Dear Author,

Please check these proofs carefully. It is the responsibility of the corresponding author to check against the original manuscript and approve or amend these proofs. A second proof is not normally provided. Informa Healthcare cannot be held responsible for uncorrected errors, even if introduced during the composition process. The journal reserves the right to charge for excessive author alterations, or for changes requested after the proofing stage has concluded.

The following queries have arisen during the editing of your manuscript and are marked in the margins of the proofs. Unless advised otherwise, submit all corrections using the CATS online correction form. Once you have added all your corrections, please ensure you press the “Submit All Corrections” button.

Please review the table of contributors below and confirm that the first and last names are structured correctly and that the authors are listed in the correct order of contribution.

<table>
<thead>
<tr>
<th>Contrib. No.</th>
<th>Prefix</th>
<th>Given name(s)</th>
<th>Surname</th>
<th>Suffix</th>
<th>Degree(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>Alberto José</td>
<td>Cerrillo Urbina</td>
<td></td>
<td>MSc</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>Antonio</td>
<td>Garcia-Hermoso</td>
<td></td>
<td>PhD</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>Mairena</td>
<td>Sánchez-López</td>
<td></td>
<td>PhD</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>Vicente</td>
<td>Martínez-Vizcaíno</td>
<td></td>
<td>MD, PhD</td>
</tr>
</tbody>
</table>

**AUTHOR QUERIES**

Q1: The sentence “Pooled data were…” says there are three categories but listed more than that. Kindly check and confirm.

Q2: Kindly note that since references 40 and 42 in originally given are identical we have changed the citations of 42 as 40 and rest are renumbered accordingly. Please check and confirm that all the references have been cross-referred correctly and amend if necessary.

Q3: A declaration of interest statement reporting no conflict has been inserted. Please confirm the statement is accurate.

Q4: Please provide the last accessed date of the website for ref. 58.

Q5: Please provide last page range.

Q6: Please provide better quality artwork for all figures.
Effect of Exercise Programs on Symptoms of Fibromyalgia in Peri-Menopausal Age Women: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Alberto José Cerrillo Urbina, MSc1, Antonio García-Hermoso, PhD2, Mairena Sánchez-López, PhD1,3, and Vicente Martínez-Vizcaíno, MD, PhD2

1Social and Health Care Research Centre, University of Castilla-La Mancha, Cuenca, Spain, 2Facultad de Ciencias de la Salud, Universidad Autónoma de Chile, Talca, Chile, and 3School of Education, University of Castilla-La Mancha, Ciudad Real, Spain

ABSTRACT

Objectives: The aim of this review and meta-analysis was to summarize evidence regarding the effect of physical exercise programs on fibromyalgia syndrome symptoms in peri-menopausal age women, and the characteristics of these programs.

Findings: Nineteen randomized controlled trials \(N = 1077\) women satisfied the inclusion criteria. Methodological quality of papers was assessed using the PEDro scores. Data on the study, subject, and exercise program characteristics as well as assessment of changes in depression, fatigue, global well-being [overall feeling of well-being and health-related quality of life], pain, sleep, and stiffness were extracted. The studies were grouped according to the intervention program: land interventions [aerobic, combined [aerobic endurance, strength, and flexibility], vibrations, and alternative programs], and aquatic interventions. Nineteen studies were selected for systematic review, but clinical heterogeneity limited the meta-analysis to two aerobic, three combined, two alternative, and five aquatic studies.

Conclusions: In general, exercise programs have a positive effect on the symptoms of fibromyalgia in women in peri-menopausal age. The meta-analysis indicates that programs based on combined exercise and aquatic exercises have, respectively, a moderate \(d = 0.63; I^2 = 0\%\) and small effect \(d = 0.41; I^2 = 30\%\] on functional global well-being [assessed using the Fibromyalgia Impact Questionnaire total score]. Short-term interventions [12 weeks], including two to three sessions lasting 30–60 min each per week seem to improve symptoms in peri-menopausal age women with fibromyalgia, although high-quality studies with larger sample sizes are necessary to confirm these results.

KEYWORDS: Menopausal, perimenopause, fibromyalgia, exercise, global well-being, randomized controlled trial, systematic review, meta-analysis

INTRODUCTION

Fibromyalgia syndrome [FMS] is a syndrome characterized by widespread pain, fatigue, sleep disturbance and/or joint stiffness, paresthesia, anxiety, and stress (1,2). In addition, it has been associated with restrictions to participating in daily life activities and, in general, with a worse quality of life (2). The prevalence of FMS in the general population is estimated to be 0.5–5% (3), and it is higher in women [73–95%] than in men (4).

Women with FMS are less active than women without this condition (5). The symptoms characteristic of this syndrome might stop many patients performing sufficient physical activity to gain...
health benefits (6). However, studies have found that
programs including aquatic exercises (7), a combina-
tion of aerobic exercise and stretching at home (8),
pilates (9), yoga (10), qigong (11), or tai chi (12)
might relieve the symptoms of FMS and improve the
patient’s quality of life. Increasing benefits have been
reported when combined with exercise self-manage-
ment education (13,14).

During menopause, women frequently face vaso-
motor symptoms [hot flashes, night sweats], insom-
nia, paresthesia, nervousness, dizziness, weakness,
joint pain/muscle pain, headache, and palpitations
(15). These symptoms are often accompanied by
anxiety and stress, which facilitate the occurrence of
depression and weight gain (16,17). Around 3% of
women with FMS are at an age at which menopause
appears (3), and it is assumed that these women not
only experience the symptoms of both conditions
(15,16) but that the conditions also exacerbate each
other (18).

Physical exercise might be an effective strategy
to reduce the symptoms of both menopause (19,20)
and FMS, but to our knowledge the evidence
regarding its effectiveness has not yet been synthe-
sized. The purpose of the present systematic review
and meta-analysis was thus to summarize, in peri-
menopausal age women with FMS, evidence regard-
ing the ability of physical exercise programs to
control FMS symptoms, and the characteristics of
these programs.

METHODS

Data sources and searches
Five databases covering the period from 1980 to
October 2014 [PubMed, Scopus, Science Direct,
EBSCO [E-journal, CINAHL, SportDiscus], and The
Cochrane Library] were searched. Manual searches
were also conducted, but resulted in the inclusion of
no further articles. The search terms used were:
[“menopause” OR “postmenopausal” OR “premenopausal” OR “peri-menopause” OR “menopause
symptoms” OR “early menopause” OR “elderly
woman” OR “women” OR “female”] AND [“fibromyalgia” OR “fibromyalgia syndrome” OR “therapy
fibromyalgia” OR “treatment fibromyalgia”] AND
[“exercise” OR “physical fitness” OR “physical
activity” OR “mind-body therapies” OR “tai chi”
OR “yoga” OR “pilates” OR “qigong”].

