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Exercise for Fibromyalgia: A Systematic Review

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ABSTRACT. ***Objective.*** Fibromyalgia (FM) is a syndrome expressed by chronic widespread pain often associated with reduced physical function. Exercise is a common recommendation in management of FM. We evaluated the effects of exercise training on global well-being, selected signs and symptoms, and physical function in individuals with FM.

Methods. We searched Medline, Embase, CINAHL, SportDiscus, PubMed, PEDro, and the Cochrane Central Register for Controlled Trials to July 2005 and included randomized trials evaluating cardiorespiratory endurance, muscle strength, and flexibility. Methodological quality was assessed using the van Tulder and Jadad instruments. Training protocols were evaluated using American College of Sports Medicine (ACSM) guidelines. Clinical heterogeneity limited metaanalysis to 6 aerobic and 2 strength studies.

Results. There were 2276 subjects across the 34 studies; 1264 subjects were assigned to exercise interventions. Metaanalysis of 6 studies provided moderate-quality evidence that aerobic-only exercise training at ACSM-recommended intensity levels has positive effects on global well-being (SMD 0.49, 95% CI 0.23–0.75) and physical function (SMD 0.66, 95% CI 0.41–0.92) 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 underevaluated; however, strength training may have a positive effect on FM symptoms.

Conclusion. Aerobic-only training has beneficial effects on physical function and some FM symptoms. Strength-only training may improve FM symptoms, but requires further study. Large, high-quality studies of exercise-only interventions that provide detailed information on exercise prescription and adherence are needed. (First Release May 1 2008; J Rheumatol 2008;35:1130–44)

Key Indexing Terms:
FIBROMYALGIA EXERCISE METAANALYSIS TREATMENT OUTCOME

Fibromyalgia (FM) is 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"[1]. The American College of Rheumatology diagnostic criteria include widespread pain for longer than 3 months' duration, with pain on palpation on at least 11 of 18 specified tender points on the body[2]. Prevalence rates in individuals of all ages have been reported to be 2% (female 3.4%, male 0.5%)[3]. Limitations in activities associated with daily living have been reported to be as high in patients with FM as in patients with rheumatoid arthritis[4]. In individuals who seek medical attention, the condition is chronic and nonremitting, with symptoms affecting every aspect of life, including work, family life, and leisure[5]. The effect of FM on the ability to work and productivity is substantial, with 20% to 50% of persons with FM able to work few or no days[6,7], 36% experiencing an average of 2 or more absences from work per month, and 26.5% to 55% receiving disability or social security payments[7,8].

Despite investigation of a wide range of options, optimal management of FM is still unknown. Evidence-based guidelines[9,10] and reviews[11-17] have examined a range of pharmacologic and nonpharmacologic management options. Nonpharmacologic strategies include interventions classified as mind-body cognitive/cognitive-behavioral, exercise, complementary, and alternative therapies. Goldenberg, *et al*[9] 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."

Many individuals with FM have been shown to be sedentary[18] with levels of cardiorespiratory fitness well below average[18-21]. While the underlying pain, fatigue, and depression are likely to contribute to sedentary lifestyles and there-

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fore low levels of fitness, the exercise studies indicate that individuals with FM are able to perform maximal tests of cardiorespiratory fitness, low and moderate intensity aerobic exercise, and flexibility and muscle-strengthening exercises. Additionally, while exercise is recognized as one part of the management of FM, not all of the clinically relevant and practically important aspects of exercise prescription have been identified.

The primary objective of this systematic review is 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. Determining the effectiveness of various types and training volumes of exercise for improvement of FM signs and symptoms, and which outcomes are most affected by exercise, will help to guide clinicians in exercise prescription and assist individuals with FM to approach exercise with realistic expectations of benefits and difficulties.

MATERIALS AND METHODS

We searched the literature for randomized trials comparing an intervention that included an exercise component with an untreated control (randomized controlled trials) or a non-exercise intervention (randomized clinical trials) for individuals with FM. We included studies using published diagnostic criteria[2,22-25]. 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. We classified exercise interventions into 2 types: composite interventions included both an exercise and non-exercise component(s) delivered simultaneously; and exercise-only interventions that had no additional non-exercise component. Exercise-only interventions were subsequently classified by the predominant exercise type (excluding warm-up and cool-down). Exercise-only interventions included aerobic-only training, strength-only training, flexibility-only training, or mixed exercise-only interventions (that included some combination of aerobic, strength, and flexibility exercise). 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.

Search strategy. We searched Medline (1966 to May 2005), CINAHL (1982 to May 2005), HealthStar (1990 to May 2005), SportDiscus (1975 to May 2005), Embase (1974 to May 2005), and the Cochrane Controlled Trials Register (CENTRAL, Issue 3, 2005), using no language restrictions. We used a search strategy[26] that included keywords and MeSH headings used for FM and experimental trials and that described the wide spectrum of forms of physical activity, exercise, and exercise testing. In addition, 2 reviewers independently reviewed reference lists from identified articles, metaanalyses, and reviews of all types of management strategies for FM, and all promising references were scrutinized.

Study selection. Two reviewers independently scanned the titles and reviewed abstracts of studies generated from searches, reviews, and meta-analyses. After retrieving complete publications for the promising abstracts, full-text articles were examined independently by 2 reviewers to determine if they met the selection criteria. Disagreements between reviewers were resolved through consensus. Foreign language studies were translated and included in the review.

Data extraction and management. Two reviewers independently extracted study characteristics and results from each report and subsequently checked point-estimates for outcome measures. Discrepancies were rechecked and consensus achieved by discussion. In the case of missing data or when further clarification was needed, we contacted authors. Responses were received from 10 authors.

Methodological quality assessment. Two instruments for assessing methodological quality were applied after agreement on a consistent interpretation of each instrument. The van Tulder Methodological Quality Criteria[27,28] were applied with the following 2 deviations from van Tulder[27]. 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 analyzed at completion of the primary short-term endpoint of the study, or if all subjects who entered the study were analyzed at completion (i.e., intention-to-treat analysis). We also applied the Jadad Methodological Quality Criteria as described by Jadad, *et al*[29].

Two or 3 reviewers independently applied the quality assessment tools to each study and then met to compare results. Differences in ratings were resolved by consensus. Interrater reliability, calculated using kappa coefficients, ranged from K = 0.864 for studies evaluated by 3 reviewers to K = 0.914 for studies evaluated by 2 reviewers, indicating "almost perfect" agreement according to Landis and Koch[30].

Using the 11 items of the van Tulder instrument that reflect internal validity[28] we classified studies into high, moderate, and low quality categories using arbitrary groupings of 8–11 for high quality, 5–7 for moderate quality studies, and ≤ 4 for low quality studies. In this way, moderate quality represented scores of 50% or greater because one of the 11 items (the blinding of the care provider) is seldom achieved in exercise studies. In this review, we placed greater weight on high and moderate quality studies.

Evaluation of congruence of exercise/physical activity with recognized guidelines. We evaluated exercise interventions using the American College of Sports Medicine (ACSM) guidelines for exercise training[31,32] and the US Centers for Disease Control (CDC) guidelines for physical activity[33]. Two reviewers independently classified studies as either meeting or not meeting the ACSM and CDC guidelines, and then met to reach a consensus by discussion.

