediately following the intervention or at the 12 week follow-up. Neither Jentoft 2001 nor Redondo 2004 found any significant between-group differences at 46 and 52 weeks respectively. Ramsay 2000 who had only one significant between group difference at the end of intervention (HAD-anxiety) between a weekly supervised aerobic exercise class and an unsupervised home program found no between group differences at 24 or 48 weeks.

5. Adverse Effects

Norregaard 1997 noted that “many patients in the training group actually reported a deterioration of symptoms and did not want to complete the study”. Verstappen 1997 commented that, “17% (of completers) reported that their complaints got worse during the intervention period, that the exercise aggravated the feelings of soreness and tiredness afterwards, or that the pain exceeded their tolerance level during the exercises”. Mannerkorpi 2000 reported a reduction of planned intensity of exercise because “many patients reported increased pain for 3–4 days after the training sessions”. In contrast, Mengshoel 1992 noted that “fibromyalgia patients may perform a low-intensity dynamic endurance exercise ... without exacerbating their general pain and fatigue symptoms”. While Richards 2002 reported no adverse effects, they cited increased pain and stiffness as a reason for attrition (for unknown numbers of participants). Schachter 2003 also reported that some participants reported increased pain, stiffness and fatigue (unknown numbers of participants). Wigers 1996 reported that nine subjects experienced increased stress. Aside from these general comments, only five of the 1264 subjects assigned to exercise interventions were designated as having had an adverse effect possibly related to exercise. These included one metatarsal stress fracture (Schachter 2003), one case of ischialgia (Wigers 1996), and two cases of transient knee pain (McCain 1988).

With regards to strength training, Jones 2002 reported a worsening of pain (n=3). Conversely, Hakkinen 2001 did not report any adverse effects and stated “even heavy resistance training can be safely used in the treatment of fibromyalgia”. Valkeinen 2004 reported no adverse effects and commented that “it is noteworthy that, after the initial phase of training, the patients did not com-

plain of any unusual exercise induced pain or muscular soreness during the experimental period, and even intensive strength training did not worsen the symptoms.”

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In mixed exercise intervention studies, both vanSanten 2002a and vanSanten 2002b describe post exercise soreness as an important barrier to a compliance with mixed exercise training. They noted that despite continuous encouragement, about 50% of the participants in both the high intensity and self-selected intensity mixed exercise training groups were not able to comply with the training sessions and patients in the high intensity group “felt completely ‘broken down’ for more than 24 hours after the training sessions.” Among studies with composite interventions, Cedraschi 2004 speculated that increased pain may have contributed to high attrition rates in the exercise group, but this was not quantified.

DISCUSSION

Summary of main results (benefits and harms)

The main results of our review are as follows:

- 1) Moderate quality evidence exists that aerobic-only exercise training at recommended intensity levels has medium-sized positive effects on global outcome measures and medium-sized positive effects on measures of physical function; the effect of such exercise on pain and tender points is less certain but we cannot rule out the possibility that aerobic exercise has a large positive effect on these variables;
- 2) Strength and flexibility exercise remain under-evaluated as exercise prescriptions for people with FM;
- 3) Despite the increasing number of studies investigating the effect of combination treatments with exercise, this question has also received inadequate study, principally because there is underutilization of appropriate research designs;
- 4) There is limited evidence on a variety of other outcomes including stiffness, fatigue, and depression;
- 5) The analysis of percentage change reinforced the results of meta-analysis.

In aerobics-only interventions, clinically significant improvements were found sporadically in six variables: depression, tender points, global well-being, physical function, self-efficacy and symptoms.

Aerobic-only

The evidence has been steadily accumulating to the degree that we were now able to meta-analyze a body of six studies of moderate to high quality comparing aerobic-only protocols of ASCM-

recommended intensity to an untreated control group. With respect to our a priori primary outcomes, we identified the existence of moderate quality evidence that short-term aerobic-only exercise training at recommended intensity levels (ACSM 2006) produced medium-sized positive effects on global outcome measures (Buckelew 1998, Gowans 2001, King 2002, Schachter 2003) and medium-sized positive effects on measures of physical function (Gowans 2001, King 2002, Schachter 2003, Wigers 1996). Effects on pain and tender points were statistically insignificant. With respect to the secondary outcomes (depression, fatigue/sleep), there is conflicting evidence regarding the effect of aerobic exercise on depression, with two studies reporting medium to large effects (Buckelew 1998, Gowans 2001) and two others, no evidence of effect (Schachter 2003, Wigers 1996). There is limited evidence from one medium quality study (Schachter 2003) that aerobic-only exercise prescribed at ACSM levels has no effect on fatigue in individuals with FM.

Although the meta-analysis indicates there is a positive effect of aerobic exercise on global well-being and physical function, our appraisal is moderated by several factors. Attrition rates were high in most studies (range 13-44%) and all studies had relatively small sample sizes (range 16-51). In addition, although adherence is rarely well documented, there many indications that adherence to both exercise intensity and frequency is poor. It must also be noted that more high-quality studies are needed as our analysis only includes one such study (Wigers 1996) and that study had a small sample size (n=16 in the intervention group).

Strength-only

Currently, there is limited evidence that strength-only exercise has a large effect on pain (Hakkinen 2001), global well-being (Hakkinen 2001, Valkeinen 2004), physical function (Hakkinen 2001, Valkeinen 2004), tender points (Valkeinen 2004) and depression (Hakkinen 2001). There is also limited evidence that strength-only exercise compared to flexibility exercise has a medium size positive effect on pain and global well-being, but no effect on muscle strength (Jones 2002). However, only one of these studies was even of medium quality (Jones 2002) and all three had small sample sizes (range 11-28) and inadequate adherence reporting information. Of interest, Hakkinen 2001 and Valkeinen 2004 reported the strength-only exercise had no adverse effects and zero attrition, which is a promising finding given the mean attrition rate of 23.3% reported in the aerobic-only studies. Despite some intriguing results from the available literature however, at this time we are unable to recommend strength training past the suggestion that additional studies, preferably of high quality, are needed to confirm the effect of such exercise on people with FM.

Flexibility-only

There were no studies comparing flexibility-only exercise to a non-exercise control group. There is limited evidence from one mod-

erate quality study (Jones 2002) that flexibility-only exercise compared to strength exercise has a large positive effect on flexibility, but no effect on tender points or depression. Thus more studies, again preferably of high quality, are needed to confirm and extend the effects of flexibility exercise.

Mixed Studies

There were not enough studies to enable meta-analysis of mixed-exercise studies, in which comparisons included untreated controls, high versus low intensity, water versus land, relaxation, balneotherapy (immersion of part or all of the body in a mineral water bath), and Cognitive Behaviour Training. Without exception, the evidence for any particular comparison was limited and arose from a single medium quality study. There were no positive effects of any mixed intervention on signs and symptoms of FM with the exception of objective measures of physical function (vanSanten 2002a, versus untreated control; Martin 1996, versus relaxation).

Composite studies

Composite studies were widely varied, with interventions including Aerobic-and-Education, Exercise-and-Self Help, Mixed Exercise-and-Education, Exercise-and-Spa Treatment, and Exercise-and-Self Management Strategies. Comparisons included untreated controls, education and relaxation. Evidence for effects was limited for every comparison, with a mix of positive and no-difference effects for the active intervention. Only in the case of Aerobics-and-Education versus untreated control did more than one study (Burckhardt 1994, Gowans 1999; both low quality) contribute to the results that indicated limited evidence of no difference in pain and a medium effect on measures of physical function in favour of the intervention.

A concern with all the composite studies is that the experimental designs did not permit a comparison between the individual composite interventions and control groups. Thus there is no way to determine the independent effect of, for example, aerobic exercise or education, or their potential interaction. Use of 2x2 factorial designs is recommended for all such composite studies to maximize information. While this would add to the complexity of organizing the study and require more participants, such designs would help to clarify the effects of both composite and "pure" interventions.

Relative Change

Our analysis across all interventions revealed only sporadic occurrences of clinically significant improvements (defined as > 30%, Farrar 2001), and these improvements were observed only when exercise interventions were compared to untreated control groups. In reference to our primary outcome variables, clinically significant improvements were observed and reported in: a) pain in one strength-only intervention; b) global well-being in one aerobic-only, two strength-only, and one composite intervention; c) physical performance-aerobic in no interventions, physical per-

formance-musculoskeletal in one aerobics-only intervention, and physical performance-flexibility in no interventions; and d) in tender points in two aerobic-only interventions. Clinically significant improvement was found in the following secondary outcome measures: a) depression in seven studies (two aerobic, one strength-only, one mixed exercise-only, and three composite interventions); b) fatigue in no interventions; and c) sleep (rested in morning) in one aerobic-only intervention. A 30% relative improvement probably aligns with a large effect size. These sporadic clinically significant effects were in general agreement with the occurrences of moderate to large effects in the meta-analyses and the effect size analyses.

Harms

Adverse effects of exercise were not always well reported in studies. Available information was quite variable, with some studies reporting no adverse effects, some reporting vague effects (e.g. increased stress) and others attributing high attrition rates to exacerbations of typical signs and symptoms of FM. On occasion it seemed to be difficult to separate adverse effects caused by the exercise protocol from normal fluctuations in signs and symptoms of FM (e.g. Richards 2002). The reported adverse effects suggest that researchers regarded adverse effects primarily as problems outside of the sphere of symptoms of fibromyalgia. It is possible that participants experiencing increased FM symptoms regarded them as adverse effects to exercise. Verstappen 1997 for example reported that 17% of completers/people who responded to a questionnaire about perceived benefits of the exercise program felt "that their complaints got worse during the intervention period, that the exercise aggravated the feelings of soreness and tiredness afterwards, or that the pain exceeded the tolerance level" (pp. 23. Greater attention to ensuring that a definition of adverse effects is shared by researchers and participants is warranted in the future.

Overall, it is our impression that most exercise programs reviewed in this update can be safely completed by people with FM. Clinicians prescribing exercise are reminded to increase intensity slowly, check frequently with participants for adverse effects, and be prepared to back off the exercise program until such effects subside.

Overall completeness and applicability of evidence

There is still a lack of studies, particularly good quality studies, to fully meet the objectives of this review. With the exception of aerobic-only exercise, there are only one or two studies at any level of quality that address many of our specific comparisons. This may be in part because of the large number of exercise modes that have been employed and also in part because research has not been guided by convincing results in previous literature. Fibromyalgia syndrome is also a difficult syndrome to study because of the exacerbations and accompanying signs and symptoms that make participation in exercise problematic for many people. However, with respect to aerobic-only exercise, we now have a pool of six moderate to high quality studies that do permit meta-analysis, with

results indicating a positive effect of such exercise on important outcomes.

With respect to participants, studies continue to overwhelmingly recruit women, as per the well-established demographics of FM, but studies of men with FM would provide welcome information. There are overly numerous interventions; the issues around mixed and composite interventions have been identified above. There is also a bewildering array of outcome measures assessing the same constructs that may contribute to the large variability in some of our meta-analyses.

The primary objective of this systematic review was to evaluate the effects of exercise training including cardiorespiratory (aerobic), muscle strengthening, and/or flexibility exercise on global well-being, selected signs and symptoms, and physical function in individuals with FM. We have critically appraised and summarized 34 studies, all of which are relevant to this question, at least to some degree. Despite the noted limitations in study quality and sample size, we are thus confident of the external validity of our review, that is to say, this review is a valid reflection of the current literature on the effects of exercise on FM.

Methodological Quality

Quality of the evidence

We reviewed 21 new studies in this update, for a cumulative total of 34 including the first review (Busch 2002). Despite this larger pool, there are still too few studies to allow definitive conclusions regarding the effect of strength or flexibility exercise in people with FM. However there are now six studies, of moderate to high quality that have investigated the effect of short-term aerobic-only exercise (at recommended intensity levels) in people with FM. These studies permit the conclusion (derived from meta-analysis) that such exercise has medium-size positive effects on pain, small to medium-sized positive effects on global outcome measures and medium-sized positive effects on measures of physical function. The sample size in these six studies ranged from 16 to 51 in the intervention groups. Their internal validity scores on the van Tulder scale ranged from 5-9, and they scored between 2 and 3 on the Jadad scale. Attrition ranged between 13 and 44% and adherence to the prescribed training programs was generally poorly reported.

Adherence

The studies reviewed do not present a sufficiently clear picture of: a) the intensity and progression of exercise prescribed by researchers, or b) the intensity and progression of exercise performed by the participants. Intended target exercise intensities were expressed in broad terms (for example, 60-80% of age predicted maximal heart rate, as in Martin 1996). This represents a large range of intensities: 60% of maximum heart rate is now considered light intensity exercise, while 80% is considered to be within the low end of the range classified as hard intensity (ACSM 2006). Greater detail about exercise intensity (such as presented in Meyer

2000) is desirable. In addition, consistent use of one system for the classification of exercise intensity is needed in future studies so that researchers, clinicians and individuals with FM have the same understanding of light, moderate and vigorous intensity exercise. Furthermore, the studies reviewed do not present a consistent picture of actual level of exercise performed. No study analyzed and reported intensity of exercise performed in a systematic manner. Without further reporting of adherence to targets within each exercise session, the reviewers were left without a definitive understanding of intensities of exercise tolerated by individuals with fibromyalgia. Researchers such as [McCain 1988](#) presented a picture in which individuals with fibromyalgia can successfully perform vigorous aerobic training. In contrast, a number of researchers noted poor adherence to the prescribed exercise. [Meyer 2000](#) used exercise logs to monitor adherence to individual sessions and stated that “it appears that whereas exercising at high intensity is tolerated for a limited duration over a short period of time, prolonged exposure to a high-intensity exercise regime is not well tolerated and may have an adverse effect on function. On the other hand, exercising at a low-intensity level is well tolerated and may be associated with improved function as adherence continues.” [vanSanten 2002a](#) supported Meyer’s findings but also reported that 50% of participants following a less vigorous exercise prescription had difficulty performing the prescribed exercise intensity. In [Norregaard 1997](#), the researchers stated that while the planned level of performance of the aerobic dance program corresponded to 40-50% VO₂ max, “the majority of the subjects could not achieve target heart rate levels”.