Study selection

The criteria for inclusion were as follows: [1]
Patients: peri-menopausal age women [or mean
age 45–60 years] diagnosed with FM syndrome based
on American College of Rheumatology criteria (1);
[2] Type of study: randomized controlled trial
[RCT], in which the control group received no
physical exercise intervention; [3] Type of interven-
tion: physical exercise programs, participants that
were taking regular medication and could not
change the pharmacological treatment during the
trials, studies in which exercise was part of a multi-
component therapy involving a combination of
exercise and alternative therapy were excluded
(21); and also excluding those limited to testing
the effect of exercise on improving the components
of fitness and/or strength without reporting the
effect on the symptoms of FMS and menopause; [4]
Main outcome: for the meta-analysis we only
selected trials that used the Fibromyalgia Impact
Questionnaire [FIQ] as a measure of global well-
being, as previous research suggested that the
pooling of global well-being instruments might
result in biased meta-analyses (22); and [5] in
English or Spanish language. Finally, no restrictions
on frequency or duration of training were imposed.
The search was conducted between the 1st and the
15th of October 2014.

A protocol for data extraction was designed in
order to obtain the information from each selected
study according to predefined criteria listed below.
Verifcation was performed first by title and
abstract, considering the following questions: Is
the effect of exercise studied? Does the study
include peri-menopausal age women [or mean age
45–60 years] diagnosed with FMS syndrome? Does
it include women with FMS? Are symptoms or
quality of life in postmenopausal age women and/
or FMS reported? Does exercise with menopause
and/or FMS? Two negative responses were the
criterion for exclusion; therefore, when there was
one or no negative response, the evaluators [A.J.
and A.G.] proceeded to full text verifcation. When
there were doubts about a study’s eligibility from
the abstract, the authors examined the full text
of the article.

Data collection

A codebook was designed for data extraction
including the following major categories: [1] char-
acteristics of trial participants [number, age, year of
symptoms, and diagnosis]; [2] intervention features
[type, duration, frequency, and intensity of physical
exercise]; [3] results of outcomes [before and after
the intervention]. The two above-mentioned authors
independently extracted the data from each selected
article.
Quality assessment [risk of bias]

The quality of the studies was evaluated using Physiotherapy Evidence Database [PEDro] criteria: Trials [but not reviews or guidelines] were rated using the PEDro scale which includes 11 items designed for rating the methodological quality of RCTs. These items evaluate some quality criteria, including random allocation, concealment of allocation, comparability of groups at baseline, blinding of patients, therapists and assessors, analysis by intention to treat and adequacy (23).

Data analysis

For the data analysis, effect sizes $[d_{\text{Cohen}}]$ and 95% confidence intervals [CI] were calculated using $t$ scores, number of subjects, and standard deviation [standardized mean differences]. Cohen’s categories were used to evaluate the magnitude of the effect size, calculated according to the standardized mean difference $[d]$ statistic and considering scores of $d \geq 0.8$ as a large effect, scores from $0.5 \leq d < 0.8$ as medium, scores from $0.2 \leq d < 0.5$ as small, and scores $0.1 \leq d < 0.2$ as trivial (24). Pooled data were calculated for the studies, which were grouped into three categories: aerobic (8,13), combined (13,25,26), vibration (27), alternative (10,28) and aquatic (7,29–32) programs. Due to the heterogeneity of the outcome measures of the studies, only the changes in global well-being as assessed by the total score from the FIQ were considered for meta-analysis.

Assessment of heterogeneity

The heterogeneity of the studies was assessed using Cochran’s $Q$-statistic applied to the $d$ (33). The percentage of total variation across the studies due to heterogeneity was determined using $I^2$. The magnitude of the inconsistency was assessed as follows: small if $0 \leq I^2 \leq 25\%$, medium if $25\% < I^2 \leq 50\%$, and large if $I^2 > 50\%$ (34).

Sensitivity analysis

In order to analyze the influence of each study on the overall results, each study was deleted from the model once and the pooled analyses were conducted without this study in the model.

Assessment of bias

Given the small number of studies as well as the lack of between-study heterogeneity, bias assessment results were not incorporated into the statistical analysis (35).

RESULTS

Study selection

After screening all 572 studies identified by the literature search strategy, 501 did not meet the inclusion criteria, and thus 71 potentially relevant references were included in the next stage, during which the publication was re-evaluated based on the full text. Fifty-one studies were subsequently rejected, and the remaining 19 RCTs were grouped, according to the content of the intervention, into land interventions [aerobic, combined, vibrations, and alternative programs] and aquatic interventions [Figure 1].

Study characteristics and interventions

The characteristics of the 19 studies included in this review (7,8,10,11,13,25–32,36–41) are detailed in Table 1.

Exercises were supervised in eight studies by an instructor [a physical therapist] (7,10,11,28–30, 39,40). The other three were supervised in the first session and then subjects received a prescription for exercise at home (8,13,38). In some cases participants were taught how to monitor their heart rate and adjust their activity to maintain the correct exercise intensity (8). For their part, the studies did not report whether the subjects were unable to perform the exercises. Two studies included educational sessions (29,40). In one study, all the patients were asked not to change their medication during the study period (28). Finally, the studies, with one exception (29), did not take into account whether the subjects took medication.

Aerobic programs

Five studies evaluated the effectiveness of aerobic exercise in women with FM (8,13,36,38,39). The program content was based on aerobic work and stretching. In four of the studies, aerobic exercise consisted of walking (13,36,38,39), sometimes supplemented with dance (36); the remaining study involved conducting aerobic exercises at home (8). Exercise intensity began at 60–70% of maximum heart rate [HRmax] and was gradually increased to a maximum of 75–85%.

Combined programs

Four studies evaluated a combined exercise program [aerobic, endurance, strength, and flexibility] in women with FM (13,25,26,37). Aerobic exercise consisted of walking or dancing (37), and began at 60–70% of HRmax and was gradually increased to as
high as 75–85%, depending on the subjects’ adaptation. Muscle strengthening involved performing 12 sets of 8–10 repetitions with several muscle groups, using machines, dumbbells, or the subjects’ own weight. Finally, the program included 10 min of flexibility training with eight to nine exercises [one set of three repetitions, maintaining the stretched position for 30 s].