ACSM guidelines were used to assess 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. For cardiorespiratory endurance (aerobic training), the required exercise stimulus was as follows: (a) frequency of exercise at least 3 days per week; (b) intensity of exercise sufficient to achieve or exceed 40% of heart rate reserve (range 40% to 85%) or 64% of predicted maximum heart rate (range 64% to 94%); (c) sessions of at least 20 minutes' duration (range 20 to 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; and (d) a total time period of at least 6 weeks. For muscle strengthening, the exercise dosage requirements were: (a) frequency of 2 to 3 days per week; and (b) a minimum of one set of 8 to 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. Flexibility training dosage requirements were: (a) frequency of exercise ≥ 2 days per week; (b) intensity to a position of mild discomfort; and (c) 3 to 4 repetitions of each stretch held for a duration of 10 to 30 seconds.

We used the Centers for Disease Control and Prevention physical activity guideline[33] to evaluate whether interventions had provided an exercise or physical activity stimulus that could improve health. These guidelines are supported by epidemiological studies addressing 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 5 or more days of the week or at least 20 minutes of vigorous intensity exercise at least 3 days per week, represents a public health statement to the general population.

Measures of treatment effect. We grouped the outcome measures into 6 constructs representing global well-being, commonly experienced signs and symptoms of FM, and observer-measured physical function. Primary outcomes represented 4 constructs: (1) pain; (2) global well-being (overall feeling of well-being) or perceived improvement in FM symptoms as assessed by the study participant or observer; (3) physical function (reflected by tests evaluating the cardiorespiratory system, muscle strength, or flexibility); and (4) tender points. Secondary outcomes represented 2 constructs: depression, and fatigue and sleep. When researchers reported more than one measure for any one construct, we used the following order of preference for analysis: (1) Pain: visual analog scale (VAS), Fibromyalgia Impact Questionnaire (FIQ) VAS subscale, ordinal scale. (2) Global: FIQ Total, subject-rated VAS or ordinal scale, health professional-rated change, Quality of Life scale, Sickness Impact Profile Total. (3) Physical Function: selected on a case by case basis depending on researchers' stated objectives. (4) Tender Points: dolorimetry, total myalgic score, tender point count. (5) Depression: Beck Cognitive, Beck Total, Center for Epidemiologic Studies-Depression, FIQ-Depression, Arthritis Impact Measurement Scales-Depression subscale.

We calculated standardized mean differences (SMD), using 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 pre-test and post-test standard deviations (or standard errors) where these were provided.

Evaluation of clinically important differences. Recent literature suggests use of relative difference in change scores or percentage change as a guide for determining clinically important difference. The magnitude of change constituting clinically important difference ranges from 15%[34] to approximately 30%[35]. We chose a conservative estimate of 30% relative percentage improvement as a benchmark for clinical importance based on the work of Farrar, *et al*[35] in the area of chronic pain. This is consistent with the findings of Dunkl, *et al*[36], 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.

Assessment of heterogeneity. Heterogeneity among the trials was assessed using the heterogeneity statistics (chi-squared, I^2). We considered values of $p \leq 0.1$ to be indicative of significant heterogeneity. Where $p < 0.1$ and/or $I^2 > 50\%$, the results were examined for sources of clinical heterogeneity as well as methodological differences. Reviewers identified important sources of heterogeneity as: variations in intervention type (exercise-only or composite), exercise type(s) and dosage, disparate comparators (e.g., intervention versus a control group or versus a second intervention), timing of measurement of outcome measures, and methodological quality. If no methodological or clinical reason could be found to explain the statistical heterogeneity, we proceeded with the metaanalysis using a random-effects model.

Data synthesis. Statistical analyses were conducted using RevMan Analyses software[37]. We carried out metaanalysis of trials that compared the effects of one type of exercise (aerobic-only or strength-only interventions) to control conditions that did not involve any form of active treatment. The control conditions we accepted were: treatment as usual, attention-only, and wait-list control strategies. For aerobic-only studies, we included only moderate and high quality studies. We did not impose quality restrictions when analyzing strength-only interventions due to the limited number of trials available. When multiple interventions were compared in a single study, we analyzed the comparisons for each exercise intervention separately. We preferentially analyzed intention-to-treat (ITT) data when available. Mean change scores were compared, and weighted and combined using a random-effects model. All other studies were analyzed using effect sizes (SMD) and confidence intervals.

When interpreting the results of the metaanalyses, we used Cohen's categories for effect size[38] to evaluate the magnitude of the effect (0.2 = small effect, 0.5 = medium effect, 0.8 = large effect). We applied the van Tulder[28] recommendations regarding levels of evidence as follows.

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

We defined "inconsistent evidence" when analysis showed one of: (1) an absence of high quality studies, where at least one RCT clearly favored control while at least one RCT clearly favored treatment; and (2) when more than one high quality study is available, and at least one high quality RCT clearly favored control while at least one high quality RCT clearly favored treatment. We defined "consistent" evidence as analysis in which: all studies clearly favored treatment (or control) or some studies clearly favored treatment, while the remainder are inconclusive (that is, they do not exclude the null). We defined "clearly favor" when the confidence interval excluded zero.

Assessment of biases. When appropriate, publication bias was assessed using a visual assessment of the funnel plot generated using RevMan Analyses software[37,39]. 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 low quality studies versus the moderate to high quality aerobic-only studies.

RESULTS

We inspected 3989 titles generated from searches conducted in 2002 and 2005 and found 86 citations of full-length articles describing experimental trials in subjects with FM that examined the effects of interventions including an exercise component. Excluded studies are listed in Table 1. Of the 27 excluded studies, 4 did not adequately characterize the population, 19 were not randomized trials, and 4 did not include an intervention that we characterized as exercise.

Thirty-four trials were included in this review. Three were followed by subsequent reports about the same subjects. Hakkinen, *et al*[68] and Hakkinen, *et al*[69] were counted as one study for analysis. Gowans, *et al*[70] and Mannerkorpi, *et al*[71] presented information on longterm uncontrolled followup of RCT they studied, thus these reports were treated as secondary studies and were excluded from analysis. The basic characteristics of the studies included are summarized in Table 2. There were 2276 subjects across the 34 studies with a confirmed diagnosis of FM; 1264 subjects were assigned to exercise interventions. The average sample size for the smallest experimental group was 24.7 (SD 16.4, range 5–80). Mean age in the studies ranged from 27.5 to 60.2 years in 33 studies (unspecified in Ramsay[72]). For the 2197 subjects for whom gender was reported, 96.4% were female.

The 34 studies evaluated 47 interventions including exercise. Subjects were randomized to at least one aerobic-only intervention in 15 studies, to strength-only interventions in 3 studies, to flexibility-only interventions in 3 studies, to

Table 1. Excluded studies. From The Cochrane Library 2007, Issue 4, with permission.

Study	Reason for Exclusion
Ahlgren 2001[40]	Diagnosis: trapezius myalgia
Astin 2003[41]	Did not meet exercise criteria (QiGong)
Bailey 1999[42]	One-group design
Bakker 1995[43]	Between-group analysis not done
Dawson 2003[44]	One-group before-after design
Gandhi 2000[45]	Not randomized
Geel 2002[46]	Not randomized
Gowans 2002[47]	Examines measurement issues of selected variables already reported in an included study; new variables did not include standard deviations
Guarino 2001[48]	Diagnosis: Gulf War syndrome
Han 1998[49]	Not randomized
Hunt 2000[50]	Unspecified diagnostic criteria for FM
Karper 2001[51]	Not randomized
Kendall 2000[52]	Did not meet exercise criteria (body awareness)
Kingsley 2005[53]	Use of published diagnostic criteria not verified
Mason 1998[54]	Not randomized
Meiworm 2000[55]	Not randomized
Mobily 2001[56]	Case study
Nielens 2000[57]	Not randomized
Offenbacher 2000[58]	Non-experimental narrative review
Oncel 1994[59]	No description of exercise
Peters 2002[60]	Diagnosis: persistent unexplained symptoms
Pfeiffer 2003[61]	One-group before-after design
Piso 2001[62]	Not randomized
Rooks 2002[63]	One-group design
Thieme 2003[64]	Did not meet exercise criteria (passive physiotherapy with light movement in water)
Tiidus 1997[65]	One-group repeated-measures design
Vlaeyen 1996[66]	Insufficient description of exercise
Worrel 2001[67]	One-group design

mixed exercise-only interventions in 11 studies, and to a composite aerobic exercise plus education intervention in 4 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.