Systematic monitoring and reporting of exercise intensity, duration, and frequency for each mode of exercise examined, is important to more clearly identify the types and modes of exercise best tolerated by individuals with fibromyalgia as well as to determine any dose-response curve for various exercise types and to a lesser extent, within each type, modes of exercise. Examining participants’ impressions of, and reactions to exercise, with special attention to those who drop out of programs, may yield valuable information that would help clinicians understand more fully the impact of, and problems with, exercise for individuals with FM. More detailed reporting of the exercise program and adherence to exercise sessions is required to explore this more fully in order to design future programs with improved adherence and lower attrition rates among participants.

The intensity of aerobic exercise in the six studies in the aerobic-only meta-analysis does comply with the ACSM guidelines but generally falls into the low domain of the recommended intensity range. Progression of intensity and/or duration for the treatment protocols was largely unsuccessful. Thus, these studies involved intensity levels that fall into that described by ACSM guidelines as appropriate for the early part of an aerobic training protocol (i.e. the first 4 weeks). Typically, greater initial improvement is expected when sedentary, deconditioned individuals become more active;

beyond that, unless the exercise regimen is progressed, a tapering off of improvements would be expected. Because training volume did not increase in many of the included studies, it is unclear if the initial reported improvements would continue if programs had continued for longer duration.

Heterogeneity

The effect sizes for our primary outcomes were small to medium and several I² statistics for the meta-analyses were greater than 50%, indicating heterogeneity, or lack of consistency, between studies. In examining possible sources of heterogeneity, we noted that demographics of study participants, the duration of disease, and the types of outcome measurements were reasonably similar between the studies. Publication bias was ruled out as a source of heterogeneity based on funnel plot analysis. Attrition and drop-outs may contribute, but we are unable to quantify their impact. Heterogeneity due to differences in methodological quality, type and duration of exercise intervention and training dosage were addressed by subgroup analysis. The remaining heterogeneity of the results could not be readily explained, therefore, we used a random effects meta-analysis model rather than a fixed-effects model.

Visual scanning of forest plots for subgroup analysis suggested a random distribution with results in the same direction for most subgroups of studies, suggesting that though the study effects differed in size, their results were mostly in the same direction. This is supported by the P-value tests of significance associated with the meta-analysis.

Sample size

There is no agreement as to the sample size needed to demonstrate clinically important effects. In this review, most of the studies were underpowered and few formal power calculations were reported. None of the intervention groups was larger than 85 subjects per group, the median of the size of intervention groups 22.5 (min= 5, Q1=15.75, Q3=30.5, max = 84). Therefore, we must be cautious when making decisions about “no effect”. The average sample size for the smallest experimental group was 24.7 (SD=16.4, range: 5-80) for the 34 original studies. Similar concerns about sample size were raised in our initial review ([Busch 2002](#)) and it is somewhat disheartening to see that little progress has been made in the intervening period. However, mean sample size for the intervention groups in our initial review (16 studies) was 19.4 subjects; in the additional 18 studies since 2002, mean sample size increased to 39, so this must be considered a positive trend towards reaching more fully-powered studies.

Outcome measures

There has also been little progress with respect to developing any agreement around a common set of tests and measures for this population. In our initial review (16 studies), more than 60 instruments were used to evaluate outcomes ([Busch 2002](#)). In this update (19 studies) more than 100 tests and instruments were

used including eight for pain, nine for cardiovascular fitness and thirteen for physical function. The plethora of tests and measures to evaluate outcomes make it difficult to combine data via meta-analysis without inducing heterogeneity, although many of the measures have acceptable levels of reliability and validity. Nevertheless, it would improve consistency of reporting and confidence in analysis if there were more agreement around “gold standards” for assessing outcomes of interest. We thus repeat our previous call for establishing a core set of outcome measures for research into non-medical treatments for FM.

Potential biases in the review process

There are limitations inherent in the primary literature including incomplete description of the exercise protocols, inadequate sample sizes, inappropriate designs for assessing composite exercise programs, and inadequate documentation of adherence to exercise prescriptions.

In our review process, we attempted to control for biases as follows:

- we did not limit our search to English-only publications
- we assessed the reliability of our selection of relevant studies and our grading of the quality of the studies
- we contacted primary authors for clarification and additional information where indicated, although responses were not always obtained
- we examined clinical sources of heterogeneity
- our description of the results was based on a careful consideration of intervention characteristics, study population, methodologic rigour, pre-identification of levels of evidence and group discussion of evidence tables to reach consensus
- we used a multi-disciplinary team with expertise in critical appraisal, pain, clinical rheumatology, physical therapy, exercise physiology and knowledge translation
- where researchers evaluated treatment effects at multiple points, we used the data points closest to 12 weeks to standardize our comparisons.

Agreements and disagreements with other studies or reviews

Our findings are supported in the work of other reviews. [Goldenberg 2004](#) examined overall management of FM and concluded that among studies comparing exercise to wait-list or flexibility controls but not blinded trials, there is strong evidence for efficacy for the use of cardiovascular exercise as part of symptom management and moderate evidence for efficacy of strength training. The authors go on to say, “a stepwise program emphasizing education, certain medications, exercise, cognitive therapy, or all 4 should be recommended” (P 2388). Differences between

[Goldenberg 2004](#) and our review can be explained by the classification of evidence ([Goldenberg 2004](#) has classified strong evidence as positive results from a meta-analysis or consistently positive results from more than one RCT and moderate evidence as positive results from 1 RCT or consistently positive results from multiple non-RCT studies), and from the Goldenberg’s inclusion of flexibility training as a control treatment.

In the Guideline for the Management of Fibromyalgia Syndrome Pain in Adults and Children ([Burckhardt 2005](#)), the American Pain Society also recommend multifaceted management that combines pharmacologic and non-pharmacologic therapies. The latter includes cognitive-behavior therapy that includes self-management strategies, aerobic exercise and clinician-assisted treatments such as hypnosis, acupuncture, therapeutic massage and chiropractic manipulation. The American Pain Society Guidelines ‘strongly encourage’ moderately intense aerobic exercise at least two or three times a week using a slow and gradual progression to avoid exercise-induced pain exacerbation and possible discontinuation of the exercise. The American Pain Society Guidelines are consistent with findings of this review.

In their systematic review, [Mannerkorpi 2003](#) report that low intensity aerobic exercise, such as walking, can improve function and symptoms, that moderate intensity exercise can improve aerobic capacity and reduce tenderness but that high intensity exercise be undertaken with caution. They also report that strength training can improve strength without exacerbation of symptoms. These findings are consistent with the current review. The absence of information about the search strategy used by these authors prohibits further comparisons with findings of this study.

In a systematic review of mind body therapies (MBT) for FM that included interventions such as cognitive behavioral therapy, biofeedback and relaxation training, [Hadhazy 2000](#) found exercise to be superior to MBT for pain and function. Examining interventions that included MBT plus exercise versus controls, the reviewers found moderate evidence of improvement in self-efficacy and quality of life favoring the combined intervention and limited evidence for the intervention for all other outcomes.

AUTHORS’ CONCLUSIONS

Implications for practice

There is moderate quality evidence that short-term aerobic training (at the intensity recommended for increases in cardiorespiratory fitness) produces important benefits in people with FM in global outcome measures, physical function, and possibly pain and tender points. There is limited evidence that strength training improves a number of outcomes including pain, global wellbeing, physical function, tender points and depression. There is insufficient evidence regarding the effects of flexibility exercise. Adher-

ence to many of the aerobic exercise interventions described in the included studies was poor.

Implications for research

Numerous implications for further research arose from this review. They include:

- further research to elucidate a dose-response relationship, particularly for aerobic exercise given the high attrition rates and the difficulty reported with adherence to high intensity protocols
- more detail with respect to progression of exercise prescriptions in order to understand responses to training
- additional evaluations for both strength and flexibility exercise, particularly high-quality studies, are needed to enable meta-analysis of results
- longer formal follow-up periods to assess stability of responses and minimal program parameters (intensity, duration, frequency) needed to maintain gains
- assessment of adherence to frequency and intensity of exercise as an integral part of the Results section of all primary papers
- determination of the predictors of exercise adherence in this population

- better characterization of previous physical activity levels of participants in exercise trials

- the use of multiple research sites to enable adequately-sized clinical trials

- the use of factorial designs (2 x 2) for composite treatment programs including exercise, to allow assessment of the independent contribution of each component as well as any potential interactions between the two

- identification of a core set of outcome measures and related tests for researchers in this area to standardize reporting and interpretation of results

- determination of the minimum clinically important difference (MCID) and responsiveness of the core measures

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Altan 2004

Methods	2 groups. LENGTH: Phase 1 (active tx) 12wks, Follow-up (controlled) 12 wks	
Participants	FEMALE:MALE= 46:0, AGE: 31-56(43.9). INCLUSION: Dx: FMS (ACR1990), women. EXCLUSION: Rheumatoid disease, unstable hypertension, severe cardiopulmonary problems, heat intolerance, psychiatric disorder affecting compliance, abnormal blood count and chemistry, ESR, urinalysis	
Interventions	Pool exercise in heated pool (37°C) (n=24), balneotherapy without exercise (n=22)	
Outcomes	Pain, tender points, fatigue, sleep, stiffness, muscle endurance, patient-rated disability (status), HP-rated disability (status), FIQ, depression	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Bucklelew 1998

Methods	4 groups. LENGTH: Phase 1 (active tx) 6 wks, Phase 2 (maintenance) 2 yrs	
Participants	FEMALE:MALE= 108:9, AGE: 41.9(8.1) to 45.6(9.4). INCLUSION: Dx: FMS (Yunus 1981, 1982, 1984). EXCLUSION: Organic brain syndrome, psychotic disorder, unstable or uncontrolled medical conditions, major communicative disorder, RA, widespread OA, subjective pain < 4 of 10, current participation in regular aerobic exercise, biofeedback in past year	
Interventions	Biofeedback (n=25), Exercise (n=26), Biofeedback + Exercise (n=23), Education + attention control (n=27)	
Outcomes	Pain, tender points, physical function (self-report), global, self-efficacy, fatigue and sleep, psychological function	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Burckhardt 1994

Methods	3 groups. LENGTH: 12wks.	
Participants	FEMALE:MALE= 99:0, AGE: 46.5(8.3). INCLUSION: Dx: FMS (ACR 1990), understands Swedish. EXCLUSION: Abnormal lab tests (Hb, free thyroxine, ESR, ANA, RF, CK), other rheumatic disease	
Interventions	Wait List Control (n=30),Education (n=28),Education + Exercise (n=28)	
Outcomes	Pain, tender points, physical function (cardio-respiratory fitness, self-report, muscle-skeletal tests), global, self-efficacy, fatigue, sleep, psychological function	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Cedraschi 2004

Methods	2 groups. LENGTH: Phase 1 (active tx) 6 wks, Follow-up (controlled) 6 months.	
Participants	FEMALE:MALE= 152:12, AGE: 48.9(9.7) to 49.8 (9.8). INCLUSION: Dx: FMS (ACR 1990), fluency in French. EXCLUSION: Specific medical disorders requiring immediate treatment (fractures, infectious diseases), medical disorders that prevented physical activity (cardiovascular problems), medical disorders that precluded participation in swimming pool sessions (skin diseases, allergy to chlorine)	
Interventions	Multidisciplinary program (n=84), Wait List Control (n=80).	
Outcomes	Pain, tender points, HP-rated disability (status), SF-36, FIQ, quality of life	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

DaCosta 2005

Methods	2 groups. LENGTH: Phase 1 (active tx) 12 wks, Follow-up (controlled) 9 months.	
Participants	FEMALE:MALE= 79:0, AGE: 49.2(8.7) to 52.3(10.8). INCLUSION: Confirmed diagnosis of primary FMS, female. EXCLUSION: Concomitant diseases precluding participants in exercise, contraindications to exercise identified by examining physician, regular participation in moderate intensity exercise, recent	

DaCosta 2005 (Continued)

	change in medications. in previous 2/52	
Interventions	Home-Based Exercise (n=39), Treatment as Usual Control (n=40)	
Outcomes	Pain, CR (Max), FIQ.	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Genc 2002

Methods	2 groups. LENGTH: 3 wks.	
Participants	FEMALE:MALE= 32:0, AGE: 27.9(5.4) to 27.5(5.6). INCLUSION: Dx: FMS (ACR 1990), female. EXCLUSION: unknown	
Interventions	Stretch + Strength (stretching, posture, strengthening group) (n=16), Remedial Exercise (n=16)	
Outcomes	Flexibility, FIQ.	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Gowans 1999

Methods	2 groups. LENGTH: 6 wks.	
Participants	FEMALE:MALE= 32:9, AGE: 44.3(10.7) to 46.6(12.2). INCLUSION: Dx: FMS (ACR 1990), physician referral, willing to attend in daytime hours. EXCLUSION: <50% attendance	
Interventions	Exercise + Education (n=20), Wait List Control (n=21).	
Outcomes	Pain, physical function (cardio-respiratory fitness, self-report), global, self-efficacy, fatigue, sleep, psychological function	
Notes		

<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Gowans 2001

Methods	2 groups. LENGTH: 23 wks.
Participants	FEMALE:MALE= 44:6, AGE: 44.6(8.7) to 49.8(7.3). INCLUSION: Dx: FMS (ACR 1990), willing to comply with experimental protocol. EXCLUSION: Diagnosis of hypertension or symptomatic cardiac disease, other serious systemic diseases (SLE, cancer, diabetes), intended to change medications or seeking professional help for anxiety or depression during the study period, were enrolled in or intended to begin an aerobic exercise program
Interventions	Exercise (n=27), Untreated Control (n=23).
Outcomes	Tender points, CR (functional performance), muscle strength, FIQ, self-efficacy, depression, anxiety
Notes	

Risk of bias

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

Hakkinen 2001

Methods	3 groups. LENGTH: 4 wks control for all groups, 21 wks intervention phase
Participants	FEMALE:MALE= 33:0, AGE: 37(6) to 39(6). INCLUSION: Dx: FMS (ACR 1990), pre-menopausal women. EXCLUSION: Unspecified
Interventions	FMS Control (n=10), Strength Training A (FMS: n=11), Strength Training B (healthy subjects: n=12)
Outcomes	Pain, muscle strength, global, fatigue, sleep, depression.
Notes	