Vibration programs

Two studies evaluated the effect of aerobic exercise combined with a vibration platform in women with FMS (27,39). Vibration programs consisted of a series of six exercises [30 s each] repeated six times with a recovery of 3 min between repetitions. The whole body vibration [WBV] intensity was kept constant at 30 Hz (39), with six repetitions of tilting WBV at a frequency of 12.5 Hz, and a rest interval of 60 s between each repetition; the duration of each repetition was 30–60 s (27).

Alternative programs

Three studies evaluated the effect of yoga (10) or qigong (11,28) exercise in women with FMS. Each yoga class included ~40 min of gentle stretching poses, 25 min of mindfulness meditation, 10 min of breathing techniques, 20 min of didactic presentations on the application of yogic principles to optimal coping, and 25 min of group discussion. Qigong, within Chinese medicine, is one of the four main methods aimed at improving health, vitality, and healing (11). The sessions had a duration of ~90 min, body awareness therapy comprised various breathing and postural techniques and qigong. Relaxation, grounding, breathing, and concentration were performed either in a supine or standing position.

Aquatic programs

Seven studies evaluated the effect of aquatic exercise on women with FMS (7,29–32,40,41). Only two

FIGURE 1. Flowchart for the selection of studies. Three studies (13,36,39) were included in several groups as they had two experimental groups [aerobic and combined program interventions] and a control group.
<table>
<thead>
<tr>
<th>Study</th>
<th>Participants ((n, \text{years}))</th>
<th>Interventions EG</th>
<th>CG ((n))</th>
<th>Duration ((\text{weeks}))</th>
<th>Follow-up ((\text{weeks}))</th>
<th>Outcomes (symptoms)</th>
<th>Adherence (%)</th>
<th>PEDro score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Da Costa et al. (8)</td>
<td>(n = 79, 49.2)</td>
<td>Aerobic: aerobic exercise and stretching at home. Four sessions of 90° in the first 12 weeks. At home 60–120° weekly aerobic exercise and stretching</td>
<td>None ((n = 40))</td>
<td>12</td>
<td>12, 24, and 36</td>
<td>- Pain, fatigue, stiffness, anxiety, depression (FIQ)</td>
<td>77.21</td>
<td>8</td>
</tr>
<tr>
<td>Rooks et al. (13)</td>
<td>(n = 207, 48.0)</td>
<td>EG1 ((n = 51)): Aerobic: aerobic exercise (walking 45°) and flexibility, two times per week in sessions of 60°</td>
<td>Edu ((n = 50))</td>
<td>16</td>
<td>–</td>
<td>- Pain, fatigue, sleep, stiffness, anxiety (FIQ)</td>
<td>65.21</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EG2 ((n = 51)): Combined: aerobic and flexibility both for 20° and strength training for 25° (six exercises combination machines)</td>
<td></td>
<td></td>
<td></td>
<td>- HRQoL and physical function (SF-36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>EG3 ((n = 51)): Combined: EG1, Strength training (8–10 reps 8 muscle groups) and flexibility, sessions lasted 60°–90°</td>
<td></td>
<td></td>
<td></td>
<td>- Depression (BDI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>EG4 ((n = 51)): Combined: EG1, Strength training (8–10 reps 8 muscle groups) and flexibility, two times per week in sessions of 60°</td>
<td></td>
<td></td>
<td></td>
<td>- Self-efficacy scale pain and other symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sañudo et al. (36)</td>
<td>(n = 64, 55.9)</td>
<td>EG1 ((n = 22)): Aerobic exercise (walking and aerobic dance), two times per week in sessions of 60°</td>
<td>None ((n = 20))</td>
<td>24</td>
<td>12 and 24</td>
<td>- Pain, fatigue, sleep, stiffness (FIQ)</td>
<td>85.93</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EG2 ((n = 21)): Combined: EG1, Strength training (8–10 reps 8 muscle groups) and flexibility, sessions lasted 60°–90°</td>
<td></td>
<td></td>
<td></td>
<td>- Depression (BDI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>EG3 ((n = 21)): Combined: EG1, Strength training (8–10 reps 8 muscle groups) and flexibility, two times per week in sessions of 60°</td>
<td></td>
<td></td>
<td></td>
<td>- HRQoL (SF-36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>EG4 ((n = 21)): Combined: EG1, Strength training (8–10 reps 8 muscle groups) and flexibility, two times per week in sessions of 60°</td>
<td></td>
<td></td>
<td></td>
<td>- Depression (BDI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sañudo et al. (37)</td>
<td>(n = 42, 55.9)</td>
<td>Combined: Aerobic exercise (walking, running or dancing), strength training (8–10 reps 8 muscle groups) and flexibility, two times per week in sessions of 60°</td>
<td>None ((n = 20))</td>
<td>24</td>
<td>–</td>
<td>HRQoL (SF-36)</td>
<td>90.47</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Depression (BDI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sañudo et al. (25)</td>
<td>(n = 42, 55.5)</td>
<td>Combined: Aerobic exercise (walking), strength training (8–10 reps 8 muscle groups) and flexibility, two times per week in sessions of 60°</td>
<td>None ((n = 20))</td>
<td>24</td>
<td>–</td>
<td>Pain, fatigue, sleep, stiffness, anxiety, depression (FIQ)</td>
<td>90.47</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Depression (BDI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HRQoL (SF-36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Participants (n, years)</td>
<td>Interventions EG</td>
<td>Interventions CG (n)</td>
<td>Duration (weeks)</td>
<td>Follow-up (weeks)</td>
<td>Outcomes (symptoms)</td>
<td>Adherence (%)</td>
<td>PEDro score</td>
</tr>
<tr>
<td>-------</td>
<td>------------------------</td>
<td>------------------</td>
<td>---------------------</td>
<td>-----------------</td>
<td>-----------------</td>
<td>---------------------</td>
<td>---------------</td>
<td>------------</td>
</tr>
<tr>
<td>Meyer and Lemley (38)</td>
<td>n = 21, 49.5</td>
<td>EG1 (n = 8). Aerobic: low-intensity aerobic exercise (walking), three times a week, gradually increasing 12°–30°</td>
<td>None (n = 5)</td>
<td>24</td>
<td>12 and 24</td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression, physical function, wellness (FIQ). - Pain (HAQ) - Anxiety (SAI) - Depression (BDI) - Self-report functional ability (HQA-SDI)</td>
<td>38.09</td>
<td>2</td>
</tr>
<tr>
<td>Garcia-Martínez et al. (26)</td>
<td>n = 28, 59.3</td>
<td>EG2 (n = 8). Aerobic: EG1 high intensity</td>
<td>None (n = 14)</td>
<td>12</td>
<td>–</td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression (FIQ) - HRQoL (SF-36). - Self-esteem (The Rosenberg Self-Esteem Scale)</td>
<td>89.28</td>
<td>4</td>
</tr>
<tr>
<td>Alentorn-Geli et al. (39)</td>
<td>n = 36, 55.2</td>
<td>EG1 (n = 12). Aerobic: Aerobic activities (dance), stretching and relaxation techniques, two times per week in sessions of 90°</td>
<td>None (n = 12)</td>
<td>6</td>
<td>–</td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression (FIQ)</td>
<td>91.66</td>
<td>6</td>
</tr>
<tr>
<td>Olivares et al. (27)</td>
<td>n = 41, 53.0</td>
<td>EG2 (n = 12). Vibration: EG1 and WBV, six exercises on platform (30 s each), 30 Hz frequency and intensity amplitude 2 mm</td>
<td>None (n = 20)</td>
<td>12</td>
<td>–</td>
<td>- Health and physical function (FIQ) - HRQoL (15D)</td>
<td>87.80</td>
<td>8</td>
</tr>
<tr>
<td>Study</td>
<td>Sample Size</td>
<td>Intervention Details</td>
<td>Control Group</td>
<td>Duration</td>
<td>Outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------------</td>
<td>-------------</td>
<td>---------------------------------------------------------------------------------------</td>
<td>---------------</td>
<td>----------</td>
<td>--------------------------------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burckhardt et al. (40)</td>
<td>n = 86, 46.5</td>
<td>Pool exercise: two pool therapy sessions, and individual time to ride, walk or swim and Education Program (EG1)</td>
<td>None (n = 30)</td>
<td>12</td>
<td>- Pain, fatigue, stiffness, anxiety, depression, wellness (FIQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>12 and 32</td>