Outcomes. A large variety of measures (n = 166) were used to evaluate the effects of the 6 outcomes. To evaluate pain, most studies (n = 22) used a 10-cm VAS. The FIQ was the test most commonly used to measure for global well-being (n = 13). The tests most commonly used to measure physical performance (aerobic) were the 6-minute walk test (n = 6) and maximum oxygen uptake (n = 7)**.** 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 5 studies and using the depression VAS in 5 studies. The most common measure of fatigue was the FIQ-fatigue VAS, which was reported in 10 studies.

Methodological quality of studies. Results of the methodological assessment are provided in Table 3. The mean of van Tulder scores for internal validity was 5.06 (out of a total possible of 11); the mode was 4 (range 1–9). Four studies were classified as high quality, 15 as moderate quality, and 14 as low quality. More than half the studies were deficient in 6 or more internal validity criteria (concealment of treatment allocation, compliance with treatment, patient blinding, care provider blinding, control of cointervention, valid randomization).

Evaluation of training stimulus. Twenty studies described exercise interventions that met ACSM recommendations: 17 for aerobic training (Table 3), 3 for strength training[69,82,98], and 2 for flexibility[83,86]. 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. Of the remaining studies, in Norregaard, *et al*[92], we judged that ACSM guidelines had not been met because authors reported the subjects were unable to achieve intended intensity levels. In Mannerkorpi, *et al*[86], exercise was not designed to elicit a training effect and in Zijlstra, *et al*[103] the duration of the exercise program was too short (15 days).

Three studies examining aerobic training interventions met CDC recommendations for physical activity[88,90,93]. Seven of those 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[72,74,75,78,81,84,96]. The remaining studies employed interventions that provided insufficient frequency and/or duration of exercise to satisfy the CDC standards for either moderate or vigorous physical activity.

Potential sources of bias. Small sample size is a methodological weakness of most included studies; only 5 studies of the 34 included studies met the standard of 50 subjects per group[104].

Adverse effects. Five of the 1264 subjects assigned to aerobic exercise interventions experienced adverse effects possibly related to exercise, including one metatarsal stress fracture[95], one case of ischialgia[102], and 2 cases of transient knee pain[88].

All other reports of adverse effects focused on increases in FM symptoms. There was no agreement about whether protracted increases in FM symptoms (especially pain, stiffness, and/or fatigue) should be reported as adverse effects of exercise. A number of studies using aerobic exercise interventions reported increased FM symptoms that may have affected performance, adherence, and attrition[86,92,94,95,101]. Only one of the 3 strength-only interventions reported worsening pain; 11% of participants in Jones, *et al*[83] reported increased pain. Conversely, Hakkinen, *et al*[69] did not report any adverse effects and stated "even heavy resistance training can be safely used in the treatment of fibromyalgia."

Table 2. Studies included in the metaanalysis. From The Cochrane Library 2007, Issue 4, with permission.

Study	Method	Participants, F:M; age range (yrs)	Interventions (n)	Type of Exercise	Outcomes
Altan 2004[73]	RClinT, active therapy 12 wks, followup (controlled) 12 wks	46:0; 31–56 (43.9)	Pool-based exercise in heated pool (24), balneotherapy (22)	Mixed	Pain, tender points, fatigue, sleep, stiffness, muscle endurance, patient-rated disability (status), HP-rated disability (status), FIQ, depression
Buckelew 1998[74]	RCT, active therapy 6 wks, maintenance 2 yrs	108:9; 41.9 (8.1) to 45.6 (9.4)	Aerobic + HP (26), biofeedback + aerobic (23), biofeedback (25); education + attention control (27)	Aerobic composite	Pain, tender points, physical function (self-report), global, self-efficacy, fatigue and sleep, psychological function
Burckhardt 1994[75]	RCT, 12 wks	99:0; 46.5 (8.3)	Exercise + education (28), education (28); wait-list control (80)	Composite	Pain, tender points, physical function (CR fitness, self-report, muscle-skeletal tests), global, self-efficacy, fatigue, sleep, psychological function
Cedraschi 2004[76]	RCT, active therapy 6 wks, followup (controlled) 6 mo	152:12; 48.9 (9.7) to 49.8 (9.8)	Multidisciplinary program including mixed exercise (84); wait-list control (80)	Composite	Pain, tender points, HP-rated disability (status), SF-36, FIQ, quality of life
Da Costa 2005[77]	RCT, active therapy 12 wks, followup, (controlled) 9 mo	79:0; 49.2 (8.7) to 52.3 (10.8)	Home-based exercise (39); treatment as usual control (40)	Aerobic	Pain, CR (max), FIQ
Genc 2002[78]	RClinT 3 wks	32:0; 27.9 (5.4) to 27.5 (5.6)	Exercise (16), remedial exercise (16)	Mixed	Flexibility, FIQ
Gowans 1999[79]	RCT 6 wks, followup 3 mo	32:9; 44.3 (10.7) to 46.6 (12.2)	Exercise + education (20); wait-list control (21)	Composite	Pain, physical function (CR fitness, self-report), global, self-efficacy, fatigue, sleep, psychological function
Gowans 2001[80]	RCT 23 wks	44:6; 44.6 (8.7) to 49.8 (7.3)	Exercise (27); untreated control (23)	Aerobic	Tender points, CR (functional performance), muscle strength, FIQ, self-efficacy, depression, anxiety
Hakkinen 2001[69]	RCT; pre-therapy control (for all groups) 4 wks; active therapy 21 wks	33:0; 37 (6) to 39 (6)	FM strength (11); FM untreated control (10), healthy subject strength control (12)	Strength	Pain, muscle strength, global, fatigue, sleep, depression
Hakkinen 2002[68]	RCT 21 wks	33:0; 37 (5) to 39 (6)	FM strength (11); FM untreated control (10), healthy subject strength control (12)	Strength	Musculoskeletal (strength), anthropometric measures, hormonal responses (testosterone, free test, DHEAS, IGF-I, GH)
Isomeri 1993[81]	RClinT 15 wks	39:6; 43.7 (24–55)	Aerobic (15), aerobic + amitriptyline (14), flexibility + amitriptyline (16)	Mixed	Pain, tender points
Jentoft 2001[82]	RClinT, active therapy 20 wks, followup (controlled) 6 mo	34:0; 39.4 (8.8) to 42.9 (8.6)	Pool-based exercise (18), land-based exercise (16)	Mixed	Pain, tender points, fatigue, stiffness, CR (predicted max), CR (functional performance), muscle strength, muscle endurance, patient-related disability (status), FIQ, self-efficacy, depression, anxiety
Jones 2002[83]	RClinT 12 wks	56:0; 46.4 (8.6) to 49.2 (6.3)	Strength (28), flexibility (28)	Strength, flexibility	Pain, tender points, fatigue, muscle strength, flexibility, FIQ, quality of life, self-efficacy, depression, anxiety
Keel 1998[84]	RClinT, active therapy 15 wks, followup 4 mo	24:3; 48 to 50	Exercise + self-management training (14), relaxation training (13)	Mixed	Pain, fatigue, sleep
King 2002[85]	RCT, active therapy 12 wks, followup (controlled) 3 mo	170:0; 44.9 (10) to 47.4 (9)	Aerobic (42), education (41), exercise + education (35); control (34)	Aerobic	Tender points, CR (functional performance), FIQ, self-efficacy

Table 2. Continued.