Risk of bias

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

Hakkinen 2002

Methods	3 groups. LENGTH: 21 wks.
Participants	FEMALE:MALE= 33:0, AGE: 37(5) to 39(6). INCLUSION: Dx: FMS (ACR 1990), pre-menopausal. EXCLUSION: None
Interventions	FMS Training (n=11), FMS Control(n=10), Healthy Training Control (n=12)
Outcomes	Musculoskeletal (strength), anthropometric measures, hormonal responses (testosterone, free test, DHEAS, IGF-I, GH)
Notes	

Risk of bias

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

Isomeri 1993

Methods	3 groups. LENGTH: 15 wks.
Participants	FEMALE:MALE= 39:6, AGE: 43.7 (range=24-55). INCLUSION: Dx: FMS (Yunus 1981, Wolfe 1985) . EXCLUSION: Unable to participate in strenuous physical training due to medical conditions or medication, other disease causing pain
Interventions	Flexibility + Amitriptyline (n=16), Aerobic Exercise (n=15), Aerobic Exercise + Amitriptyline (n=14)
Outcomes	Pain, tender points.
Notes	

Risk of bias

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

Jentoft 2001

Methods	2 groups. LENGTH: Phase 1 (active tx) 20 wks, Follow-up (controlled) 6 months. (46 wks after initiation).
Participants	FEMALE:MALE= 34:0, AGE: 39.4(8.8) to 42.9(8.6). INCLUSION: Women aged 20 to 60, Dx: FMS (ACR 1990). EXCLUSION: Inflammatory rheumatic disease, hypothyroidism, heart and lung disease, pregnancy

Jentoft 2001 (Continued)

Interventions	Pool (pool based exercise) (n=18), Land (land based exercise) (n=16)	
Outcomes	Pain, tender points, fatigue, stiffness, CR (predicted max), CR (functional performance), muscle strength, muscle endurance, patient-related disability (status), FIQ, self-efficacy, depression, anxiety	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Jones 2002

Methods	2 groups. LENGTH: 12 wks.	
Participants	FEMALE:MALE= 56:0, AGE: 46.4(8.6) to 49.2(6.3). INCLUSION: Dx: FMS (ACR 1990), female, age 20 to 60. EXCLUSION: Current or past history of CV, pulmonary, neurological, endocrine, or renal disease that would preclude exercise program, current use of medications that would affect normal physiological response to exercise, current cigarette smoking, score = 29 on Beck Depression Scale modified for FMS, current participant in a regular exercise program	
Interventions	Strength (n=28), Flexibility (n=28).	
Outcomes	Pain, tender points, fatigue, muscle strength, flexibility, FIQ, quality of life, self-efficacy, depression, anxiety	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Keel 1998

Methods	2 groups. LENGTH: Phase 1 (active tx) 15 wks, Follow-up 4 months. after post-test	
Participants	FEMALE: MALE= 24:3, AGE: 48 to 50. INCLUSION: Dx: FMS (Muller 1990), proficiency in German, written consent. EXCLUSION: Severe mental disorders (including drug addiction) requiring continuing psychiatric care	
Interventions	Self-Management Training (n=14), Relaxation Training (n=13).	

Keel 1998 (Continued)

Outcomes	Pain, fatigue, sleep.	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

King 2002

Methods	4 groups. LENGTH: Phase 1 (active tx) 12 wks, Follow-up (controlled) 3 months.	
Participants	FEMALE:MALE= 170:0, AGE: 44.9(10) to 47.4(9). INCLUSION: Dx: FMS (ACR 1990), women, age 18-65, willing to meet 3 wks x 12 wks. EXCLUSION: Conditions precluding ability to exercise (severe cardiac arrhythmia, dizziness, severe shortness of breath), inflammatory arthritis, SLE MRA	
Interventions	Exercise (n=42), Education (n=41), Exercise + Education (n=35), Control (n=34)	
Outcomes	Tender points, CR (functional performance), FIQ, self-efficacy	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Mannerkorpi 2000

Methods	2 groups. LENGTH: Exercise 24 wks. (includes 6 wks of education)	
Participants	FEMALE:MALE= 69:0, AGE: 45(8.0) to 47(11.6). INCLUSION: Dx: FMS (ACR1990). EXCLUSION: Other rheumatic diseases, other severe somatic or psychiatric disorders, chlorine allergy, plans to start other treatments during study	
Interventions	Exercise + Education (n=28), Treatment as Usual Control Group (n=29)	
Outcomes	Pain, physical function (cardio-respiratory fitness, self-report, muscle-skeletal tests), global, self-efficacy, fatigue, sleep, psychological function	
Notes		

Mannerkorpi 2000 (Continued)

<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Martin 1996

Methods	2 groups. LENGTH: 6 wks.
Participants	FEMALE:MALE= 37:1, AGE: 43.9(9.7) to 45.7(9.9). INCLUSION: Dx: FMS (ACR 1990). EXCLUSION: cardiovascular, pulmonary, neurological or renal disease that precluded participation in exercise, medication that changed physiological response to exercise
Interventions	Aerobic Exercise (n=18), Relaxation (n=20).
Outcomes	Pain, tender points, physical function (cardio-respiratory fitness, muscle-skeletal tests), global, self-efficacy
Notes	

<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

McCain 1988

Methods	2 groups. LENGTH: 20 wks.
Participants	FEMALE:MALE= mixed, details unspecified, AGE: 35.8(11.1) to 45.9(8.2). INCLUSION: Dx: FMS (Smythe 1988), successful treadmill stress test. EXCLUSION: Amytriptyline within previous 3 mo., ischemic heart disease, symptomatic cardiac arrhythmias, exercise induced asthma
Interventions	Aerobic Exercise (n=18), Flexibility (n=20).
Outcomes	Pain, tender points, physical function (cardio-respiratory fitness), global, fatigue, sleep, psychological function
Notes	

<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Mengshoel 1992

Methods	2 groups. LENGTH: 20 wks.
Participants	FEMALE:MALE= 25:0, AGE: 34 (range= 25-38) to 35.5 (range= 21-47). INCLUSION: Dx: FMS (ACR 1990). EXCLUSION: Abnormal lab tests (ESR, Hb, liver enzymes, serum creatinine, ANA, Waaler, latex, thyroxine)
Interventions	Aerobic Exercise (n=11), Physical Activity as Usual Control Group (n=14)
Outcomes	Pain, physical function (cardio-respiratory fitness, muscle-skeletal tests), fatigue, sleep, psychological function
Notes	

Risk of bias

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

Meyer 2000

Methods	3 groups. LENGTH: 24 wks.
Participants	FEMALE:MALE= 8:0, AGE: 49.5(6.3). INCLUSION: Dx: FMS (ACR 1990). EXCLUSION: Uncontrolled hypertension, history of heart or respiratory disease, orthopedic dysfunction that would prevent participation in walking program
Interventions	Low Intensity Exercise (n=8 at pretest), High Intensity Exercise (n=8 at pretest), Physical Activity as Usual Control (n=5 at pretest). (Note: Began with 21 subjects but only 8 completed, original group assignment not retained)
Outcomes	Pain, tender points, physical function (cardio-respiratory fitness, self-report), global, psychological function
Notes	

Risk of bias

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

Nichols 1994

Methods	2 groups. LENGTH: 8 wks.	
Participants	FEMALE:MALE= 17:2, AGE: 47.8(11.1) to 50.8(11.8). INCLUSION: Dx: FMS (ACR 1990). EXCLUSION: Heart, lung disease, uncontrolled hypertension, orthopedic disorder, regular physical activity in previous 6 mo	
Interventions	Aerobic Exercise (n=10), Sedentary Control (n=9).	
Outcomes	Pain, physical function (self-report), psychological function	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Norreagaard 1997

Methods	3 groups. LENGTH: 12 wks.	
Participants	FEMALE:MALE= unspecified, AGE: 44(8) to 55(10). INCLUSION: Dx: FMS (ACR 1990), age 20 to 70 yrs. EXCLUSION: Pregnancy, lactation, alcoholism, cardiovascular, lung, renal or rheumatic disease, anticoagulant medication	
Interventions	Aerobic Exercise (n=5), Mixed Exercise (n=11), Hot Packs (n=7)	
Outcomes	Pain, tender points, physical function (cardio-respiratory fitness, muscle-skeletal tests), global, fatigue, sleep, psychological function	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Ramsay 2000

Methods	2 groups. LENGTH: 12 wks.	
Participants	FEMALE:MALE= unspecified, AGE: unspecified. INCLUSION: Dx: FMS (ACR 1990), stable medication use for 1 mo. prior to entry into study (tricyclic antidepressants, analgesics, NSAIDs). EXCLUSION: Unspecified	

Ramsay 2000 (Continued)

Interventions	Single Exercise + Home Program (n=35), Exercise Class + Home Program (n=15)	
Outcomes	Pain, tender points, global, fatigue, sleep, psychological function	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Redondo 2004

Methods	2 groups. LENGTH: Phase 1 (active tx) 8 wks, Follow-up (controlled) 6 mo., 12 mo.	
Participants	FEMALE:MALE= 40:0, AGE: 52.5(8.8). INCLUSION: Women, Dx: FMS (ACR 1990). EXCLUSION: Serious concomitant disease, poor CV. fitness on initial test	
Interventions	Physical exercise (n=19), Cognitive Behavioral Therapy (n=21)	
Outcomes	Tender points, CR (Max), physical function, patient-rated change (improvement), SF-36, FIQ, self-efficacy, depression, anxiety, coping	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Richards 2002

Methods	2 groups. LENGTH: Phase 1 (active tx) 12 wks, Follow-up 1 yr from entry (evaluation at 6 & 12 mo. post-entry)	
Participants	FEMALE:MALE= 126:10, AGE: 45(38-52) to 48(38-56). INCLUSION: Female and male, ages 18-70, Dx: FMS (ACR 1990), able to give informed consent. EXCLUSION: Individuals with alternative diagnoses that could explain current symptoms, unable to attend exercise classes (too busy, lived too far away, too incapacitated, other reasons), severe pulmonary, CV, renal, neurological disease precluding involvement in aerobic exercise, inability to co-operate	
Interventions	Aerobic exercise (n=69), Relaxation (n=67).	

Richards 2002 (Continued)

Outcomes	Pain, tender points, fatigue, patient-rated change (improvement), SF-36, FIQ	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Schachter 2003

Methods	3 groups. LENGTH: 16 wks.	
Participants	FEMALE:MALE= 143:0, AGE: 41.3(8.67) to 42.5(6.69). INCLUSION: Women aged 20 to 55 yrs old from Saskatoon, Dx: FMS (ACR 1990), sedentary, family MD permission, informed consent for study, willingness to be randomly assigned. EXCLUSION: More than 2 CAD risk factors (ACSM 1995), known CV or respiratory disease, metabolic, musculoskeletal, or neurological conditions interfering with moderate intensity aerobic exercise	
Interventions	No exercise (n=36), Short Bout Exercise (n=56), Long Bout Exercise (n=51)	
Outcomes	Pain, tender points, sleep, stiffness, CR (max), other CR, self reported function, patient-rated disability (status), HP-rated disability (status), FIQ, self-efficacy, depression, anxiety	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Sencan 2004

Methods	3 groups. LENGTH: Phase 1 (active tx) 6 wks, Follow-up (controlled) 6 wks.	
Participants	FEMALE:MALE= 60:0, AGE: 32.6(9.4) to 35.5 (7.9). INCLUSION: Women, Dx: FMS (ACR 1990). EXCLUSION: Tumoral, infectious, metabolic, cardiovascular, endocrine disease, drug dependency, other pharmacological treatment, co-morbid disease	
Interventions	Aerobic exercise (n=20), Antidepressant (Paroxetine) (n=20), Placebo (n=20)	
Outcomes	Pain, tender points, sleep, depression.	

Sencan 2004 (Continued)

Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Valim 2003

Methods	2 groups. LENGTH: 20 wks.	
Participants	FEMALE:MALE= 76:0, AGE: 47(10) to 44(11). INCLUSION: Sedentary women, 18-60 yrs, Dx: FMS (ACR 1990), never previously treated, newly diagnosed. EXCLUSION: Cardiorespiratory disorders limiting exercise, neurological disorders, BMI >35, hyperthyroidism, other rheumatologic diseases	
Interventions	Aerobic exercise (n=32), Stretching exercise (n=28).	
Outcomes	Pain, tender points, CR (max), CR (submax), flexibility, SF-36, FIQ, depression, anxiety	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Valkeinen 2004

Methods	3 groups. LENGTH: 21 wks.	
Participants	FEMALE:MALE= 36:0, AGE: 59.1(3.5) to 60.2(2.5). INCLUSION: Dx: FMS (ACR 1990), age = 55 years, women. EXCLUSION: No other diseases, no injuries, no experience of regular strength training exercises, willingness to participate in study protocol	
Interventions	FMS Training (n=13), FMS Control (n=13), Healthy Control Training (n=10)	
Outcomes	Pain, tender points, fatigue, sleep, other CR, muscle strength, self-reported function, depression	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description

Valkeinen 2004 (Continued)

Allocation concealment?	Unclear	B - Unclear
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vanSanten 2002a

Methods	3 groups. LENGTH: 24 wks.
Participants	FEMALE:MALE= 129:0, AGE: 42.8(26-59) to 46.2(26-59). INCLUSION: Female, 18-60 years, living within 30 km of either rheumatology depts., Dx: FMS (ACR1990). EXCLUSION: Known co-morbidities, female with more localized myalgia, ischemic heart disorder, arrhythmias, exercise induced asthma, unsettled disability compensation, incapacitating psych. distress, pregnancy, wait list for elective surgery, vacation during trial
Interventions	Fitness (with/without compliance strategy)(n=50), Biofeedback (with/without compliance strategy) (n=50), Treatment as Usual Control (n=29)
Outcomes	Pain, tender points, fatigue, cardio-respiratory fitness, CR (max), other CR, self-reported function, SIP
Notes	