<td>- Sense of control over her disease (FAI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Scale Quality of life (QOLS-S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Self-Efficacy (Self-Efficacy scale)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Depression (BDI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- HRQoL (SF-36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Self-Efficacy (ASES-S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Quality of life (QOLS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Anxiety and depression arthritis impact (AIMS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression (FIQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- HRQoL (SF-36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Self-Efficacy (ASES-S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Quality of life (QOLS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Anxiety and depression arthritis impact (AIMS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression, wellness (FIQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- HRQoL (SF-36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Self-Efficacy (ASES-S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Quality of life (QOLS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Anxiety and depression arthritis impact (AIMS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mannerkorpi et al. (29)</td>
<td>n = 58, 45.0</td>
<td>Pool exercise: one time a week for 35°-and Education Program (coping strategies and symptoms) for six sessions of 1 h</td>
<td>None (n = 30)</td>
<td>24</td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression (FIQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Self-Efficacy (ASES-S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Quality of life (QOLS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Anxiety and depression arthritis impact (AIMS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression, wellness (FIQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- HRQoL (SF-36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Self-Efficacy (ASES-S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Quality of life (QOLS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Anxiety and depression arthritis impact (AIMS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression, wellness (FIQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- HRQoL (SF-36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Self-Efficacy (ASES-S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Quality of life (QOLS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Anxiety and depression arthritis impact (AIMS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression, wellness (FIQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- HRQoL (SF-36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Self-Efficacy (ASES-S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Quality of life (QOLS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Anxiety and depression arthritis impact (AIMS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression, wellness (FIQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- HRQoL (SF-36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Self-Efficacy (ASES-S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Quality of life (QOLS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Anxiety and depression arthritis impact (AIMS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression, wellness (FIQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- HRQoL (SF-36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Self-Efficacy (ASES-S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Quality of life (QOLS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Anxiety and depression arthritis impact (AIMS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression, wellness (FIQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- HRQoL (SF-36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Self-Efficacy (ASES-S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Quality of life (QOLS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Anxiety and depression arthritis impact (AIMS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression, wellness (FIQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- HRQoL (SF-36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Self-Efficacy (ASES-S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Quality of life (QOLS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Anxiety and depression arthritis impact (AIMS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression, wellness (FIQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- HRQoL (SF-36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Self-Efficacy (ASES-S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Quality of life (QOLS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Anxiety and depression arthritis impact (AIMS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression, wellness (FIQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- HRQoL (SF-36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Self-Efficacy (ASES-S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Quality of life (QOLS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Anxiety and depression arthritis impact (AIMS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression, wellness (FIQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- HRQoL (SF-36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Self-Efficacy (ASES-S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Quality of life (QOLS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Anxiety and depression arthritis impact (AIMS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression, wellness (FIQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- HRQoL (SF-36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Self-Efficacy (ASES-S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Quality of life (QOLS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Anxiety and depression arthritis impact (AIMS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression, wellness (FIQ)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Study</th>
<th>Participants (n, years)</th>
<th>Interventions EG</th>
<th>CG (n)</th>
<th>Duration (weeks)</th>
<th>Follow-up (weeks)</th>
<th>Outcomes (symptoms)</th>
<th>Adherence (%)</th>
<th>PEDro score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Munguia-Izquierdo and Legaz-Arrese (32)</td>
<td>n = 60, 50.0</td>
<td>Pool exercise: Exercises in pool hot water (32 °C) at breast height, slow walking and mobility 10’, slow progressive force exercises 10’–20’, aerobics 20’–30’ and low intensity exercises 10’, three times a week.</td>
<td>None (n = 25)</td>
<td>16</td>
<td>–</td>
<td>- Pain (VAS) - Pain, fatigue, stiffness, anxiety, depression, wellness (FIQ) - Cognitive function (PASAT and TMT)</td>
<td>88.33</td>
<td>5</td>
</tr>
<tr>
<td>Tomas-Carus et al. (7)</td>
<td>n = 33, 50.7</td>
<td>Pool exercise: Aerobic exercise, lower extremity strength with water resistance to waist (four sets of 10 knee flexion-extension) in hot water pool and upper limb strength exercises without water resistance (four sets of 10 repetition lifting arms over head), three times per week in sessions of 60’.</td>
<td>None (n = 16)</td>
<td>32</td>
<td>–</td>
<td>- Pain, fatigue, sleep, stiffness, anxiety, depression (FIQ) - Anxiety and Somatic disorders (STAI)</td>
<td>90.90</td>
<td>6</td>
</tr>
<tr>
<td>Munguia-Izquierdo and Legaz-Arrese (41)</td>
<td>n = 60, 50</td>
<td>Pool exercise: aerobic exercise, resistance exercise with slow strength in hot water up to his chest in pool (exercise multiple muscle groups) and relaxation, three times per week in sessions of 60’.</td>
<td>None (n = 25)</td>
<td>16</td>
<td>16 and 48</td>
<td>- Tender points (Syringe calibrated) - Health (FIQ) - Sleep Quality (PSQI) - Psychological State (SAI) - Cognitive Function (PASAT)</td>
<td>78.33</td>
<td>7</td>
</tr>
<tr>
<td>Mannerkorpi et al. (28)</td>
<td>n = 36, 45</td>
<td>Qigong: The qigong movements were performed for 20’ while standing still, focusing on relaxation, grounding and concentration. The sessions were completed with a short discussion about the movements. One time per week in sessions of 90’.</td>
<td>None (n = 17)</td>
<td>12</td>
<td>–</td>
<td>- Pain, fatigue, anxiety, depression (FIQ)</td>
<td>63.15</td>
<td>5</td>
</tr>
<tr>
<td>Haak and Scott (11)</td>
<td>n = 57, 53.3</td>
<td>Qigong: Practice of the Qigong, known as the Lotus method (He Hua Gigong). Nine group sessions, the total amount of time was 11.5h.</td>
<td>None (n = 28)</td>
<td>7</td>
<td>–</td>
<td>- Anxiety (STAI) - Depression (BDI) - Quality of Life (WHOQOL-BREF) - Daily self-recordings,</td>
<td>92.98</td>
<td>5</td>
</tr>
</tbody>
</table>
Exercise and Fibromyalgia in Women