Study	Method	Participants, F:M; age range (yrs)	Interventions (n)	Type of Exercise	Outcomes
Mannerkorpi 2000[86]	RCT 24 wks (includes 6 wks of education)	69:0; 45 (8.0) to 47 (11.6)	Exercise + education (28); treatment as usual control (29)	Composite	Pain, physical function (CR fitness, self-report, muscle-skeletal tests), global, self-efficacy, fatigue, sleep, psychological function
Martin 1996[87]	RClinT 6 wks	37:1; 43.9 (9.7) to 45.7 (9.9)	Exercise (18), relaxation (20)	Mixed	Pain, tender points, physical function (CR fitness, muscle-skeletal tests), global, self-efficacy
McCain 1988[88]	RClinT 20 wks	Sexes mixed but unspecified; 35.8 (11.1) to 45.9 (8.2)	Aerobic (18), flexibility (20)	Aerobic flexibility	Pain, tender points, physical function (CR fitness), global, fatigue, sleep, psychological function
Mengshoel 1992[89]	RCT 20 wks	25:0; 34 (25–38) to 35.5 (21–47)	Aerobic (11); physical activity as usual control (14)	Aerobic	Pain, physical function (CR fitness, muscle-skeletal tests), fatigue, sleep, psychological function
Meyer 2000[90]	RCT 24 wks	8:0; 49.5 (6.3)	Low intensity aerobic (8), high intensity aerobic (8); physical activity as usual control (5). (Note: original group assignment not retained)	Aerobic	Pain, tender points, physical function (CR fitness, self-report), global, psychological function
Nichols 1994[91]	RCT 8 wks	17:2; 47.8 (11.1) to 50.8 (11.8)	Aerobic (10); sedentary control (9)	Aerobic	Pain, physical function (self-report). psychological function
Norregaard 1997[92]	RCT 12 wks	Sexes unspecified; 44 (8) to 55 (10)	Aerobic (5), mixed exercise (11); hot packs control (7)	Aerobic	Pain, tender points, physical function (CR fitness, muscle-skeletal tests), global, fatigue, sleep, psychological function
Ramsay 2000[72]	RClinT 12 wks	Sexes unspecified; age unspecified	Single exercise + HP (35), exercise class + HP (15)	Mixed	Pain, tender points, global, fatigue, sleep, psychological function
Redondo 2004[93]	RClinT, active therapy 8 wks, followup (controlled) 6 mo, 12 mo	40:0; 52.5 (8.8)	Exercise (19), cognitive behavioral therapy (21)	Mixed	Tender points, CR (max), physical function, patient-rated change (improvement), SF-36, FIQ, self-efficacy, depression, anxiety, coping
Richards 2002[94]	RClinT, active therapy 12 wks, followup 1 yr from entry	126:10; 45 (38–52) to 48 (38–56)	Aerobic (69), relaxation/flexibility (67)	Aerobic	Pain, tender points, fatigue, patient-rated change (improvement), SF-36, FIQ
Schachter 2003[95]	RCT 16 wks	143:0; 41.3 (8.67) to 42.5 (6.69)	Short-bout aerobic (56), long-bout aerobic (51); untreated control (36)	Aerobic	Pain, tender points, sleep, stifness, CR (max), other CR, self-reported function, patient-rated disability (status), HP-rated disability (status), FIQ, self-efficacy, depression, anxiety
Sencan 2004[96]	RCT, active therapy 6 wks, followup (controlled) 6 wks	60:0; 32.6 (9.4) to 35.5 (7.9)	Aerobic (20), antidepressant (paroxetine) (20); placebo (20)	Aerobic	Pain, tender points, sleep, depression
Valim 2003[97]	RClinT 20 wks	76:0; 47 (10) to 44 (11)	Aerobic (32), stretching (28)	Aerobic	Pain, tender points, CR (max), CR (submax), flexibility, SF-36, FIQ, depression, anxiety
Valkeinen 2004[98]	RCT 21 wks	36:0; 59.1 (3.5) to 60.2 (2.5)	FM strength (13); FM untreated control (13), healthy subject strength control (10)	Strength	Pain, tender points, fatigue, sleep, other CR, muscle strength, self-reported function, depression
vanSanten 2002[99]	RCT 24 wks	129:0; 42.8 (26–59) to 46.2 (26–59)	Exercise (with/without compliance strategy) (50), biofeedback (with/without compliance strategy) (50); treatment as usual control (29)	Mixed	Pain, tender points, fatigue, CR fitness, CR (max), other CR, self-reported function, SIP
vanSanten 2002[100]	RClinT 20 wks	37:0; 39 (20–54) to 45 (25–58)	Exercise at self-selected intensity (15), exercise at high intensity (18)	Mixed	Pain, tender points, CR (max), CR (submax), other CR, patient-rated severity, general health status, depression, anxiety, other psychological problems

Table 2. Continued.

Study	Method	Participants, F:M; age range (yrs)	Interventions (n)	Type of Exercise	Outcomes
Verstappen 1997[101]	RCT 6 mo	72:0; 42.8 (8.4) to 46.6 (8.3)	Aerobic + HP (45), non-intervention (27)	Mixed	Physical function (CR fitness, muscle-skeletal tests)
Wigers 1996[102]	RCT, active therapy 14 wks, followup 4.5 yrs	55:5; 44 (10)	Aerobic (16), stress management (15); treatment as usual control (17)	Aerobic	Pain, tender points, physical function (CR fitness), global, fatigue, sleep, psychological function
Zijlstra 2005[103]	RCT, active therapy 2.5 wks, followup (uncontrolled) 12 mo from baseline	28:6; 47 (24–64) to 48 (22–64)	Spa (58); treatment as usual control (76)	Composite	Pain, tender points, fatigue, sleep, CR (submax), patient-rated general health status, FIQ, depression

RCT: randomized controlled trial; RClinT: randomized clinical trial, comparing various treatments without a control group; HP: home exercise program; CR: cardiorespiratory fitness; FIQ: Fibromyalgia Impact Questionnaire; SIP: Sickness Impact Profile.

Valkeinen, *et al*[98] 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." Worsening pain was reported with one flexibility exercise intervention[83] (incidence not reported). In mixed exercise intervention studies, both vanSanten, *et al*[99] and vanSanten, *et al*[100] describe post-exercise soreness as an important barrier to adherence to mixed exercise training in about 50% of participants performing either high intensity or self-selected intensity interventions. Among studies with composite interventions, Cedraschi, *et al*[76] speculated that increased pain may have contributed to high attrition rates in the exercise group, but this was not quantified.