Risk of bias

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

vanSanten 2002b

Methods	2 groups. LENGTH: 20 wks.
Participants	FEMALE:MALE= 37:0, AGE: 39(20-54) to 45(25-58). INCLUSION: Dx: FMS (ACR 1990), female, 18 to 60 yrs, living within 30 km radius of Maastricht. EXCLUSION: Known cardiopulmonary or psychiatric co-morbidity, IHD, arrhythmia, EIA, unsettled disability compensation dispute, incapacitating psychological distress
Interventions	Self Selected Intensity Training (n=15), High Intensity Training (n=18)
Outcomes	Pain, tender points, CR (max), CR (submax), other CR, patient rated severity, general health status, depression, anxiety, other psychological problems
Notes	

Risk of bias

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

Verstappen 1997

Methods	2 groups. LENGTH: 6 mo.	
Participants	FEMALE:MALE= 72:0, AGE: 42.8(8.4) to 46.6(8.3). INCLUSION: Dx: FMS (Wolfe 1988), age 18-60 yrs, female. EXCLUSION: Ischemic heart disease, cardiac arrhythmias, exercise induced bronchospasm, psychiatric disorders, current involvement in health insurance procedures	
Interventions	Aerobic Exercise (n=45), Non-intervention (n=27).	
Outcomes	Physical function (cardio-respiratory fitness, muscle-skeletal tests)	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Wigers 1996

Methods	3 groups. LENGTH: Phase 1 (active tx) 14 wks, Follow-up 4.5 years	
Participants	FEMALE:MALE= 55:5, AGE: 44(10). INCLUSION: Dx: FMS (Smythe 1979 + Yunus criteria 1981) (58 of 60 met ACR 1990 criteria, evaluated retrospectively). EXCLUSION: None	
Interventions	Aerobic Exercise (n=16), Stress Management Training (n=15), Treatment as Usual Control (n=17)	
Outcomes	Pain, tender points, physical function (cardio-respiratory fitness), global, fatigue, sleep, psychological function	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Zijlstra 2005

Methods	2 groups. LENGTH: Phase 1 (active tx) 2.5 wks., Follow-up (uncontrolled) 12 mo. from baseline.	
Participants	FEMALE:MALE= 28:6, AGE: 47(24-64) to 48(22-64). INCLUSION: Dx: FMS (ACR 1990), 18 to 65 yrs, willingness to undergo in-patient treatment of some wks. EXCLUSION: Secondary FMS (pre-sume of another underlying disease that causes chronic pain), co-morbidity interfering with spa, other co-morbidity, dependency on wheelchair or help from other people, current involvement in a law proce-	

	dure concerning disability or employment, recent spa treatment for musculoskeletal disorders, difficulty understanding Dutch	
Interventions	SPA (n=58), Treatment as Usual Control (n=76).	
Outcomes	Pain, tender points, fatigue, sleep, CR (submax), patient-rated general health status, FIQ, depression	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Ahlgren 2001	Diagnosis - trapezius myalgia
Astin 2003	Did not meet exercise criteria (QiGong)
Bailey 1999	One group design
Bakker 1995	Between group analysis not done
Dawson 2003	One group before-after design
Gandhi 2000	Not randomized - 3 group design: (1)Non-exercising control(n=12), (2) hospital-based exercise group (n=10), (3) home based videotaped exercise program (n=10)
Geel 2002	Not randomized
Gowans 2002	Focuses on measurement issues of selected variables already reported in an included study; new variables did not include standard deviations
Guarino 2001	Diagnosis - Gulf War Syndrome
Han 1998	Not randomized (geographic control)
Hunt 2000	Diagnosis of FMS was not clear, even when the author was contacted to clarify the diagnostic criteria that were used
Karper 2001	Not randomized (program evaluation)

(Continued)

Kendall 2000	Did not meet exercise criteria (Body Awareness)
Kingsley 2005	Diagnosis of FMS made by physician or rheumatologist but when contacted, the authors did not verify the use of published criteria (e.g., ACR 1990 classification)
Mason 1998	Not randomized (subjects enrolled in a multimodal treatment compared to subjects who were unable to participate due to insurance reasons)
Meiworm 2000	Not randomized (subjects self selected their group)
Mobily 2001	Case study
Nielen 2000	Not randomized (cross-sec. case control study of fitness)
Offenbacher 2000	Non-experimental - Narrative review
Oncel 1994	Insufficient description of exercise (one group received "medical therapy and exercise"; no further information about the exercise intervention given)
Peters 2002	Diagnosis - Persistent unexplained symptoms
Pfeiffer 2003	One group before-after design
Piso 2001	Not randomized - Our translator reported: "The authors wrote only how they recruited nine of the patients. They wrote nothing about if and how the patients were allocated to the two groups." We were unsuccessful on several attempts to contact the authors for clarification
Rooks 2002	One-group design
Thieme 2003	Did not meet exercise criteria (passive PT with light movement in water - the active exercise was too small a component, not described or quantified sufficiently)
Tiidus 1997	One group repeated measures design
Vlaeyen1996	Insufficient description of the mode of exercise. "Each session ended with a physical exercise such as swimming or bicycling, excluding systematic physical or fitness training."
Worrel 2001	One-group design.

DATA AND ANALYSES

Comparison 1. *Aerobic Only - Moderate to High Quality by ACSM (restricted to untreated control groups)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain	4	223	Std. Mean Difference (IV, Random, 95% CI)	0.81 [0.15, 1.47]
1.1 Pain - Did Not Prescribe ACSM	1	40	Std. Mean Difference (IV, Random, 95% CI)	1.34 [0.65, 2.04]
1.2 Pain - Did Prescribe ACSM	3	183	Std. Mean Difference (IV, Random, 95% CI)	0.65 [-0.09, 1.39]
2 Global	4		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 Global - Prescribed ACSM	4	269	Std. Mean Difference (IV, Random, 95% CI)	0.49 [0.23, 0.75]
3 Physical Function	4		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 Physical Function - Prescribed ACSM	4	253	Std. Mean Difference (IV, Random, 95% CI)	0.66 [0.41, 0.92]
4 Tender points	6	349	Std. Mean Difference (IV, Random, 95% CI)	0.76 [-0.01, 1.53]
4.1 Tender Points - Did Not Prescribe ACSM	1	40	Std. Mean Difference (IV, Random, 95% CI)	3.90 [2.80, 4.99]
4.2 Tender Points - Prescribed ACSM	5	309	Std. Mean Difference (IV, Random, 95% CI)	0.23 [-0.18, 0.65]
5 Depression	5	273	Std. Mean Difference (IV, Random, 95% CI)	0.54 [0.14, 0.94]
5.1 Depression - Did Not Prescribe ACSM	1	40	Std. Mean Difference (IV, Random, 95% CI)	1.22 [0.54, 1.90]
5.2 Depression - Prescribed ACSM	4	233	Std. Mean Difference (IV, Random, 95% CI)	0.40 [0.04, 0.76]

Comparison 2. *Strength Training versus Control

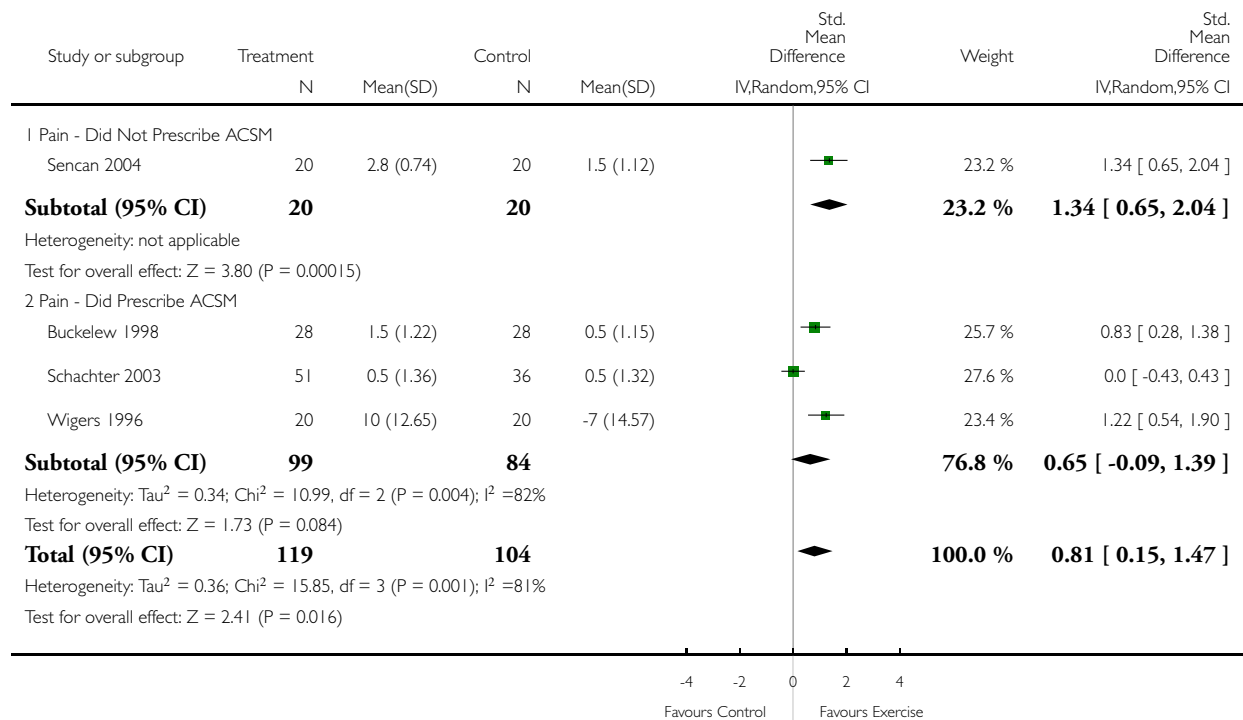
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Global Well Being	2	47	Std. Mean Difference (IV, Fixed, 95% CI)	1.43 [0.76, 2.10]
3 Physical Function	2	47	Std. Mean Difference (IV, Fixed, 95% CI)	0.52 [-0.07, 1.10]
4 Tender Points	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5 Depression	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1 *Aerobic Only - Moderate to High Quality by ACSM (restricted to untreated control groups), Outcome 1 Pain.

Review: Exercise for treating fibromyalgia syndrome

Comparison: 1 *Aerobic Only - Moderate to High Quality by ACSM (restricted to untreated control groups)

Outcome: 1 Pain

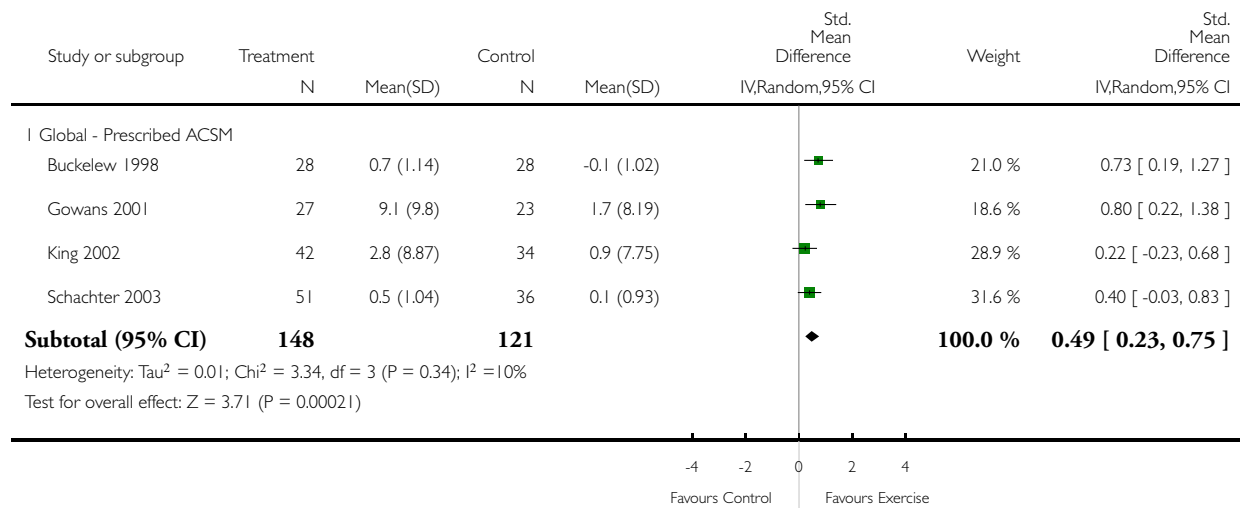


Analysis 1.2. Comparison 1 *Aerobic Only - Moderate to High Quality by ACSM (restricted to untreated control groups), Outcome 2 Global.

Review: Exercise for treating fibromyalgia syndrome

Comparison: 1 *Aerobic Only - Moderate to High Quality by ACSM (restricted to untreated control groups)

Outcome: 2 Global

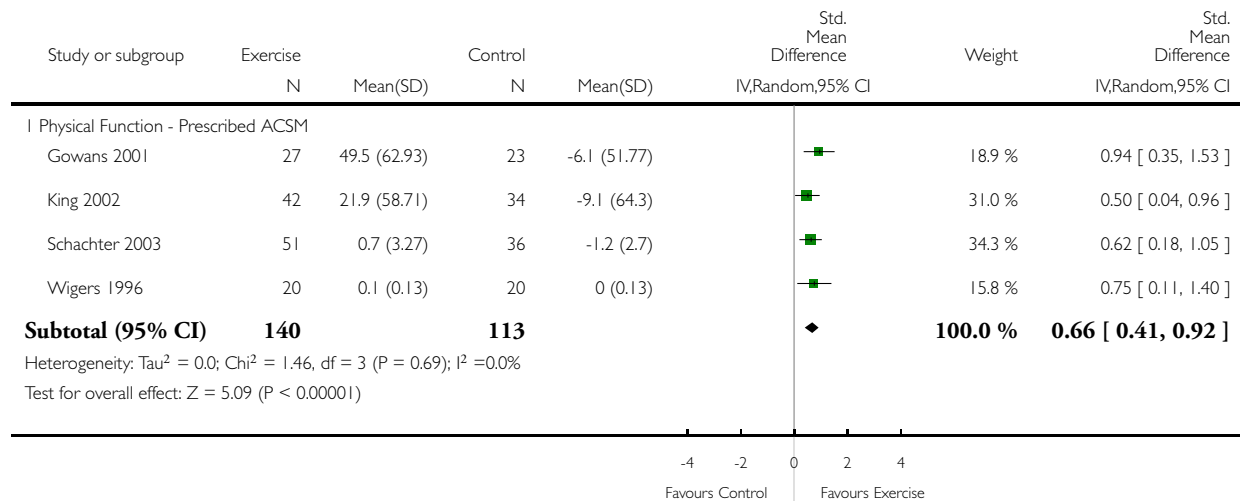


Analysis 1.3. Comparison 1 *Aerobic Only - Moderate to High Quality by ACSM (restricted to untreated control groups), Outcome 3 Physical Function.