Pain, sleep and psychological health and distress (VNS)

Carson et al. (10)

None (n=28)

n=53, 53.7

n=25. Yoga: stretching, relaxation, and meditation. One session per week in sessions of 75–90 min.

Methodological quality of studies

A total of 89.47% of the studies fulfilled at least 50% [5/10] of the PEDro criteria (23) [Table 1].

Participants

The 1077 women included were recruited mostly from general inquiries of Associations of Rheumatology and FMS, and ranged in age from 45 to 60 years [mean 51.53 years; SD 7.94 years]. Of these, 200 participated in aerobic activities, 50 participated in combined activities, 45 in vibration programs, 73 in alternative activities, and 167 in aquatic exercise programs. The average sample size of all groups was 28.16 subjects. The mean duration of symptoms was 13.43 ± 8.34 years (7,8,11,26–29, 31,32,40,41), the mean number of years after diagnosis was 7.63 ± 4.1 (8,10,13,39), and the mean number of tender points was 14.69 ± 2.85 (7,8,10, 11,27–29,31,32,40,41). However, five of the studies included in this systematic review did not provide information about these issues (25,30,36–38).

Adherence, dropouts and adverse effect

The adherence rate was high in all studies [greater than 65%], although in one study subjects abandoned the program due to illness and refusal to participate in a regular walking program [38.09%] (38). One study reported increased pain after the first 3–4 d due to the initial exercise intensity, requiring a reduction in the latter (29). A study presented low adherence, the reasons were time restrictions, surgery, feeling depressed, muscle inflammation, and high pain intensity (28). Another patient experienced an anxiety attack during the first session of WBV (39). To calculate the compliance of home-based exercise (8), following each exercise session, participants completed exercise logs which included information regarding the type of exercise performed; this methodology has previously been validated (42). Average weekly adherence rates were calculated as the ratio of the number of exercise sessions reported to the number of exercise sessions prescribed. 

studies reported the water temperature. The exercises were conducted in shallow pools with water temperatures of 32–33 °C (31,32). Aerobic exercises were performed at an intensity of 65–75% HRmax for 45–50 min, and were combined with exercises for strength in the lower extremities [four sets of ten repetitions of knee flexion and extension] and flexibility (7,31). The session ended with 10 min of cool-down with low intensity exercises and relaxation (7,41).

<table>
<thead>
<tr>
<th>Scale</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-36</td>
<td>Short-Form health survey with only 36 questions</td>
</tr>
<tr>
<td>GSI</td>
<td>The symptom checklist 90-revised</td>
</tr>
<tr>
<td>SCL-90R</td>
<td>The symptom checklist 90-revised</td>
</tr>
<tr>
<td>VAS</td>
<td>Visual Analogue Scale</td>
</tr>
<tr>
<td>BDI</td>
<td>Beck Depression Inventory</td>
</tr>
<tr>
<td>HAQ</td>
<td>The Pain scale of the health Assessment Questionnaire</td>
</tr>
<tr>
<td>SCL-90R</td>
<td>The symptom checklist 90-revised</td>
</tr>
<tr>
<td>GSI</td>
<td>The global severity index</td>
</tr>
<tr>
<td>BAI</td>
<td>Beck Anxiety Inventory</td>
</tr>
<tr>
<td>PASAT</td>
<td>The Paced Auditory Serial Addition Task</td>
</tr>
<tr>
<td>STAI</td>
<td>State-Trait Anxiety Inventory</td>
</tr>
<tr>
<td>PSQI</td>
<td>Pittsburgh Sleep Quality Index</td>
</tr>
<tr>
<td>CPAQ</td>
<td>The Chronic pain acceptance questionnaire</td>
</tr>
<tr>
<td>VMPCI</td>
<td>Vanderbilt Multidimensional Coping Inventory</td>
</tr>
<tr>
<td>WHOQOL-BREF</td>
<td>The World Health Organization Quality of Life BREF</td>
</tr>
<tr>
<td>VNS</td>
<td>Visual Numerological Scale</td>
</tr>
</tbody>
</table>

Ed: education program; None: no intervention; FIO: Fibromyalgia Impacts Questionnaire; SF-36: Short-Form health survey; GSI: The global severity index; BDI: Beck Depression Inventory; HAQ: Health Assessment Questionnaire; FIQ: Fibromyalgia Impact Questionnaire; QOL-S: Quality of Life scale; ASB: Arthritis Self-Efficacy Scales; AIMS: Arthritis Impact Measurement Scales; CPAQ: The Chronic pain acceptance questionnaire; VMPCI: Vanderbilt Multidimensional Coping Inventory; WHOQOL-BREF: The World Health Organization Quality of Life BREF; VNS: Visual Numerological Scale.
of sessions prescribed. In general, dropouts were mainly for reasons unrelated to the study [work problems, family, and FMS-unrelated diseases].