Adherence. The requirement that exercise must be tolerated by individuals with FM is fundamental to application of exercise as an intervention for FM. While a few researchers reported good adherence to high intensity cycle ergometry[88] and strength training[69,98], other researchers reported that participants had serious problems adhering to the exercise programs because of increased FM symptoms[86,92,99,101]. Such difficulties with exercise combined with high attrition rates in exercise studies suggest the importance of employing more tools to measure exercise adherence in order to identify the dose-response curves for FM signs and symptoms for different types and modes of exercise.

Attrition. Attrition rates for the 17 aerobic exercise intervention groups averaged 27.0% (SD 18.9%, range 0 to 67%); there was no attrition in the 2 strength training interventions. In 2 flexibility interventions, attrition was 12.5% (range 9% to 16%; one study did not report attrition per group). The 13 mixed exercise interventions had attrition rates of 14.6% (SD 11.8%, range 0 to 40%). The 11 composite interventions had dropout rates of 14.8% (SD 9.6%, range 0 to 27%). Mean attrition in the 20 nontreatment control groups was 12.3% (SD 11.8%, range 0 to 47%) and in the comparator groups was 18.0% (SD 14.1%, range 0 to 49%).

Metaanalyses. Results of the metaanalyses of aerobic-only exercise interventions compared to untreated controls are displayed in Figures 1 to 4. There was moderate evidence that short-term (6 to 23 weeks) aerobic-only exercise training prescribed at ACSM-recommended levels resulted in:

- a medium-size positive effect (nonsignificant) on pain (SMD 0.65, 95% CI –0.09 to 1.39) pooled from 183 subjects in one high quality[102] and 2 moderate quality studies[74,95] (Figure 1);
- a medium-size positive effect on global measures of well-being (SMD 0.49, 95% CI 0.23 to 0.75) pooled from 269 subjects from 4 moderate quality studies[74,80,85,95] (Figure 2);
- a medium-size positive effect on objective measures of physical function (SMD 0.66, 95% CI 0.41 to 0.92) pooled from 253 subjects in one high quality[102] and 3 moderate quality studies[80,85,95];
- a small-size positive effect (nonsignificant) for tender points (SMD 0.23, 95% CI –0.18 to 0.65) pooled from 309 subjects. One high quality study[102] reported a significant large positive effect, 3 moderate quality studies[74,80,95] found small nonsignificant positive effects, and one moderate quality study[85] found a small nonsignificant effect (Figure 3).

There was conflicting evidence that the effect of short-term (6 to 23 weeks) aerobic-only exercise training prescribed at ACSM-recommended levels resulted in a small to medium size positive effect on depression (SMD 0.40, 95% CI 0.04 to 0.76) pooled from 233 subjects from one high quality[102] and one medium quality study[95] that showed no evidence of effect, and 2 moderate quality studies[74,80] that demonstrated medium to large size effects (Figure 4).

There was limited evidence (one medium quality study[95], 87 subjects) that 16 weeks of aerobic-only exercise prescribed at ACSM-recommended levels had *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 was limited evidence from 2 low quality studies[69,98] that 21 weeks of strength-only exercise prescribed at ACSM-recommended levels resulted in:

Table 3. Methodological quality and congruence with American College of Sports Medicine (ACSM) aerobic training guidelines. From The Cochrane Library 2007, Issue 4, with permission.

Study	van Tulder Internal Validity Subscale* Items A, B, C, D, E, F, G, H, I, J, K	Internal Validity Total	Jadad Criteria Randomization, Blinding, Dropout	Total Score	ACSM Aerobic Training Guidelines
Altan 2004[73]	+++−−−−+++−	6	2, 0, 1	2	+
Buckelew 1998[74]	−−+−+−++++−	6	1, 0, 1	2	+
Burckhardt 1994[75]	−−+−−−−+++−	5	1, 0, 1	2	−
Cedraschi 2004[76]	+++−++−−+++	8	2, 0, 1	3	−
Da Costa 2005[77]	++−−−+−++++	7	2, 0, 1	3	+
Genc 2002[78]	−−+−−−−−+++	4	1, 0, 1	2	−
Gowans 1999[79]	−−+−−−−−++−	3	1, 0, 1	2	+
Gowans 2001[80]	−−+−+−−+−++	5	1, 0, 1	2	+
Hakkinen 2001[69]	−−+−−−−−+++	4	1, 0, 1	2	NA
Isomeri 1993[81]	−−+−−−−−++−	3	1, 0, 1	2	−
Jentoft 2001[82]	+−−−−+−+++−	5	2, 0, 1	3	+
Jones 2002[83]	+−+−−+−+−+−	5	2, 0, 0	2	NA
Keel 1998[84]	−++−+−+N/A++−	6	0, 0, 1	1	−
King 2002[85]	+++−+−−+−++	7	2, 0, 1	3	+
Mannerkorpi 2000[86]	−−+−++−+−+−	5	0, 0, 1	1	−
Martin 1996[87]	+−+−+−−+−++	6	2, 0, 1	3	+
McCain	−−−−++++++−	6	1, 0, 1	2	+
Mengshoel 1992[89]	−−+−−−−+−+−	3	1, 0, 1	2	+
Meyer 2000[90]	−−−−−−−−−+−	1	1, 0, 1	2	+
Nichols 1994[91]	−−−−+−−−−+−	2	1, 0, 1	2	+
Norregaard 1997[92]	+−−−+−−+−+−	4	2, 0, 1	3	−
Ramsay 2000[72]	−−−−−−−−+++	3	1, 0, 1	2	−
Redondo 2004[93]	+−+−−−−+−++	5	2, 0, 1	3	+
Richards 2002[94]	++++−−−++++	8	2, 0, 0	2	−
Schachter 2003[95]	+++−++−−−++	7	2, 0, 1	3	+
Sencan 2004[96]	−−+−+−+−+++	6	1, 0, 1	2	−
Valim 2003[97]	+−+−−−−+−+−	4	1, 0, 1	2	+
Valkeinen 2004[98]	+−+−−−−−+−+	4	2, 0, 1	3	NA
vanSanten 2002[99]	+++−−−−++++	7	1, 0, 1	2	−
vanSanten 2002[100]	+++−−−+++++	8	1, 0, 1	2	+
Verstappen 1997[101]	−−+−−−−+++−	4	1, 0, 1	2	−
Wigers 1996[102]	+−+++++++++	9	2, 0, 1	3	+
Zijlstra 2005[103]	+++−−−+−−−−	4	2, 0, 0	2	−

* van Tulder internal validity items; congruence with ACSM aerobic training guidelines: +: met the criterion, –: did not meet the criterion; NA: not applicable. van Tulder Internal Validity Subscale: 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? F: Was the outcome assessor blinded to the intervention? G: Were cointerventions avoided or similar? H: Was the compliance acceptable in all groups? I: Was the dropout 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?

• a large positive effect on global well-being[69,98] (47 subjects, SMD 1.43, 95% CI 0.76 to 2.10; Figure 5);
• a medium positive effect (nonsignificant) on objective measures of physical function[69,98] (47 subjects, SMD 0.52, 95% CI –0.07 to 1.10).

There was limited evidence from low quality studies[69,98] that 21 weeks of strength-only exercise prescribed at ACSM-recommended levels resulted in:
• a large positive effect on pain[69] (21 subjects, SMD 3.00, 95% CI 1.68 to 4.32);
• a large positive effect on tender points[98] (26 subjects, SMD 1.52, 95% CI 0.63 to 2.41);
• a large positive effect on depression[69] (21 subjects, SMD 1.14, 95% CI 0.20 to 2.08).