Review: Exercise for treating fibromyalgia syndrome

Comparison: 1 *Aerobic Only - Moderate to High Quality by ACSM (restricted to untreated control groups)

Outcome: 3 Physical Function

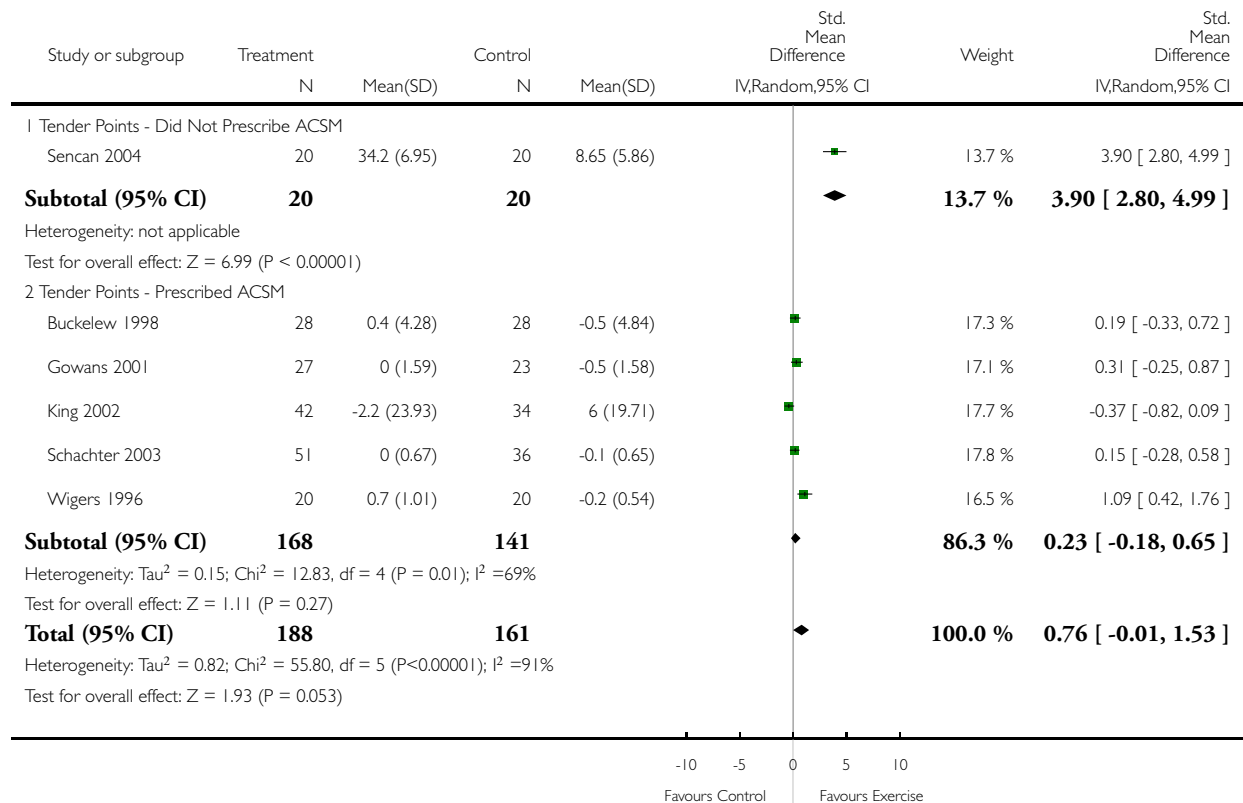


Analysis 1.4. Comparison 1 *Aerobic Only - Moderate to High Quality by ACSM (restricted to untreated control groups), Outcome 4 Tender points.

Review: Exercise for treating fibromyalgia syndrome

Comparison: 1 *Aerobic Only - Moderate to High Quality by ACSM (restricted to untreated control groups)

Outcome: 4 Tender points

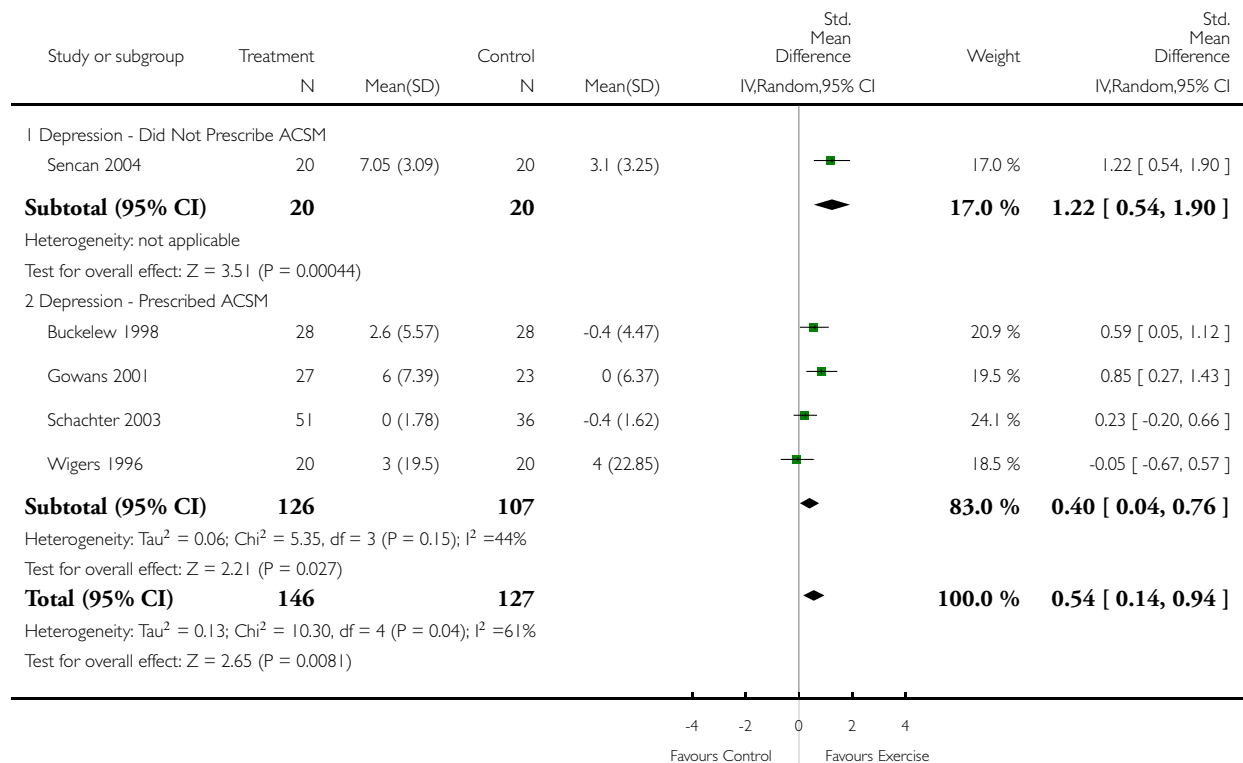


Analysis 1.5. Comparison 1 *Aerobic Only - Moderate to High Quality by ACSM (restricted to untreated control groups), Outcome 5 Depression.

Review: Exercise for treating fibromyalgia syndrome

Comparison: 1 *Aerobic Only - Moderate to High Quality by ACSM (restricted to untreated control groups)

Outcome: 5 Depression

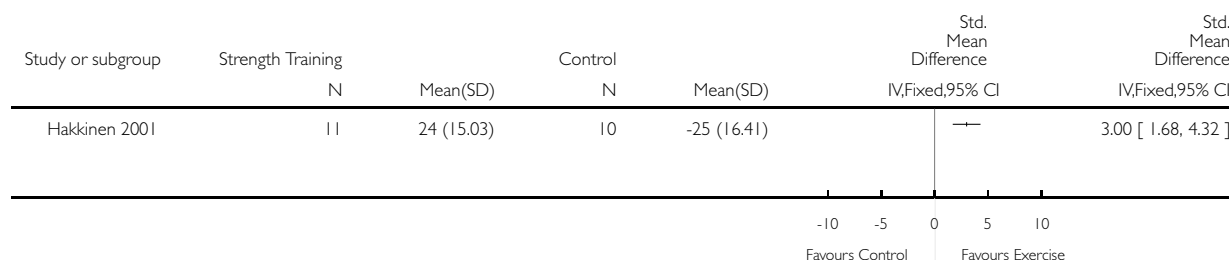


Analysis 2.1. Comparison 2 *Strength Training versus Control, Outcome 1 Pain.

Review: Exercise for treating fibromyalgia syndrome

Comparison: 2 *Strength Training versus Control

Outcome: 1 Pain

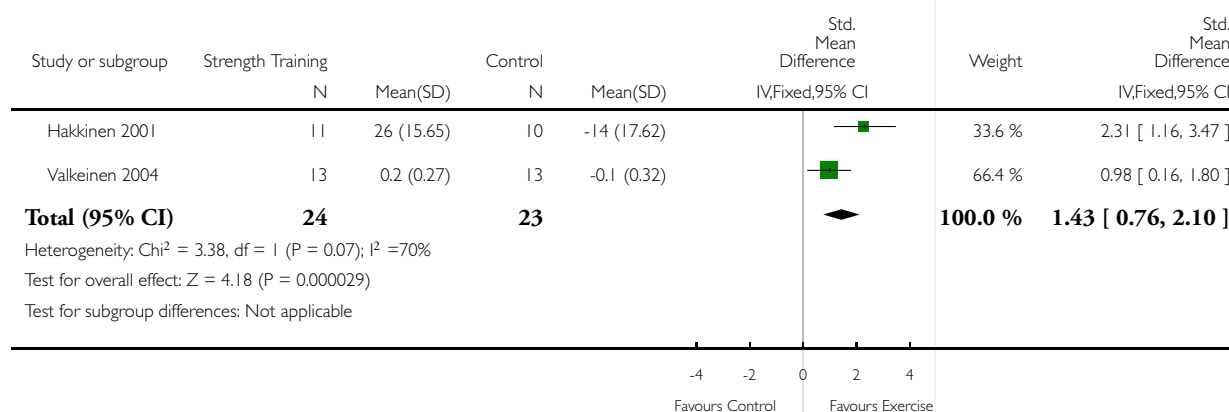


Analysis 2.2. Comparison 2 *Strength Training versus Control, Outcome 2 Global Well Being.

Review: Exercise for treating fibromyalgia syndrome

Comparison: 2 *Strength Training versus Control

Outcome: 2 Global Well Being

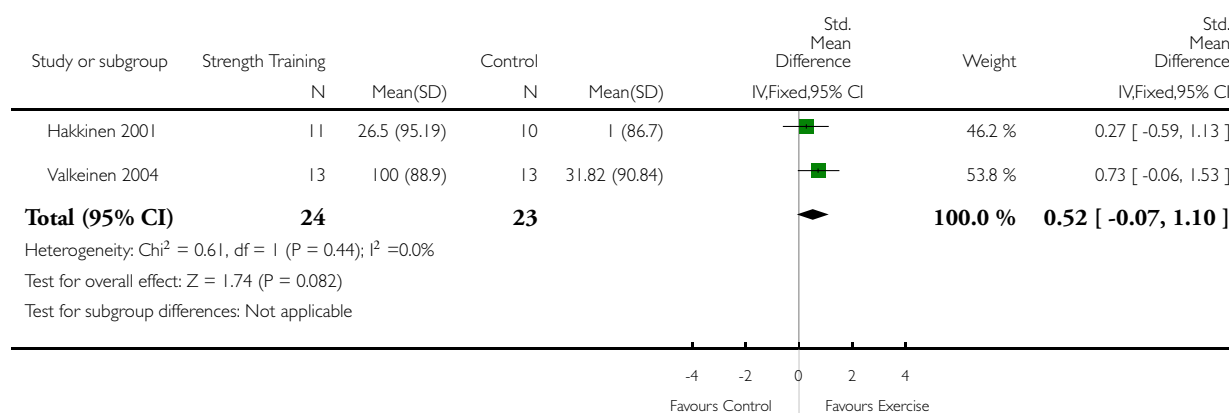


Analysis 2.3. Comparison 2 *Strength Training versus Control, Outcome 3 Physical Function.

Review: Exercise for treating fibromyalgia syndrome

Comparison: 2 *Strength Training versus Control

Outcome: 3 Physical Function

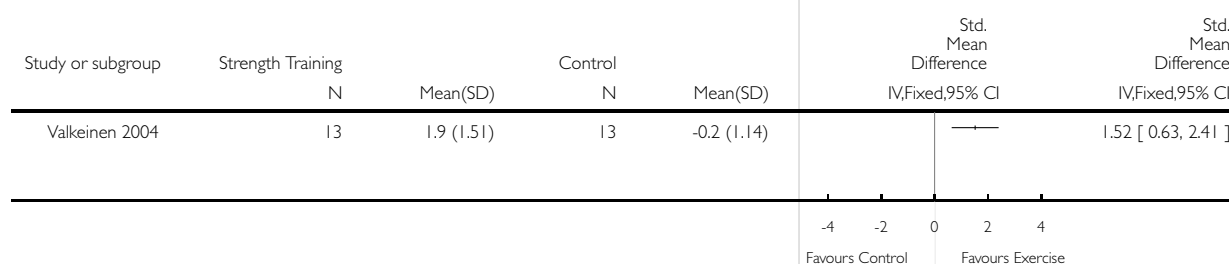


Analysis 2.4. Comparison 2 *Strength Training versus Control, Outcome 4 Tender Points.