Outcomes measures

There was much variability in outcomes measures [Table 1]. The most commonly evaluated symptoms were functional global well-being and pain.

Synthesis of results

Table 2 describes the effect of physical exercise on each of the symptoms evaluated in women with FMS. Pain, fatigue, sleep, stiffness, and anxiety improved with all types of exercise. Depression and quality of life were also positively influenced by all types of program, with the exception of yoga exercises. Finally, self-esteem was only assessed in combined programs, which also had a positive effect. Finally, somatic disorders improved only with aquatic exercises, which had a positive influence on all symptoms.

Meta-analysis [findings for global well-being using the FIQ]

Figure 2 shows the $d$ [95% CI] for each study and each pooled subgroup. Overall, combined $d = -0.63, 95\%$ CI, $-0.99$ to $0.27$] and aquatic programs $d = -0.41, 95\%$ CI, $-0.68$ to $-0.14$] improved the global well-being of women with FMS $p < 0.05$ using fixed effect models. No statistically significant within-group heterogeneity was found [combined, $Q = 1.61, p = 0.43, I^2 = 0\%$; aquatic, $Q = 5.73, p = 0.22, I^2 = 30\%$]. There were not enough vibration studies with controlled comparison groups to carry out a meta-analysis.

Sensitivity analysis

With each outcome deleted from the model once, the results remained statistically significant across all deletions for both combined and aquatic programs. The results were also the same after removing studies including peri-menopausal age women (8,13,29,38,40).

DISCUSSION

To the best of our knowledge, this manuscript is the first systematic review and meta-analysis examining the evidence for the effect of physical exercise programs in peri-menopausal age women with FMS. In view of the results of the meta-analysis, the pooled analysis of the evaluated studies reveals that the effectiveness of exercise on controlling FMS symptoms is: [1] moderate for combined programs including aerobic endurance, strength, and flexibility exercises; [2] low for aquatic programs; and [3] not sufficiently proven to be able to recommend aerobic programs and yoga, although it should be noted that yoga is a promising alternative. Therefore, our findings are in accordance with previous reviews and recommendations for FMS management in other less specific populations (21,35,43–45).

Aerobic programs

Two meta-analyses (21,35) have reported a beneficial effect on global well-being in FMS patients. Our results, although showing a positive effect on some symptoms such as pain, stiffness, and depression, even after 9 months follow-up (8), did not confirm an improvement in global well-being $d = -0.10, 95\%$ CI, $-0.43$ to $0.24; p > 0.05$ [Figure 2]. It should be noted that some studies evaluating the
effectiveness of aerobic exercise did not meet our inclusion criteria (36,38), and that those studies revealed changes in the FIQ total score that were clinically relevant [\(\geq 14\%\)] (46). In general, analysis of the available studies indicates that low-intensity exercise might mitigate FMS symptoms in the medium-to-long term [24 weeks]; however, vigorous physical activity might increase pain in these patients (38).

Combined programs

The effectiveness of combined programs in the control of FMS symptoms has been reported in previous reviews (47). Our meta-analysis revealed an improvement [moderate effect] in global well-being \([d = -0.63, 95\% CI, -0.99 to 0.27]\) [Figure 2]. In addition, combined programs result in clinically relevant improvements in pain, health-related quality of life [HRQoL] and social well-being (25,48). Finally, it is noteworthy that this type of training does not exacerbate the symptoms of these women, and conversely diminishes their fatigue (48). For this purpose, it is essential to prescribe recovery times between workouts, and to plan the progression of both aerobic and strength exercises carefully.

In summary, our results highlight the importance of including endurance and flexibility exercises with aerobic work in physical exercise programs aimed at this population of patients (36) in order to maximize their physical function and well-being (49).

Vibration programs

The WBV vibration is a mode of exercise that has recently been utilized to improve muscle strength, bone density, and balance in healthy adults (50) and aging populations (51). The results of the current systematic review show that women who attended programs including WBV showed improvements in pain and fatigue (39), avoiding deterioration, and maintaining their HRQoL (27) to a greater extent than women in the control group. It is noteworthy that this type of exercise improves symptoms, especially pain and fatigue, from the start of the intervention, and that this improvement is maintained over time (39). A daily walking activity in addition to using WBV improves balance and prevents falls in this group of women (52). The two included studies that evaluated WBV (27,39) concluded that these programs mitigate symptoms and increase HRQoL.
Alternative programs

Several systematic reviews and meta-analyses have reported that alternative and meditative movement therapies [tai chi, yoga, and qigong] constitute a safe and effective strategy to improve FMS symptoms (53,54), although all also noted the need for high-quality studies with larger sample sizes to confirm these results. In accordance with these findings, the only study included yoga exercise in the current review testing the effectiveness of yoga in women with FMS showed that this intervention modality is moderately effective at controlling FMS symptoms in perimenopausal age women, although this requires further study. The qigong exercise showed mixed results, since one study reported that long-term programs do not appear to be generally recommendable for patients with FM with long-term symptoms due to the reported adverse effects (28), another study reported that the obtained results are merely placebo effects, even though authors concluded that their study supports that short qigong intervention has beneficial and long-lasting effects (11).

Aquatic programs

Studies that assessed aquatic training programs for patients with FMS indicated improvements in walking ability, well-being, and fatigue (29,49). The follow-up studies also indicated improvements in anxiety, depression, self-efficacy, and insight into the disease (43,55). Our meta-analysis showed that aquatic programs slightly improved global well-being [d = −0.41, 95% CI, −0.68 to −0.14] [Figure 2]. Overall, studies have shown improvements in pain threshold and a reduction in the number of tender points (32). These improvements seem to persist even in the long term (7), even in the case of anxiety and depression (43). Hot pools set at 32–33°C [a common water temperature for pool studies cited in this review] are well tolerated by people with FMS [they are more sensitive to cold] (32), generating a positive feeling of well-being and a reduction in pain and stiffness (29,49). The buoyancy of water facilitates the performance of movements, and thus also enhances the learning of relaxation and body awareness (49). Movements and exercise load can be easily adjusted to the limitations of each patient, which allows the duration of treatments in this medium to be lengthened (7). Therefore, aquatic exercise can be an effective intervention for women with FMS (43) and menopause.