Effectiveness of all other exercise interventions. SMD (effect sizes) and 95% CI for the effects in exercise-only trials excluded in the metaanalyses are summarized in Table 4. Several significant medium to large effect sizes favoring several exercise (Table 4) and composite interventions (data not shown) were found. Global well-being was the outcome most commonly shown to improve, with significant medium to large effects in 6 interventions.

Clinically significant improvements. Improvements of

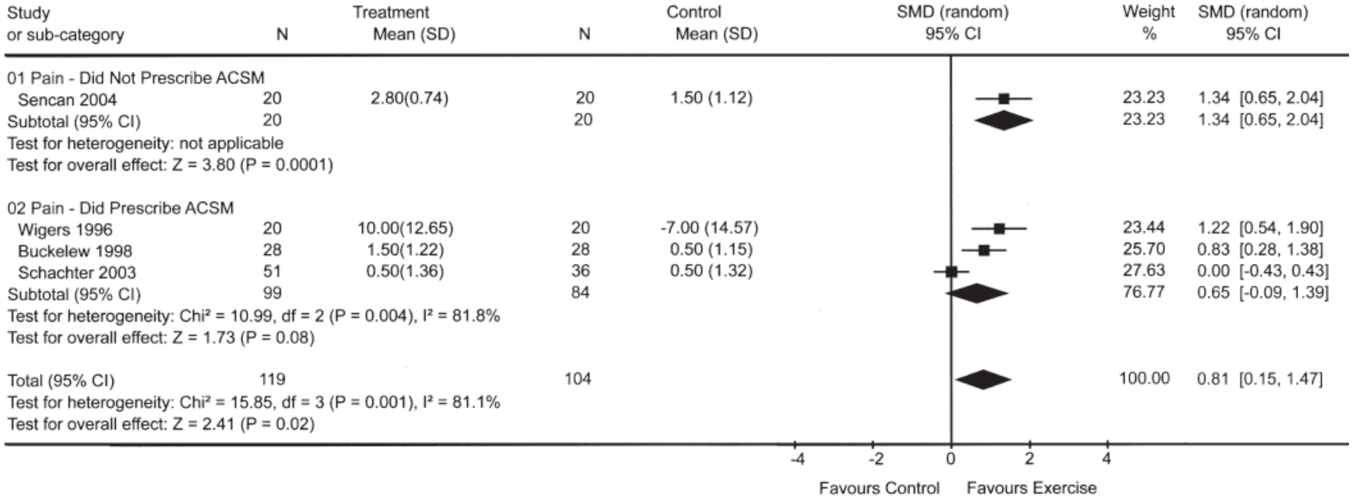

Figure 1. Metaanalysis for effect of aerobic exercise on pain (01: exercise programs did not meet ACSM standards; 02: exercise programs met ACSM standards). SMD: standardized mean difference. From The Cochrane Library 2007, Issue 4, with permission.

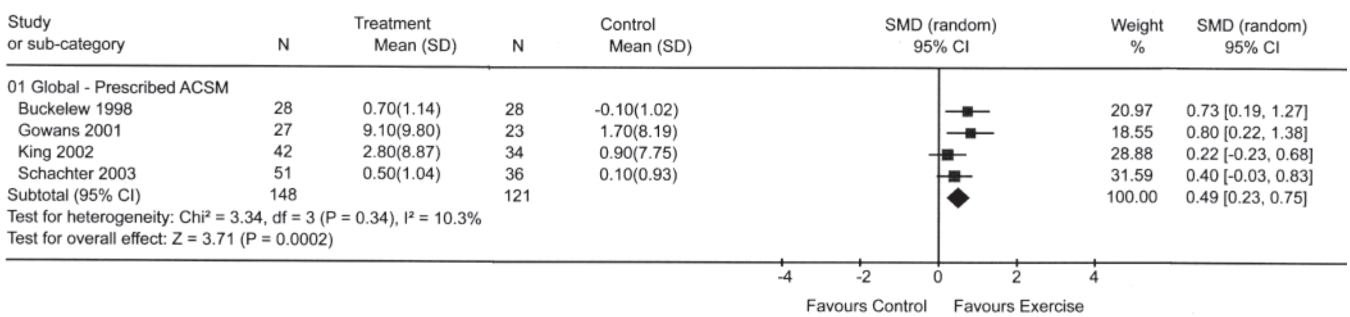

Figure 2. Metaanalysis for effect of ACSM-recommended aerobic exercise on global well-being. SMD: standardized mean difference. From The Cochrane Library 2007, Issue 4, with permission.

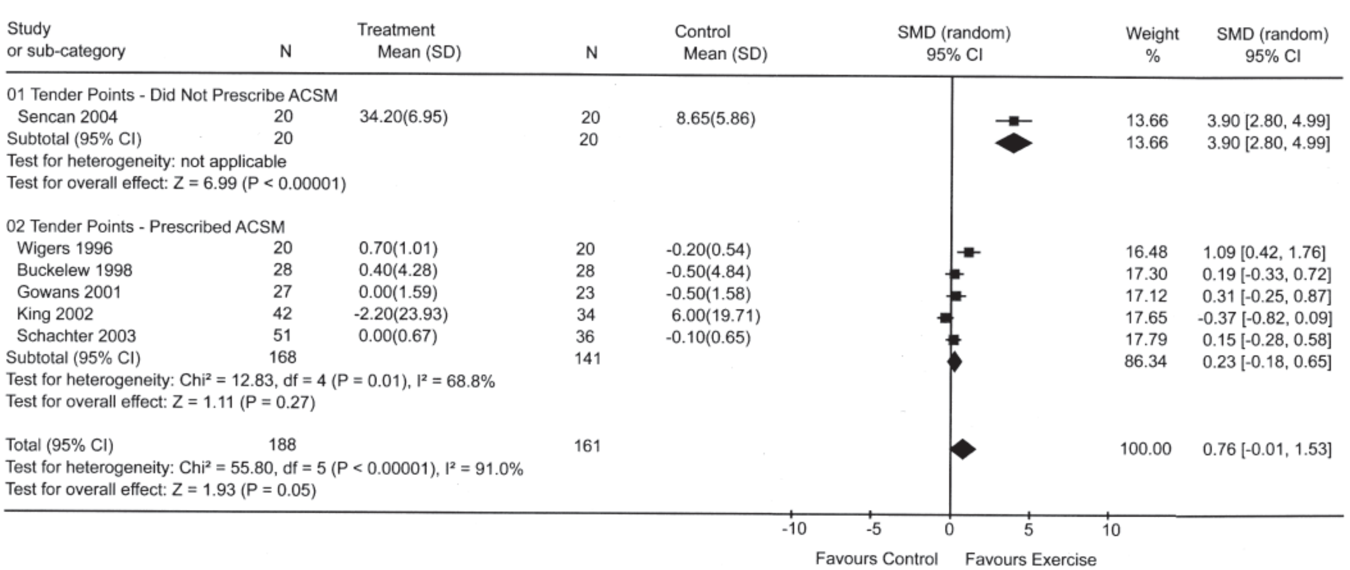

Figure 3. Metaanalysis for effect of aerobic exercise on tender points (01: exercise programs did not meet ACSM standards; 02: exercise programs met ACSM standards). SMD: standardized mean difference. From The Cochrane Library 2007, Issue 4, with permission.