Review: Exercise for treating fibromyalgia syndrome

Comparison: 2 *Strength Training versus Control

Outcome: 4 Tender Points

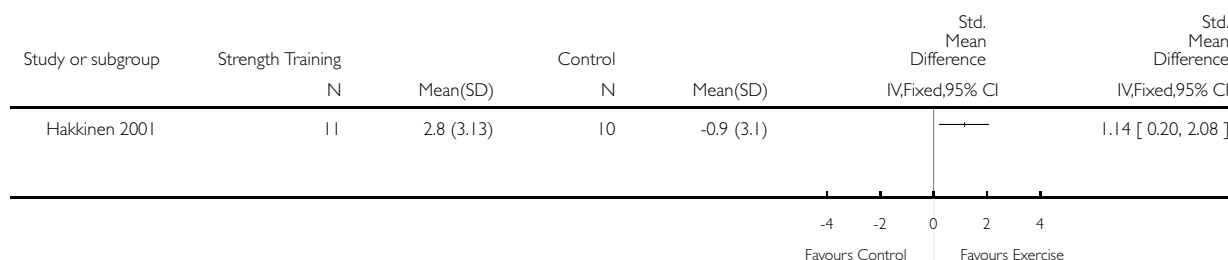


Analysis 2.5. Comparison 2 *Strength Training versus Control, Outcome 5 Depression.

Review: Exercise for treating fibromyalgia syndrome

Comparison: 2 *Strength Training versus Control

Outcome: 5 Depression



ADDITIONAL TABLES

Table 1. Search Strategy used for Busch 2002 FMS and Exercise (first edition)

Process	Particulars
Data bases used	MEDLINE (1966-12/2000), CINAHL (1982-12/2000), HealthSTAR (1990-12/2000), Sports Discus (1975 - 12/2000), EMBASE (1974 to 12/2000), the Cochrane Controlled Trials Register (Issue 4, 2000)
Adjunctive search methods	Reference lists from identified articles, meta-analyses and reviews of all types of treatment for FMS were reviewed independently by two reviewers and all promising references were scrutinized. We searched without language restriction and translated all non-English studies that were initially identified as possibly meeting the inclusion criteria
Search Strategy used for MEDLINE	Search Strategy on SilverPlatter v3.0 for Windows
	1 "Fibromyalgia"/ all subheadings 2 fibromyalgia 3 fibrositis 4 fibromyalgia or fibrositis 5 #1 or #4 6 explode "Exertion"/ all subheadings 7 "Physical-Fitness"/ all subheadings 8 explode "Physical-Therapy"/ all subheadings 9 "Exercise-Test"/ all subheadings 10 "Exercise-Tolerance"/ all subheadings 11 explode "Sports"/ all subheadings 12 "Pliability"/ all subheadings 13 #6 or #7 or #8 or #9 or #10 or #11 or #12

Table 1. Search Strategy used for Busch 2002 FMS and Exercise (first edition) (Continued)

14 exertion*
15 exercis*
16 physical 17 motion
18 fitness
19 therapy
20 therapies
21 (physical or motion) near (fitness or therapy or therapies)
22 physical
23 endurance
24 physical near endurance
25 manipulation*
26 skating
27 running
28 jogging
29 swimming
30 bicycling
31 cycling
32 walking
33 rowing
34 weight
35 training
36 muscle
37 strengthening
38 skating or running or jogging or swimming or bicycling or cycling or walking or rowing or weight training or muscle strengthening
39 #13 or #14 or #15 or #21 or #24 or #25 or #38
40 #5 and #39
41 explode "Research-Design"/ all subheadings
42 explode "Clinical-Trials"/ all subheadings
43 #41 or #42
44 #40 and #43
45 PT = "CLINICAL-TRIAL"
46 #40 and (PT = "CLINICAL-TRIAL")
47 #44 or #46

Table 2. Detailed Description of Exercise Protocol

Study	Group	Aerobic	Strength	Flexibility	Other
Altan 2004 (Information supplemented by author)	Length: 12 weeks POOL BASED EXERCISE GROUP Supervised group of mixed exercise	Pool exercise for 35 min / day, 3 days / wk Warm-up: walking - 5 min; Activity: jumping, rhythmic ROM for upper and lower extremities, rhythmic swimming - 20 min;	Squatting - repetitions not specified.	Active ROM, neck and extremity stretches in the pool, bending on land. Position of maximum muscle length was held for 5 seconds. Duration of stretching was 5	none

Table 2. Detailed Description of Exercise Protocol (Continued)

		Cool down: stretching and relaxing - 5 min; out of pool exercise (stretching and bending) - 5 min. Target intensity was 60 to 75% age-adjust HR max progressing to 70 to 75% HRmax. Pool was heated to 37°C. No home program		minutes without interruption. Repetitions not specified	
Bucklew 1998	1. Active Phase = 6 weeks a) EXERCISE GROUP: 1.5 hour exercise session 1/week + Home Program 2/week (unspecified duration) b) EXERCISE & BIOFEEDBACK GROUP: Exercise component identical to Exercise group 2. Maintenance Phase = 2 years a) EXERCISE GROUP: 1 hour exercise session 1/month + Home Program of unspecified duration and frequency b) EXERCISE & BIOFEEDBACK GROUP: Unknown	1a. Walking @ 60-70% HRmax. Home Program @ unspecified intensity and duration 1b. Walking @ 60-70% HRmax. Home Program @ unspecified intensity and duration 2a. unspecified 2b. unspecified 1b. unspecified 2a. unspecified 2b. unspecified	1a. unspecified 1b. unspecified 2a. unspecified 2b. unspecified	1a. Active Range of Motion - details unspecified 1b. Active Range of Motion - details unspecified 2a. unspecified 2b. unspecified	1a. Posture + body mechanics instruction 1b. Posture + body mechanics instruction 2a. none 2b. none
Burckhardt 1994	Length: 12 weeks EXERCISE & EDUCATION 1 hr, 1/wk exercise x 6 weeks followed by Home Program x 6 weeks	Walking, swimming or cycling. Details unspecified. Home Program unspecified	none	Range of Motion, stretching	Counselling on Home Program of aerobic exercise, 2 pool sessions over 6 weeks

Table 2. Detailed Description of Exercise Protocol (Continued)

Cedraschi 2004	Length: 6 weeks MULTIDISCIPLINARY PROGRAM 10 sessions of 45 min. duration	Supervised group exercise aimed at breaking inactivity patterns and learning to apply relaxation techniques - 8 x 45 min pool sessions (34 degrees C pool) - 2 x 45 min low impact land based sessions Aerobic exercise information not given - participants were instructed to find their own pace	Strengthening exercise information not specified	Flexibility exercise information not specified	none
DaCosta 2005	Length: 12 weeks HOME-BASED AEROBIC TRAINING	Individually prescribed mode, intensity, duration, and frequency using ACSM 1998 recommendations based on baseline cardio-respiratory fitness, severity of FMS, access to equipment, time constraints and activity preferences/enjoyment. Duration was 60 to 120 min/wk. Frequency not specified. Intensity began at 60 - 70% HRmax progressing to 75 - 85% HRmax aided by use of heart rate monitor and exercise logs which were collected weekly. Participant initiation and guidance was provided by an exercise physi-	Strengthening confined to warm-up/cool down individualized to participant needs	Stretching confined to warm-up/cool down individualized to participant needs	none

Table 2. Detailed Description of Exercise Protocol (Continued)

		ologist via 4 visits (at 0,1,3,9 wk)			
Genc 2002	Length: 3weeks 1. STRETCHING & STRENGTHENING 2. REMEDIAL EXERCISE	1. none 2. unknown	1. Strengthening for the cervical, thoracic and lumbar spine, 3x / wk. for 3 weeks. The structure, supervision, or details of the program (methods, equipment, reps, sets, and progression) are unknown. 2. Unknown - the term "remedial exercise" implies that an individual program was generated for each participant. Some individuals may have been prescribed strengthening exercise	1. Stretching exercise for the cervical, thoracic and lumbar spine, 3x /wk. Reps, sets, holds, and progression are unknown. 2. Post-isometric relaxation for upper trapezius, supraspinatus, and levator scapulii. It is assumed that this was administered by a physical therapist. Frequency - 3x / wk. for 3 weeks. Reps, sets, holds, and progression are unknown Mobilization - active/self mobilization for cervical, thoracic and lumbar regions. The structure, supervision, or details of this part of the program are unknown	1. none 2. none
Gowans 1999	Length: 6 weeks EXERCISE & EDUCATION 30 min. exercise, 2x / week	Warm-up: 10 min. Pool exercise: 20 min. walk/jog/side step/arm exercise @ 60-75% HRmax. Cool-down: 10 min	none	Warm-up, Cool-down only	none
Gowans 2001	Length: 23 weeks EXERCISE GROUP 30 min. 3/wk.	Supervised group pool and land exercise (Warm-up: 5 min., Aerobic exercise: 20 min., Cool-down: 5 min.) @ 60 - 75% HRmax. Progression: Wk 1: gen-	none	none	none

Table 2. Detailed Description of Exercise Protocol (Continued)

		tle arm and leg exercise in the pool, Wk 6: running in pool, Wk 7: slow continuous walking on land with arm mvt. 2x/wk + pool 1x/wk, Wk 23: intermittent jogging in gym 2x/wk + pool 1x/wk)			
Hakkinen 2001 and 2002	Length: 21 weeks EXERCISE GROUP 2 / wk	Warm-up, cool down	Muscle Groups: Hip extensors, abductors, and adductors; Knee extensors and flexors; Trunk and upper extremity flexors and extensors. Training program: moderate to heavy progressive resistance using David 200 dynamometer (Wk 1-3: 15-20 reps @ 40-60% x1RM, Wk 4-7:10-12 reps @ 60-70% 1RM, Wk 8-14: 8-12 reps @ 60-80%1RM, Wk 13-20: 5-10 reps @70-80% 1RM). Emphasis of hip and knee extensors plus a selection of four or five of eight additional exercises during each session. 20% of total leg exercises were performed according to the principle of explosive strength training (low resistance, high repetitions with emphasis on speed)	Warm-up, cool down	none

Table 2. Detailed Description of Exercise Protocol (Continued)

Isomeri, 1993	Length: 15 weeks 1. STRETCHING + MEDICATION 3 weeks in hospital, 12 weeks Home Program 2. EXERCISE GROUP same 3. EXERCISE & MEDICATION same	1. none 2. progressive physical fitness training, unspecified 3. progressive physical fitness training, unspecified	1. none 2. progressive physical fitness training, unspecified 3. progressive physical fitness training, unspecified	1. light muscle stretching, unspecified 2. unknown 3. unknown	1. none 2. none 3. none
Jentoft 2001	Length: 20 weeks Both pool-based (PE) and land-based (LE) exercise groups were given a 'standardized' exercise program based on the Norwegian Fitness Model (reference in Norwegian language given) with aim to improve CV capacity with minimal risk of injury. This program was used in its original form for the LE group and was modified for the PE group due to restrictions imposed by the water. Pool temp was 34 degrees C. LE group was in gym with wooden floor. 60 min sessions, 2x /wk for both LE and PE groups	For both groups, in at least 40-50% of the 60-minute session, the training intensity was kept within 60-80% HRmax. for the age of each patient. HR was monitored at least twice per session. The 1 hour session consisted of body awareness training, ergonomics, and warm-up (9 min), aerobic dance (22 min), cool down, stretching (9 min), strength training (15 min), and relaxation (5 min)	Dynamic muscle work for 15 min. included in each session - specifics not given in the article. Modeled on the Norwegian Aerobic Fitness Model which includes: strength training for thigh, back, abdominals including the deep muscle stabilizers 3-4 sets of 8-12 reps - no external loading, intensity adjusted by lever arm of the extremities (Intensity sufficient to increase strength and induce hypertrophy)	Specifics not given in the article.	none
Jones 2002	Length: 12 weeks 1. STRENGTH SUPERVISED GROUP 2. FLEXIBILITY SUPERVISED GROUP 1 hour, 2 / week	1 and 2: Warm Up	Muscle Groups: gastrocnemius, tibialis anterior, quadriceps, hamstrings, gluteus, abdominals, erector spinae, pectorals, latissimus	1. Warm up and Cool down. 2. Muscle Groups: gastrocnemius, tibialis anterior, quadriceps, hamstrings, gluteus, abdom-	1. none 2. none

Table 2. Detailed Description of Exercise Protocol (Continued)

			dorsi and rhomboids, deltoids, biceps, triceps Equipment: 1 to 3 lb weights &/or surgical tubing Concentric/eccentric contractions with minimized work during eccentric phase Intensity and progression directed by participant. Single set throughout, Repetitions progressed from 4-5 to 12. Participants encouraged to decrease activity during FMS flares. 1 hour program including 5 min. warm-up, 45 min. strengthening, 10 min. cool down	inals, erector spinae, pectorals, latissimus dorsi, rhomboids, deltoids, biceps, triceps Static stretch, participant controlled intensity of stretches 10 min WU, 40 min stretching, 10 min CD of guided imagery and relaxation	
Keel 1998	Length: 15 weeks EXERCISE: 20-30 min. 1/week + Home Program	Intensity, duration, mode unspecified	none	unspecified	none
King 2002	Length: 12 weeks 1. EXERCISE ONLY GROUP 2. EXERCISE AND EDUCATION GROUP Progressed from 10-40 min. over program 3 / wk	Supervised group walking, aquacize, or low impact aerobics @ 60 - 75% HRmax monitored using Polar Accurex HRM. Progression: duration began with 10 - 15 min progressed to an average of 20 to 40 minutes	1. none 2. none	Warm-up, cool down	1. none 2. none
Mannerkorpi 2000	Length: 6 months EXERCISE & EDUCATION 1x / week	see "Other" column	see "Other" column	see "Other" column	35 min. pool exercise for endurance, flexibility, coordination, relaxation. Not intended as training. Intensity and reps self selected, be-