Outcomes measures [assessments]

The outcome measure chosen [FIQ] has been one of the most frequently used assessment tools in the evaluation of FMS, and has been particularly useful as an outcome measure in FMS clinical trials. The FIQ has been translated from English into 12 languages, and is a valid 10-item instrument that assesses physical function, common symptoms, and general well-being (38). A total score may be obtained after normalization of some items and summing of all visual analog scales [pain, sleep, fatigue, morning stiffness, anxiety, and depression]. The questionnaire is scored from 0 to 100 [0–80 without job-related items], in which a higher score indicates a greater impact of the syndrome on the person.

The two most commonly used instruments in this systematic review were the Short-Form Health Survey [SF-36] and the Beck Depression Inventory [BDI]. These questionnaires cover the symptoms of both FMS and menopause. Studies often included other instruments for assessing parameters such as physical function, self-esteem, self-efficacy, cognitive function, and somatic disorders. The heterogeneity of these questionnaires makes it difficult to reach global conclusions regarding the results of these studies [Table 1].

Regarding the symptoms examined, aquatic programs evaluated all symptoms other than self-esteem [Table 2]. Meanwhile, the number of evaluated symptoms decreased gradually in aerobic, combined, vibration, and alternative programs. Studies evaluating alternative and vibration programs in perimenopausal age women with FMS syndrome are scarce, but have shown a positive effect on the few symptoms assessed. Symptoms less frequently included as outcomes of studies are self-esteem, self-efficacy, cognitive function, and somatic disorders and, in our opinion, all should be considered in future trials.

Approach of interventions

Most of the studies included in this systematic review and meta-analysis included group activities (7,10,11,13,25,27–32,36,37,39,41). Individual sessions are less expensive, although group exercise has a greater impact on health in this population (56). Individual strategies do not seem to produce psychological improvements, require more effort and perseverance, and the dropout rate is much higher (8). Thus, it seems reasonable to suggest that, in order to increase compliance, group strategies should be adopted in the implementation of physical
exercise programs in peri-menopausal age women with FMS, and that these programs might be reinforced by including individual exercises at home (8).

The lack of compliance to physical exercise in this population at the beginning of a program often depends on the appearance of pain after exercise; two sources have been suggested: sometimes interrupting the exercise causes pain (57), but sometimes pain appears as the intensity of exercise decreases (29). This problem seems to be reduced or avoided when implementing continued and progressive exercise (44). In this respect, several reports have shown improvements at 12 months (30), with relief of pain and alleviation of several emotional problems (31). The analgesic effect of physical exercise by breaking the vicious cycle of pain–immobility–pain might favor adherence (9). So, in our opinion, the intensity of exercise must be individually adjusted depending on the perception of pain (29). On the other hand, there is no evidence that high-intensity exercise produces more benefits than moderate exercise, and therefore it seems more appropriate to recommend physical exercise at low–moderate intensity for this population, and to tailor the prescription depending on the perception of pain (29,38).

Finally, some studies included educational programs in their designs (13,29,30,40). Educational programs appear to be complementary and beneficial for this population of patients (13,29). In general, these programs aim to develop self-control strategies to perform daily activities, to control symptoms, and to integrate physical activity into daily routines. Therefore, treatment programs combining education and exercise have been shown to improve function, symptoms, well-being and self-efficacy, and they may be more effective than either treatment alone (49).

Limitations
First, the search strategy was not conducted according to the Cochrane Collaboration procedures (58), although we employed exhaustive search methods. Second, due to heterogeneity between studies [there were numerous outcomes measures assessing the same constructs], it was only possible to perform a meta-analysis of global well-being measured using the FIQ (21). Similarly, some studies could not be included in the meta-analysis due to the lack of data for calculating the effect size [we repeatedly contacted primary authors for clarification and additional information, although responses were not always obtained]. Third, we limited the age range of the participants to the peri-menopause, since after this stage the characteristic symptoms of menopause often disappear, and therefore, do not overlap with the symptoms of FMS. Fourth, we have tried to contact with authors to request the age of the subjects and PEDro scale information, but have had no response from authors. Five, due to studies did not confirm the presence of peri-menopause, we decided to include all studies whose women mean age was from 45 to 60 years.

CONCLUSIONS
In our opinion, our results have clinical relevance and show that combined exercise programs [aerobic endurance, strength, and flexibility] and aquatic programs improve various symptoms in peri-menopausal age women with FMS. [pain, fatigue, sleep disorders, anxiety, depression, somatic symptoms, quality of life, well-being, and self-esteem]. Thus, the results of the meta-analysis reinforce findings showing moderate and small change in global well-being through these programs. On the other hand, there is less evidence regarding the benefits of aerobic exercise, vibration, and alternative programs [yoga and qigong]. In general, short-term interventions [12 weeks] including two to three sessions lasting 30–60 min each per week seem to mitigate FMS symptoms in peri-menopausal age women. However, due to the small number of studies on each type of intervention, the results need to be interpreted with caution.

Directions for future research
Suggestions for future research follow the EPICOT structure for formulating research recommendations (59). The main elements are: [E] Evidence [current]: physical exercise provides benefits for health-related fitness (60) and may decrease bone loss in menopausal women (61); [P] Population: studies in women with FMS syndrome and peri-menopause; [I] Intervention: aquatic exercise programs combined with educational programs; [C] Comparison: no active treatment (treatment as usual control) or education treatment group; [O] Outcomes: to evaluate the long-term effects on health in this population; [T] Time stamp: December 2015. The optional elements were: [d] Disease burden: the prevalence of FMS plus menopause is three percent (3); [i] Timeliness: long-term interventions [at least 24 weeks, two sessions a week, each lasting 60 min]; [s] Study type: randomized controlled trial.
DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