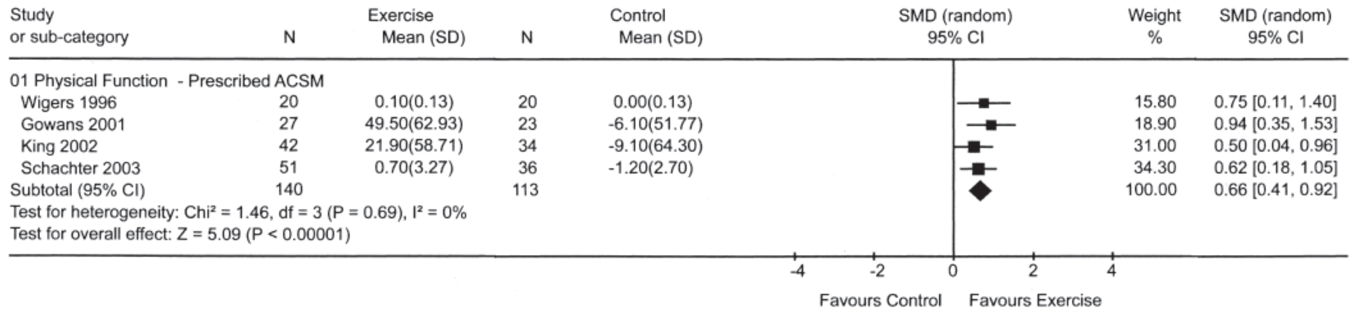

Figure 4. Metaanalysis for effect of aerobic exercise on depression (01: exercise programs did not meet ACSM standards; 02: exercise programs met ACSM standards). SMD: standardized mean difference. From The Cochrane Library 2007, Issue 4, with permission.

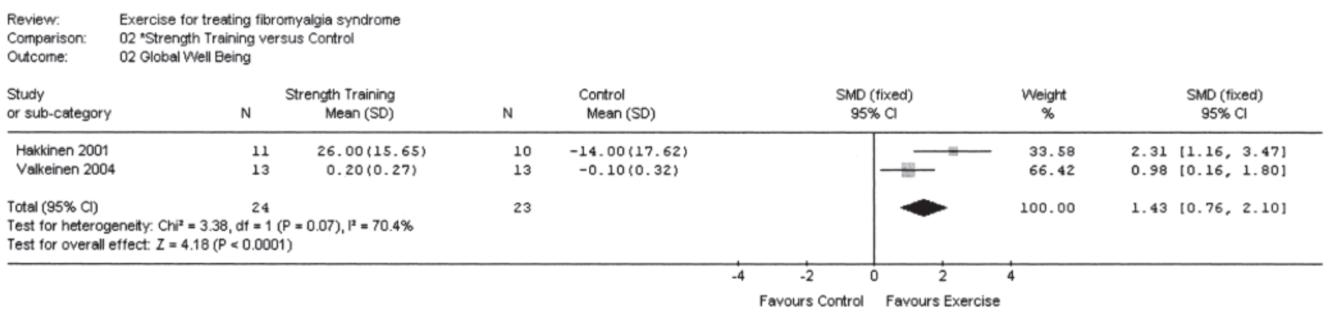

Figure 5. Metaanalysis for effect of ACSM-recommended strength training on global well-being. From The Cochrane Library 2007, Issue 4, with permission.

greater than 30% at post-test for various outcomes were sporadic (Table 5). Among our primary outcome measures, clinically significant improvements were observed in: (a) pain in one strength-only intervention; (b) global well-being in one aerobic-only, 2 strength-only, and one composite intervention; (c) musculoskeletal physical performance in one aerobic-only intervention; and (d) in tender points in 2 aerobic-only interventions. Among secondary outcome measures, clinically significant improvements were found in: (a) depression in 7 studies (2 aerobic, one strength-only, one mixed exercise-only, and 3 composite interventions), and (b) sleep (restedness in morning) in one aerobic-only intervention.

Longterm effects. Followup assessments ranged from 6 weeks to 4 years. Among aerobic-only studies, 7 reported on followup assessment (controlled[74,77,85,96] and uncontrolled[79,94,102]). Among mixed studies, 2 reported about controlled followup[73,93], one about uncontrolled[84], and among composite studies, one reported controlled followup[76] and one uncontrolled followup[103]. Maintenance of post-test improvements of FM symptoms was reported inconsistently in some but not all studies for pain, global well-being, tender points, depression fatigue, physical function, and self-efficacy (function).

DISCUSSION

There is moderate quality evidence that short-term aerobic-only exercise training at ACSM-recommended levels has medium-size positive effects on global well-being and physical function. There may also be beneficial effects on pain, tender points, and depression, but these improvements were either inconsistent or statistically insignificant. Our findings are supported by other reviews and recommendations for FM management[9,10]. There is limited evidence that strength-only exercise has a large-size positive effect on pain, global well-being, physical function, tender points, and depression. There is also limited evidence that strength-only exercise compared to flexibility exercise has medium-size positive effects on pain and global well-being, but no effect on muscle strength. While the findings pertaining to strength training are promising, more high quality studies using larger numbers and improved adherence reporting are needed before strength training can be broadly recommended. There is no evidence as to the effects of flexibility-only exercise (compared to an untreated control group) and limited evidence that flexibility-only exercise compared to strength exercise has no effect on tender points or depression. Thus further study is needed to fully understand the effects of flexibility exercise.

There were not enough similar mixed-exercise studies with controlled comparison groups to carry out metaanalysis. Without exception, the evidence for any particular comparison arose from a single medium quality study, yielding limited evidence. There were no positive effects of any mixed intervention on signs and symptoms of FM, with the exception of objective measures of physical function. While

Table 4. Short-term treatment effects expressed as standardized mean difference (SMD)* (95% CI) for exercise-only interventions excluded from meta-analysis due to clinical heterogeneity. 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. van Tulder Score is based on the 11 internal validity items as described[28]. From The Cochrane Library 2007, Issue 4, with permission.

Study	van Tulder Score[a]	Intervention 1 (n1)	Intervention 2 (n2)	Global Well-being	Pain	Tender Points	Observer-Measured Physical Function	Depression
McCain 1988[88]	6	Aerobic (18)	Flexibility (20)	—	NS	0.78 (0.12, 1.90)	1.12 (0.45, 1.79)	—
Jones 2002[83]	5	Strength (28)	Flexibility (28)	0.55 (0.02, 1.09)	0.66 (0.12, 1.20)	NS	Strength NS, flexibility –0.53 (–1.06, 0.00)	NS
Richards 2002[94]	8	Aerobic (69)	Relaxation (67)	NS	NS	NS	—	—
Martin 1996[87]	6	Mixed exercise (18)	Relaxation (20)	NS	—	1.01 (0.33, 1.69)	5.79 (4.28, 7.31)	—
Schachter 2003[95]	7	Aerobic, long-bout (51)	Aerobic, short-bout (36)	NS	NS	NS	NS	
Van Santen 2002[100]	8	Mixed exercise, high intensity (58)	Mixed exercise, self-selected intensity (85)	NS	NS	NS	NS	NS
Jentoft 2001[82]	5	Mixed exercise, water (18)	Mixed exercise, land (16)	0.93 (0.22, 1.64)	NS	—	NS	NS
Ramsay 2000[72]	3	Aerobic, supervised (35)	Aerobic, unsupervised (15)	NS	NS	NS	—	—
Da Costa 2005[77]	8	Mixed exercise, home-based (39)	Untreated control (40)	NS	—	—	—	NS
Buckelew 1998[74]	6	Aerobic (26)	Biofeedback only (25)	NS	NS	NS	—	NS
Altan 2004[73]	6	Mixed exercise (24)	Balneotherapy (22)	NS	NS	NS	NS	0.88 (0.27, 1.49)
Redondo 2004[93]	5	Mixed exercise (19)	Cognitive behaviour training (21)	NS	NS	NS	NS	NS
Van Santen 2002[99]	7	Mixed exercise (50)	Untreated control (79)	NS	NS	NS	NS	—

* Small change = 0.2, moderate change = 0.5, large change = 0.8. Data for comparison at 12 weeks or as close to 12 weeks as possible was used to calculate SMD. SMD = (mean change in Intervention 1 – mean changed in Intervention 2)/(pooled SD of change). NS: not significant.