Table 2. Detailed Description of Exercise Protocol (Continued)

					low pain and fatigue threshold
Martin 1996	Length: 6 weeks EXERCISE GROUP 3 / week	20 min. walking at 60-80% HRmax	20 min. strengthening for UE, LE, trunk (reps sets, progression unspecified)	20 min. flexibility unspecified	none
McCain 1988	Length: 20 weeks 1. AEROBIC: 3 / week 2. FLEXIBILITY: 3 / week	1. 50 min. 3/wk cycle ergometry at HR >150 bpm for increasing lengths of time, 10 min. Warm-up 2. none	1. none 2. none	1. none 2. 60 min., 3/wk, "flexibility maneuvers" (unspecified) @ HR<115 bpm	1. none 2. none
Mengshoel 1992	Length: 20 weeks EXERCISE GROUP 2 / week	60 min. aerobic dance for LE with UE exercise performed "at intervals between periods of rest", HR 120-150 bpm	none	none	none
Meyer 2000	Length: 24 weeks 1. LOW INTENSITY WALKING 3 /week 2. HIGH INTENSITY WALKING 3 /week	1. Week 1= 25% HRR; Week 2-6 increased by 5% / wk; Week 7-9= 50% HRR; Week 10-24 = 60% HRR Duration: progress from 12 to 30 min by week 20. 2. Week 1= 40% HRR; Week 2-4 increased by 10%/wk; Week 5= 75% HRR; Week 6-9 = 80% HRR; Week 10-24= 85% HRR. Duration: progress from 12 to 30 min by week 20.	none	none	none
Nichols & Glenn 1994	Length: 8 weeks EXERCISE GROUP 3 / week	20 min. walking at 60-70% HRmax + Warm-up and Cool-down	none	none	none

Table 2. Detailed Description of Exercise Protocol (Continued)

Norregaard 1997	Length: 12 weeks 1. AEROBIC GROUP 3 / week 2. EXERCISE GROUP 2 / week	1. 40 min. aerobic dance target 40-50% VO2max 2. none	1. none 2. none	1. none 2. stretching included in the 40 min. program, details unspecified	1. none 2. 40 min. body awareness, balance, motor control, stretching, unspecified, 10 min. Warm-up
Ramsay 2000	Length: 12 weeks 1. SINGLE SUPERVISED EXERCISE SESSION 1 session plus home program of unknown frequency 2. MULTIPLE SUPERVISED EXERCISE SESSION 1/ week plus Home Program of unknown frequency.	1. One-1 hr individual session with PT for demonstration of aerobic program + written instructions on how to progress the program. Home Program. Activity unspecified. 2. 1 hr graded circuit aerobic exercise (step-ups, sit to stand, skipping, jogging on the spot, alternate side bends, circling arms with increasing weights) plus warm-up. Program individualized for each subject by a PT. Intensity not specified. Progression unspecified.	1. none 2. none	1. unspecified 2. unspecified	1. none 2. none
Redondo 2004 (Information supplemented by author)	Length: 8 weeks EXERCISE GROUP 45 min. , 5 /week as follows: Cardiovascular fitness - 2/wk Exercises in warm water pool - 1/wk Flexibility & Endurance exercises - 2/wk	Included warm-up Cycle ergometer. Progression: Steeply increasing difficulty of exercise. Target intensity: HRmax 50 to 80%	Included warm up. Dynamic concentric and eccentric exercises with free weights for all major groups of the upper limbs. Specific exercise for abdominal and paraspinal muscles. Progression: graded and individualized for all subjects, beginning with 30 minutes and	Specific static exercise for upper and lower extremities and all 3 segments of the vertebral column. Duration of holds not specified	none

Table 2. Detailed Description of Exercise Protocol (Continued)

			progressing to 45 minutes. Reps and intensity were individualized and took into account perceived fatigue and a target intensity between HRmax of 50 to 80%		
Richards 2002	<p>Phase 1: Active Treatment</p> <p>Length: 12 weeks</p> <p>a) AEROBIC EXERCISE</p> <p>1 hour, 2 /wk</p> <p>b) RELAXATION/FLEXIBILITY</p> <p>1 hour, 2 /wk</p> <p>Phase 2: Follow up</p> <p>Length: 40 weeks</p> <p>a) AEROBIC EXERCISE</p> <p>b) RELAXATION/FLEXIBILITY</p>	<p>1.a) Individualized group, graded aerobic exercise, mostly treadmill walking or cycle ergometry. Usually started with two bouts of 6 min/class, progressed to two bouts of 25 min by 12 weeks at an intensity that made them perspire slightly while still being able to talk in complete sentences.</p> <p>1.b) none</p> <p>2. No organized exercise program of any type for either group</p>	<p>1. none</p> <p>2. none</p>	<p>1.a) none</p> <p>1.b) Upper and lower limb stretches, and relaxation based on regimen of Ost.</p> <p>2. none</p>	none
Schachter 2003	<p>Length: 16 weeks</p> <p>1. SHORT BOUT EXERCISE GROUP</p> <p>2. LONG BOUT EXERCISE GROUP</p> <p>Both groups did an unsupervised home-based program with exercise (to music), instruction video and booklet</p> <p>Exercise mode was "low-impact aerobics" for lower extremities.</p> <p>Intensity was mod-</p>	<p>1. 2 bouts of exercise per day, progressing duration from 5 min to 15 min; frequency from 3 to 3-5 d/wk; intensity progressing from 40-50% to 65-75% HRR, all by week 9 of 16 wk program</p> <p>2. One bout of exercise per day, progressing duration from 10 min to 30 min; frequency from 3 to 3-5 d/wk; intensity from</p>	none	Stretching exercises as part of 5 min warm-up and cool down.	none

Table 2. Detailed Description of Exercise Protocol (Continued)

	ulated through changes in music tempo, participant adjustment of vigour, self-monitored target heart rate and rating of perceived exertion	40-50% to 65-75% HRR, all by week 9 of 16 week program			
Sencan 2004	Phase 1: Active Treatment Length: 6 weeks EXERCISE GROUP 40 min., 3 /wk Phase 2: Follow-up Length: 6 months EXERCISE GROUP 3 / wk	1. Cycle ergometry 30 min @ unspecified intensity + 5 min WU, 5 min CD 2. Unsupervised Home Program (cycle ergometry 30 min @ unspecified intensity + 5 min WU, 5 min CD)	1. none 2. none	1. none 2. none	1. none 2. none
Valim 2003	Length: 20 weeks 1. AEROBIC EXERCISE GROUP 2. STRETCHING EXERCISE GROUP	1. 3x /week supervised group sessions of 45 min duration. Walking speed was determined as the speed eliciting the HR at the anaerobic threshold detected during a maximal treadmill test. 2. none	1. none 2. none	1. none 2. 3x /week supervised group sessions of 45 min duration. 2 sets of 17 static stretches for cervical and thoracic spine, upper and lower extremities with holds of no more than 30s. Exercises chosen to provide flexibility without increasing HR	1. none 2. none
Valkeinin 2004	Length: 21 weeks 1. FMS STRENGTH GROUP 2 /week individual supervised training sessions 2. HEALTHY STRENGTH CONTROL GROUP	1. none 2. none	Muscle groups/exercises: leg extensors (2 exercises), other main muscle groups of the body (5-6 exercises). Program: Weeks 1-4: 3 sets of 15-20 reps at 40-60% of 1RM; Weeks 5-11: 4 sets of 8-12 reps	1. none 2. none	1. none 2. none

Table 2. Detailed Description of Exercise Protocol (Continued)

	2 /week individual supervised training sessions identical to above		at 60-70% of 1RM; Weeks 12-21: 3 to 5 sets of 5-10 reps with 70-80% of 1 RM. 20% of leg extensor training was performed as explosive strength training. 2 sets of 8-12 reps at 40-50% 1RM performed as fast as possible		
vanSanten 2002a	Length: 20 weeks 1. LOW INTENSITY TRAINING GROUP 2. HIGH INTENSITY TRAINING GROUP	1. 2x/wk 60 min/session (encouraged to do a 3rd unsupervised 60 min session and to use sauna and/or swimming pool after all sessions). “Intensive aerobic exercises” alternated with general flexibility and balance exercises for 30 min in each session, intensity left up to each subject 2. 3x/wk 60 min/session 45 min of cycle ergometer exercise to reach and maintain 70% of max HR reached on baseline GXT	Isometric muscle strengthening (10 min) after aerobic work, before cool down	1. Stretching exercises as part of warm-up and cool down, general stretches alternated with intensive aerobic exercise in main part of program 2. Lower extremity stretching as part of warm-up (total warm-up time 10-15 min)	1. none 2. none
vanSanten 2002b	Length: 24 weeks FITNESS SUPERVISED GROUP EXERCISE 60 min, 2 /wk, led by a professional fitness instructor. Swimming/sauna encouraged after each session but not tracked.	60 min. class including 30 min. aerobics alternated with 5 min of general flexibility and balance, 10 min isometric exercise, WU (10 min) and CD (10 min). Intensity participant selected; (no more than mod-	10 min isometric exercise after aerobics for biceps, abdominals, hamstrings, hip abductors, adductors, quads	WU of postural stretching, General flexibility included in aerobic program. CD included stretching	none

Table 2. Detailed Description of Exercise Protocol (Continued)

	1 independent session/wk encouraged but not performed.	erate intensity performed) No progression achieved. WU = postural stretching CD=stretching, aerobic and relaxation exercise			
Verstappen 1997	Length: 6 months AEROBIC GROUP 2 /wk + Home Program 1-2 /wk 10 min Warm-up, 30 min exercise, 10 min Cool-down	Treadmill or cycle ergometry, duration unspecified, intensity subject controlled Home Program unspecified	Strengthening (UE, LE, abdomen) unspecified Home Program unspecified	Flexibility unspecified Home Program unspecified	Coordination unspecified Home Program unspecified
Wigers 1996	Length: 14 weeks EXERCISE GROUP 3 /wk	45 min. "whole body aerobic exercise" including 18-20 min. @ 60-70% HRmax	none	none	none
Zijlstra 2005	Phase 1: Active Treatment Length: 2.5 weeks a) SPA GROUP 7 group supervised group exercise sessions over 15 days b) HOME (non organized, individual) home program Phase 2: Follow-up 1 year from baseline	1. 60 min sessions of warm-up, light stretching and low-impact aerobic activities (treadmill walking, swimming, cycling) in which subjects were encouraged to reach 70% of their predicted maximal HR. Subjects were encouraged to do a 20-30 min swim each morning, and to do light walking or recreational swimming on mornings or afternoons with no formally scheduled treatment. 2. No organized exercise program of any type for either group	1. none 2. none	1. Light stretching as part of the seven 1-hour exercise sessions over 15 days 2. none	1. none 2. none

Table 3. van Tulder Methodological Analysis Item Rating and Total Scores

Study	VT Internal Validity	VT Total Score	Jadad Description	Jadad Total Score
	Items A, B, C, D, E, F, G, H, I, J, K	Total Score	Randomization, Blinding, Drop-out	Total Score
Altan, 2004	+ + + - - - + + -	6	2, 0, 1	2
Buckelew, 1998	- - + - - + + + + -	6	1, 0, 1	2
Burckhardt, 1994	- - + - - - + + + -	5	1, 0, 1	2
Cedraschi, 2004	+ + + - - + + - - + + +	8	2, 0, 1	3
DaCosta, 2005	+ + - - - + - + + + +	7	2, 0, 1	3
Genc, 2002	- - + - - - - + + +	4	1, 0, 1	2
Gowans, 1999	- - + - - - - + + -	3	1, 0, 1	2
Gowans, 2001	- - + - - + - - + + +	5	1, 0, 1	2
Hakkinen, 2001	- - + - - - - + + +	4	1, 0, 1	2
Isomeri, 1993	- - + - - - - + + -	3	1, 0, 1	2
Jentoft, 2001	+ - - - - + - + + + -	5	2, 0, 1	3
Jones, 2002	+ - - + - - + - - + -	5	2, 0, 0	2
Keel, 1998	- + + - - + - N/A + + -	6	0, 0, 1	1
King, 2002	+ + + - - + - - - + +	7	2, 0, 1	3
Mannerkorpi, 2000	- - + - - + + - - + -	5	0, 0, 1	1
Martin, 1996	+ - - + - - - + - + +	6	2, 0, 1	3
McCain, 1988	- - - - + + + + + -	6	1, 0, 1	2
Mengshoel, 1992	- - + - - - - + - + -	3	1, 0, 1	2
Meyer, 2000	- - - - - - - + -	1	1, 0, 1	2
Nichols, 1994	- - - - + - - - - + -	2	1, 0, 1	2
Norregaard, 1997	+ - - - + - - + - + -	4	2, 0, 1	3
Ramsay, 2000	- - - - - - - + + +	3	1, 0, 1	2

Table 3. van Tulder Methodological Analysis Item Rating and Total Scores (Continued)

Redondo, 2004	+ - - - - - + - + +	5	2, 0, 1	3
Richards, 2002	+ + + + - - - + + + +	8	2, 0, 0	2
Schachter, 2003	+ + + - + + - - - + +	7	2, 0, 1	3
Sencan, 2004	- - + - + - + - + + +	6	1, 0, 1	2
Valim, 2003	+ - - - - - + - + -	4	1, 0, 1	2
Valkeinan, 2004	+ - - - - - + - + +	4	2, 0, 1	3
vanSanten, 2002a	+ + + - - - + + + + +	7	1, 0, 1	2
vanSanten, 2002b	+ + + - - - + + + + +	8	1, 0, 1	2
Verstappen, 1997	- - + - - - + + + -	4	1, 0, 1	2
Wigers, 1996	+ - + + + + + + + +	9	2, 0, 1	3
Zijlstra, 2005	+ + + - - - + - - - -	4	2, 0, 0	2
Key to van Tulder (VT) internal validity items: (- = did not meet the criterion, + = met the criterion, N/A = not applicable)				
A) Was the method of randomization adequate?				
B) Was the treatment allocation concealed?				
C) Were the groups similar at baseline regarding the most important prognostic indicators?				
D) Was the patient blinded to the intervention?				
E) Was the care provided blinded to the intervention?				

Table 3. van Tulder Methodological Analysis Item Rating and Total Scores (Continued)

F) Was the outcome assessor blinded to the intervention?				
G) Were co-intervention avoided or similar?				
H) Was the compliance acceptable in all groups?				
I) Was the drop-out rate described and acceptable?				
J) Was the timing of the outcome assessment in all groups similar?				
K) Did the analysis include an intention-to-treat analysis?				