REFERENCES


Exercise and Fibromyalgia in Women

1081 38. Meyer BB, Lemley KJ: Utilizing exercise to affect the
1082
Fernandez-Sola J: Six weeks of whole-body vibration exercise
improves pain and fatigue in women with fibromyalgia.
1085
1086 40. Burckhardt CS, Mannerkorpi K, Hedenberg L, Bjelle A:
A randomized, controlled trial of physical activity and
physical training for women with fibromyalgia. J Rheumatol
1087
1088 41. Munguia-Izquierdo D, Legaz-Arrese A: Assessment of the
effects of aquatic therapy on global symptomatology in patients
with fibromyalgia syndrome: A randomized controlled trial.
1090
1091 42. King AC, Haskell WL, Taylor CB, Kraemer HC, DeBusk RF:
Group- vs home-based exercise training in healthy older men
and women. A community-based clinical trial. JAMA 266:
1092
1093 43. Gowans SE, deHueck A: Pool exercise for individuals with
1094
1095 44. Busch AJ, Webber SC, Brachaniec M, Bldonde J, Bello-Haas
VD, Danyliw AD, Overend TJ, et al.: Exercise therapy for
1096
1097 45. Thomas EN, Blotman F: Aerobic exercise in fibromyalgia:
1098
1099 46. Bennett RM, Bushmakin AG, Cappelleri JC, Zlateva G, Sadowsky
AB: Minimal clinically important difference in the fibromyalgia
1100
1101 47. Busch AJ, Overend TJ, Schacter CL: Fibromyalgia treatment:
The role of exercise and physical activity. Int J Clin Rheumatol
1102
1103 48. Valkeinen H, Alen M, Hakkinen A, Hannonen P, Kukkonen-
Harjula K, Hakkinen K: Effects of concurrent strength and
endurance training on physical fitness and symptoms in
postmenopausal women with fibromyalgia: A randomized
1104
1105 49. Mannerkorpi K, Iversen MD: Physical exercise in fibromyalgia
and related syndromes. Best Pract Res Clin Rheumatol 17:
1106
1107 50. Torvinen S, Kannus P, Sievanen H, Jarvinen TA, Pasanen M,
Kontulainen S, Javinen TL, et al.: Effect of four-month vertical
whole body vibration on performance and balance. Med Sci
1108
1109 51. Iwamoto J, Otaka Y, Kudo K, Takeda T, Uzawa M,
Hirabayashi K: Efficacy of training program for ambulatory
alternative exercise for fibromyalgia: A meta-analysis. J Pain
1110
1111 52. Kawanabe K, Kawashima A, Sashimoto I, Takeda T, Sato Y,
Iwamoto J: Effect of whole-body vibration exercise and muscle
strengthening, balance, and walking exercises on walking ability
1112
1113 53. Langhorst J, Klose P, Dobos GJ, Bernardy K, Haiser W:
Efficacy and safety of meditative movement therapies in
fibromyalgia syndrome: A systematic review and meta-analysis
of randomized controlled trials. Rheumatol Int 33: 193–207,
2013.
1114
1115 54. Mist SD, Firestone KA, Jones KD: Complementary and
alternative exercise for fibromyalgia: A meta-analysis. J Pain
1116
1117 55. Bowens SE, deHueck A, Voss S, Richardson M: A randomized,
controlled trial of exercise and education for individuals with
1118
1119 56. Kawanabe K, Kawashima A, Sashimoto I, Takeda T, Sato Y,
Iwamoto J: Effect of whole-body vibration exercise and muscle
strengthening, balance, and walking exercises on walking ability
1120
1121 57. Langhorst J, Klose P, Dobos GJ, Bernardy K, Häuser W:
Efficacy and safety of meditative movement therapies in
fibromyalgia syndrome: A systematic review and meta-analysis
of randomized controlled trials. Rheumatol Int 33: 193–207,
2013.
1122
1123 58. Mist SD, Firestone KA, Jones KD: Complementary and
alternative exercise for fibromyalgia: A meta-analysis. J Pain
1124
1125 59. Bowens SE, deHueck A, Voss S, Richardson M: A randomized,
controlled trial of exercise and education for individuals with
1126
1127 60. Asikainen TM, Kukkonen-Harjula K, Miilunpalo S: Exercise
and related syndromes. Best Pract Res Clin Rheumatol 17:
1128
1129 61. Munguia-Izquierdo D, Legaz-Arrese A: Assessment of the
effects of aquatic therapy on global symptomatology in patients
with fibromyalgia syndrome: A randomized controlled trial.
1130
1131 62. King AC, Haskell WL, Taylor CB, Kraemer HC, DeBusk RF:
Group- vs home-based exercise training in healthy older men
and women. A community-based clinical trial. JAMA 266:
1132
1133 63. Gowans SE, deHueck A: Pool exercise for individuals with
1134
1135 64. Busch AJ, Webber SC, Brachaniec M, Bldonde J, Bello-Haas
VD, Danyliw AD, Overend TJ, et al.: Exercise therapy for
1136
1137 65. Thomas EN, Blotman F: Aerobic exercise in fibromyalgia:
1138
1139 66. Bennett RM, Bushmakin AG, Cappelleri JC, Zlateva G, Sadowsky
AB: Minimal clinically important difference in the fibromyalgia
1140
1141 67. Busch AJ, Overend TJ, Schacter CL: Fibromyalgia treatment:
The role of exercise and physical activity. Int J Clin Rheumatol
1142
1143 68. Valkeinen H, Alen M, Hakkinen A, Hannonen P, Kukkonen-
Harjula K, Hakkinen K: Effects of concurrent strength and
endurance training on physical fitness and symptoms in
postmenopausal women with fibromyalgia: A randomized
1144
1145 69. Mannerkorpi K, Iversen MD: Physical exercise in fibromyalgia
and related syndromes. Best Pract Res Clin Rheumatol 17:
1146
1147 70. Torvinen S, Kannus P, Sievanen H, Jarvinen TA, Pasanen M,
Kontulainen S, Javinen TL, et al.: Effect of four-month vertical
whole body vibration on performance and balance. Med Sci
1148
1149 71. Iwamoto J, Otaka Y, Kudo K, Takeda T, Uzawa M,
Hirabayashi K: Efficacy of training program for ambulatory
alternative exercise for fibromyalgia: A meta-analysis. J Pain
1150
1151 72. Kawanabe K, Kawashima A, Sashimoto I, Takeda T, Sato Y,
Iwamoto J: Effect of whole-body vibration exercise and muscle
strengthening, balance, and walking exercises on walking ability
1152
1153 73. Langhorst J, Klose P, Dobos GJ, Bernardy K, Häuser W:
Efficacy and safety of meditative movement therapies in
fibromyalgia syndrome: A systematic review and meta-analysis
of randomized controlled trials. Rheumatol Int 33: 193–207,
2013.
1154
1155 74. Mist SD, Firestone KA, Jones KD: Complementary and
alternative exercise for fibromyalgia: A meta-analysis. J Pain