Table 5. Clinically significant improvements (> 30% at posttest). From The Cochrane Library 2007, Issue 4, with permission.

Outcome Measure	Aerobic-only vs Control	Strength-only vs Control	Other Interventions Including Exercise
Depression	Buckelew 1998[74], Wigers 1996[102]	Hakkinen 2001[69]	Cedraschi 2004[76], Zijlstra 2005[103], Buckelew 1998[74], Altan 2004[73]
Tender points	Wigers 1996[102], Secan 2004[96]		
Global well-being (FIQ total)	Schachter 2003[95]	Hakkinen 2001[69], Valkeinen 2004[98]	
Physical function	Mengshoel 1992[89]		
FIQ rested	Schachter 2003[95]		
Self-efficacy for function	Schachter 2003[95]		
Pain		Hakkinen 2001[69]	
Anxiety			Mannerkorpi 2000[86], Cedraschi 2004[76]
SF-36 general health, SF-36 physical role, SF-36 vitality			Mannerkorpi 2000[86]
FIQ work missed			Cedraschi 2004[76] Zijlstra 2005[103]

FIQ: Fibromyalgia Impact Questionnaire.

mixed exercise programs appeal intuitively to the clinician who seeks to facilitate positive effects of 2 or 3 types of exercise, further investigations of individual types of exercise-only prescriptions compared with controls are needed first, to allow more complete understanding of the effects of exercise on FM.

Composite interventions and comparison groups were widely varied and resulted in limited evidence of positive effects and no effects for the active interventions. The one exception was for aerobic and education versus untreated control, where there was limited evidence of a medium effect on measures of physical function in favor of the intervention. Future studies employing designs that allow comparison of both composite interventions and specific components of the composite would help to clarify the effects of both composite and "pure" interventions.

Clinically significant improvements (defined as > 30%[35]) were observed sporadically and only when exercise interventions were compared to untreated control groups. Global well-being improved with 5 interventions, tender points with 2 interventions, and depression with 7 interventions. Remaining improvements of > 30% in pain, physical function, and sleep were noted with one intervention. These sporadic clinically significant effects align with large effect sizes, and were in general agreement with the finding of moderate to large effects in the metaanalyses and effect size analyses. We reiterate our observations that small sample sizes, high attrition rates, unclear or poor adherence to exercise, and lack of high quality studies must also inform the interpretation of the clinical relevance of findings reported here.

Evidence of longterm effects of exercise is difficult to interpret due to lack of consistency in followup periods, outcome measures, and control over other activities. It is well established that cessation of training will result in a loss of training effects over time. Further study of longterm effects should clarify the training volume needed to maintain improvements in FM signs and symptoms as well as the factors associated with adherence to exercise programs. For those who continue to exercise at any level, it is important to document the effects on FM signs and symptoms.

FM is a difficult syndrome to study because of what is often an unpredictable pattern of exacerbations of symptoms that make participation in exercise problematic for many people. Adverse effects of exercise were not consistently reported in included studies. Adverse effects that were reported suggest that some researchers may have regarded adverse effects exclusively as problems outside the sphere of symptoms of FM, while other researchers and participants categorized increases in symptoms such as pain and fatigue as adverse effects. Indeed, the 2 may be difficult to consistently separate. Creating and reporting on a standardized definition of adverse effects is required. It appears that most exercise programs described here can be safely completed by people with FM. Clinicians prescribing exercise are reminded to develop prescriptions that begin with low intensity, short duration exercise, increasing intensity and duration slowly, checking frequently with participants for flares of FM symptoms, and reducing training volume until such flares subside.

Researchers continue to overwhelmingly recruit women. While this is consistent with the well established demographics of FM, exercise studies of men with FM would provide welcome information. The issues around mixed and composite interventions have been identified above. While FM may be best managed clinically with a combination of measures, advancing the understanding of effects of exercise will be understood best through isolating the effects of specific types of exercise as rigorously as possible. Multifactorial research designs that can evaluate the separate and synergistic effects of interventions should be used.

The studies reviewed do not present a clear depiction of actual intensity or duration of exercise performed by the participants: no study analyzed or reported these 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 FM. While McCain, *et al*[88] and Hakkinen, *et al*[69] assert that individuals with FM can successfully perform vigorous aerobic and strength-training, respectively, many other researchers noted particularly poor adherence and adverse effects to high intensity exercise. Exercise performed at low intensity levels appears to be better tolerated, although some studies reported that participants had difficulty with exercise even at low intensities. It is unclear why such discrepancies exist.

Future interventions should specifically address training volume using the ACSM guidelines both for prescribing exercise and describing exercise performed. This includes detailed description of the prescribed exercise progression as well as systematic monitoring and reporting of adherence to prescribed exercise (outlining the intensity, duration, and frequency of exercised performed). This information will contribute to our understanding of the dose-response relationship for tolerance of exercise intensity and FM symptom improvement with each type of exercise. Further, consistent use of the ACSM classification of exercise intensity is needed in future studies so that researchers, clinicians, and individuals with FM have the same understanding of the limits of light, moderate, and vigorous intensity 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 the influence of and problems with exercise for individuals with FM. Evaluation of interventions using the CDC physical activity recommendations is also warranted in order to identify the effectiveness of both types of programs on FM symptoms, physical fitness, and health.

There are numerous outcome measures assessing the same constructs. This contributes to the large variability in metaanalyses. Core sets of outcome measures and agreement on how best to measure them would improve the validity of this research. While progress is being made with respect to agreement about domains that should be evaluated in studies of FM management[105], much work remains to be done. In this review, over 100 tests and instruments were used, including 8 for pain, 9 for cardiovascular fitness, and 13 for physical function. Greater agreement around "gold standards" for assessing outcomes in nonmedical management for FM is needed.

Conclusions. There is moderate quality evidence that shortterm aerobic training (at the intensity recommended to elicit increases in cardiorespiratory fitness) produces important benefits in people with FM in global outcome measures, physical function, and possibly pain and tender points. Analysis of percentage change reinforces results of the metaanalyses. There is limited evidence that strength training improves a number of outcomes including pain, global well-being, physical function, tender points, and depression. There is insufficient evidence regarding the effects of flexibility exercise. Strength and flexibility remain underevaluated as exercise prescriptions for people with FM. Despite a number of studies investigating the effect of combination management strategies including exercise, this area has also received inadequate study. There is limited evidence on a variety of other outcomes including stiffness, fatigue, and depression. Adherence to aerobic exercise interventions of many of the studies was poor. In order to clarify the effects of exercise on FM and thus offer individuals with FM and clinicians definitive guidance about exercise, we recommend that further research focus on larger sample sizes, high quality studies comparing one type of exercise to untreated controls, use of ACSM and CDC exercise and physical activity guidelines, detailed reporting of exercise prescription and adherence during the intervention and during longterm followup, determination of dose-response effects, creation of standardized definitions to report adverse effects, and use of standard outcome measures.

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