Table 4. Studies including Aerobic Interventions: Quality by ACSM Criteria

	Low Quality (VT<5)	Mod to High Quality
Met American College of Sports Medicine Guidelines	Gowans 1999	Altan 2004
	Mengshoel 1992	Buckelew 1998
	Meyer 2000	DaCosta 2005
	Nichols 1994	Gowans 2001
	Valim 2003	Jentoft 2001
		King 2002
		Martin 1996
		McCain 1988
		Redondo 2004
		Schachter 2003
		Van Santen 2002b

Table 4. Studies including Aerobic Interventions: Quality by ACSM Criteria (Continued)

		Wigers 1996
Did not meet American College of Sports Medicine Guidelines	Burckhardt 1998	Cedraschi 2004
	Genc 2002	Keel 1998
	Isomeri 1993	Mannerkorpi 2002
	Norregaard 1997	Richards 2002
	Ramsey 2000	Sencan 2004
	Verstappen 1997	VanSanten 2002a
	Zijlstra 2005	

Table 5. Short-term effects (SMD, 95% CI): exercise-only interventions not meta-analyzed

Intervention 1 (n1)	Intervention 2 (n2)	Study	van Tulder Score	Global Well-being	Pain	Tender Points	Physical Function	Depression
Aerobic (26)	Biofeedback only (25)	Buckelew 1998	6	-0.26 (-0.79 0.27)	---	0.06 (-0.46 0.59)	---	0.03 (-0.49 0.56)
Aerobic (18)	Flexibility (20)	McCain 1988	6	---	0.53 (-0.12, 1.18)	0.78 (0.12, 1.90)	1.12 (0.45, 1.79)	---
Aerobic (18)	Flexibility (20)	McCain 1988	6	---	0.53 (-0.12, 1.18)	0.78 (0.12, 1.90)	1.12 (0.45, 1.79)	---
Aerobic, supervised (35)	Aerobic, unsupervised (15)	Ramsay 2000	3	0.1 (-0.35, 0.56)	0.15 (-0.31, 0.60)	0.42 (-0.04, 0.89)	---	---
Aerobic (69)	Relaxation (67)	Richards 2002	8	0.31 (-0.03, 0.65)	0.00 (-0.34, 0.34)	0.27 (-0.07, 0.61)	---	---
Aerobic, long bout (107)	Aerobic, short bout (36)	Schachter 2003	7	0.28 (-0.10, 0.66)	0.42 (-0.01, 0.85)	0.14 (-0.24, 0.52)	0.12 (-0.26, 0.50)	0.00 (-0.38, 0.38)
Strength (28)	Flexibility (28)	Jones 2002	5	0.55 (0.02, 1.09)	0.66 (0.12, 1.20)	0.25 (-0.28, 0.76)	-0.34 ^c (-0.87, 0.18)	0.41 (-0.21, 0.94)

Table 5. Short-term effects (SMD, 95% CI): exercise-only interventions not meta-analyzed (Continued)

Strength (28)	Flexibility (28)	Jones 2002	5	---	---	---	-0.53d (-1.06, 0.00)	---
Mixed exercise (24)	Balneotherapy (22)	Altan 2004	6	0.16 (-0.42, 0.74)	0.56 (-0.03, 1.15)	0.20 (-0.38, 0.78)	-0.72 (-1.32, -0.12)	0.88 (0.27, 1.49)
Mixed Exercise (Home-based) (39)	Un-treated Control (40)	DaCosta 2005	8	0.39 (-0.05, 0.84)	---	---	---	0.25 (-0.20, 0.69)
Mixed exercise, water (18)	Mixed exercise, land (16)	Jentoft 2001	5	0.93 (0.22, 1.64)	0.41 (-0.27, 1.09)	---	0.4 (-0.28, 1.09)	0.54 (-0.15, 1.23)
Mixed exercise (18)	Relaxation (20)	Martin 1996	6	0.53 (-0.12, 1.18)	---	1.01 (0.33, 1.69)	5.79 (4.28, 7.31)	---
Mixed exercise (19)	Cognitive behaviour training (21)	Redondo 2004	5	0.4 (-0.22, 1.03)	-0.06 (-0.68, 0.56)	0.46 (-0.17, 1.09)	0.42 (-0.20, 1.05)	-0.49 (-1.12, 0.14)
Mixed exercise (50)	Untreated control (79)	Van Santen 2002a	7	-0.20 (-0.64, 0.23)	0.36 (-0.08, 0.80)	-0.06 (-0.49, 0.38)	0.15 (-0.29, 0.58)	---
Mixed exercise, high intensity (58)	Mixed exercise, self-selected intensity (85)	Van Santen 2002b	8	-0.70 (-1.45, 0.05)	0.45 (-0.28, 1.19)	-0.18 (-0.90, 0.55)	0.39 (-0.34, 1.12)	-0.22 (-0.95, 0.50)
<p>Note: a. All positive values denote greater improvement in Intervention 1 versus Intervention 2. Therefore, a positive value for pain intensity would mean pain intensity has decreased with intervention</p>								

Table 5. Short-term effects (SMD, 95% CI): exercise-only interventions not meta-analyzed (Continued)

1. b. Van Tulder Score is based on the 11 internal validity items described in van Tulder et al. 2003								
c. Values provided were measured for strength.								
d. Values provided were measured for flexibility.								
Key: SMD = Standardized Mean Difference (small change = .2, moderate change = .5, large change = .8). Data for comparison at 12 weeks or as close to 12 weeks as possible was used to calculate SMD								
Formula: SMD= (Mean change in Intervention 1 - Mean changed in Inter-								

Table 5. Short-term effects (SMD, 95% CI): exercise-only interventions not meta-analyzed (Continued)

vention 2)/ (Pooled SD of change)								
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Table 6. Short-term effects (SMD, 95%CI): composite interventions, not meta-analyzed

Interven- tion 1 (n1)	Interven- tion 2 (n2)	Study	van Tulder Score	Global Well-being	Pain	Tender Points	Physical Function	Depression
Aerobic + Biofeedback (23)	Control (27)	Buckelew 1998	6	0.58 (0.25, 0.90)	0.14 (-0.35, 0.63)	0.64 (0.30, 0.98)	---	0.32 (0.00, 0.63)
Aerobic + Biofeedback (23)	Aerobic- only (27)	Buckelew 1998	6	0 (-0.53, 0. 53)	-0.5 (-1.05, 0.04)	0.2 (-0.33, 0.74)	---	-0.14 (-0. 67, 0.40)
Aerobic + Biofeedback (23)	Biofeed- back- only (27)	Buckelew 1998	6	-0.25 (-0. 80, 0.29)	-0.64 (-1. 19, -0.09)	-0.1 (-0.64, 0.44)	---	-0.1 (-0.64, 0.44)
Aerobic + Education (28)	Education- only (28)	Burckhardt 1994	4	-0.23 (-0. 75, 0.28)	0.06 (-0.46, 0.57)	---	0.09 (-0.44, 0.61)	0.05 (-0.48, 0.57)
Aerobic + Education (28)	Untreated control (30)	Burckhardt 1994	4	0.54 (0.01, 1.06)	0 (-0.42, 0. 42)	---	0.29 (0.18, 1.47)	---
Aerobic + Education (27)	Untreated control (23)	Gowans 1999	3	0.97 (0.32, 1.62)	0.25 (-0.36, 0.87)	---	0.83 (-0.23, 0.81)	0.78 (0.15, 1.42)
Ex- ercise + Edu- cation + Self Help (84)	Untreated control (80)	Cedraschi 2004	8	0.41 (0.11, 0.72)	0.38 (0.07, 0.69)	0.19 (-0.12, 0.49)	---	0.20 (-0.11, 0.50)
Ex- ercise + Self- Manage- ment (14)	Relaxation (13)	Keel 1998	6	0.31 (-0.45, 1.07)	0.55 (-0.23, 1.32)	---	---	---
Exercise + Education (28)	Untreated control (29)	Mannerko- rpi 2000	5	0.66 (0.12, 1.19)	0.45 (-0.08, 0.97)	---	1.21 (0.45, 1.79)	0.17 (-0.35, 0.69)

Table 6. Short-term effects (SMD, 95%CI): composite interventions, not meta-analyzed (Continued)

Exercise + Spa (58)	Untreated control (76)	Zijlstra 2005	4	-0.05 (-0.39, 0.29)	0.1 (-0.24, 0.44)	0.50 (0.15, 0.85)	0.13 (-0.21, 0.47)	0.04 (-0.30, 0.39)
<p>Note: a. All positive values denote greater improvement in Intervention 1 versus Intervention 2. Therefore, a positive value for pain intensity would mean pain intensity has decreased with intervention 1.</p> <p>b. Van Tulder Score is based on the 11 internal validity items described in van Tulder et al. 2003</p>								
<p>Key: SMD = Standardized Mean Difference (small change = .2, moderate change = .5, large change = .8). Data for comparison at 12 weeks or as close to 12 weeks as possible was</p>								

Table 6. Short-term effects (SMD, 95%CI): composite interventions, not meta-analyzed (Continued)

used to calculate SMD								
Formula: SMD= (Mean change in Intervention 1 - Mean change in Inter- vention 2)/ (Pooled SD of change)								

Table 7. Clinical Relevance - Aerobic Training

Outcome (scale)	# patients(# trials)	Ctl baseline m(SD)	Wt Absolute Change	Relative change %	NNT (Benefit)	Statistical sig	Quality of evidence	
Pain (10 cm VAS)	183 (3)	6.1 cm (1.97)	13% (1.3 cms less on 10 cm scale)	21%	NA	Non-sig.	Gold	
Global Outcome Measure (0-10 scale)	269 (4)	5.5 (1.33)	7% (0.7 points less on a scale of 0 to 10)	12%	5	Sig.	Gold	
Physical Function/ Fitness (peak VO2)	253 (4)	23.5 ml/ km/min (4.27)	2.8 more ml/kg/ min oxygen uptake on a max treadmill test	12%	NA	Sig.	Gold	
Tender Point (dolorimetry: pain pressure threshold)	309 (5)	3.7 (1.01)	0.23 more kg/cm ² per tender point	6%	NA	Non-sig.	Gold	
LEGEND - representative study used for								

Table 7. Clinical Relevance - Aerobic Training (Continued)

estimates related to control group values: Schachter 2003; ctl= control group; m= mean; SD= standard deviation; wt= weighted; NNT= number needed to treat, refers to a 30% improvement; sig= significance; NA=not applicable								
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Table 8. Clinical Relevance - Strength Training

Outcome (scale)	# patients (# trials)	Ctl baseline m(SD)	Wt Absolute Change	Relative Change %	NNT (Benefit)	Statistical Sig.	Quality of Evidence
Pain (0-100 scale, 0 = no pain, 100 worst possible)	21 (1)	35 (19)	49% (49 fewer points on scale of 0 to 100)	140%	2	Non-sig	Silver
Global health (disease severity scale: 0-100 scale, 0 = health, 10 = severe disease)	47 (2)	34 (29)	41% (41 fewer points on scale of 0 to 100)	122%	3	sig.	Silver
Physical Function (Max Isometric Force - Knee Extensors, Newtons)	47 (2)	415.9 Newtons (90.84)	47 Newtons (4.7 more kilograms of force generated by quadriceps)	11%	NA	non.sig.	Silver

Table 8. Clinical Relevance - Strength Training (Continued)

Number of tender points (0-18 points)	26 (1)	15.6 tender points (1.9)	2.1 fewer active tender points	13%	2	sig.	Silver
<p>LEGEND: Hakkinen 2001 used for control group data for Pain and Global Health; Valkeinen 2004 control group data used for Physical Function and Number of Tender Points. Ctl= control group; m=mean; SD=standard deviation; wt= weighted; sig= significance; NNT=number needed to treat, refers to a 30% improvement; NA=not applicable</p>							

WHAT'S NEW

Last assessed as up-to-date: 16 August 2007.

Date	Event	Description
14 June 2008	Amended	Converted to new review format. CMSG ID C036-R

HISTORY

Review first published: Issue 2, 2002

Date	Event	Description
17 August 2007	New citation required and conclusions have changed	Substantive amendment. See published notes for details

CONTRIBUTIONS OF AUTHORS

AJB: designing and reviewing protocol for review, performing literature search, data extraction, methodological analysis, writing and reviewing manuscript

CLS: designing and reviewing protocol for review, performing literature search, data extraction, methodological analysis, writing and reviewing manuscript

PMP: designing and writing protocol for review, performing literature search, methodological analysis, statistical analysis, writing and reviewing manuscript

KARB: data extraction, methodological analysis, writing and reviewing manuscript

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DECLARATIONS OF INTEREST

We confirm that any present or past affiliations or other involvement in any organisation or entity with an interest in the Review which might lead me/us to have a real or perceived conflict of interest are listed below.

- None known

SOURCES OF SUPPORT

Internal sources

- School of Physical Therapy, University of Saskatchewan, Canada.
- Department of Medicine, University of Saskatchewan, Canada.
- Institute of Health and Outcomes Research, University of Saskatchewan, Canada.
- Institute for Work and Health, Canada.

External sources

- No sources of support supplied

NOTES

This review is a major update of the previous review completed in 2002. Methodological differences between the previous review and this update included small revisions to the search terms and changes in the membership of the review team. Also in this update, 11 items of the van Tulder (2003) methodological criteria that reflect internal validity were used to classify studies into high, moderate and low quality studies. In the data synthesis, greater weight was placed on moderate to high quality studies comparing exercise-only interventions to control groups.

The previous review was based on 16 randomized trials whereas this was based on 34 randomized trials. To aid in the interpretation of a growing number of interventions and comparisons, in this update we have expanded the analysis to include calculation of relative percentage change and standardized mean differences. Despite the increased number of reports, meta-analysis continued to be restricted due to clinical heterogeneity and conclusions have not changed substantially.

INDEX TERMS

Medical Subject Headings (MeSH)

*Exercise; Exercise Tolerance; Fibromyalgia [*rehabilitation]; Randomized Controlled Trials as Topic

MeSH check words

Humans