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SYSTEMATIC REVIEW

Effects of different protocols of physical exercise on fibromyalgia syndrome treatment: systematic review and meta-analysis of randomized controlled trials

Maria Luiza L. Albuquerque[1] · Diogo Monteiro[2,3,5] · Daniel A. Marinho[1,2] · Guilherme T. Vilarino[4] · Alexandro Andrade[4] · Henrique P. Neiva[1,2]

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Abstract

Physical exercise has been used as a form of treatment for fibromyalgia, however, the results indicate the need for further investigations on the effect of exercise on different symptoms. The aim of the study was to synthesize and analyse studies related to the effect of exercise in individuals with fibromyalgia and provide practical recommendations for practitioners and exercise professionals. A search was carried out in the Web of Science, PubMed, and Scopus databases in search of randomized clinical trials (RCT) written in English. A meta-analysis was performed to determine the effectiveness of different types of exercise on the fibromyalgia impact questionnaire (FIQ), and the protocol period and session duration on the pain outcome. Eighteen articles were eligible for a qualitative assessment and 16 were included in the meta-analysis. The exercise showed large evidence for the association with a reduction in the FIQ (SMD − 0.98; 95% CI − 1.49 to − 0.48). Protocols between 13 and 24 weeks (SMD − 1.02; 95% CI − 1.53 to − 0.50), with a session time of less than 30 min (SMD − 0.68 95% CI − 1.26 to − 0.11) or > 30 min and < 60 min (SMD − 1.06; 95% CI − 1.58 to − 0.53) presented better results. Better results were found after combined training protocols and aerobic exercises. It is suggested that exercise programs lasting 13–24 weeks should be used to reduce pain, and each session should last between 30 and 60 min. In addition, the intensity should always be carried out gradually and progressively.
PROSPERO registration number CRD42020198151.

Keywords Fibromyalgia · Exercise · Intensity · Rheumatic diseases · Resistance training · Aerobic exercise

Abbreviations

ACR	American College of Rheumatology
FIQ	Fibromyalgia impact questionnaire
MHR	Maximum heart rate
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
RCT	Randomized clinical trials
RM	Repetition maximum
SMD	Standardized mean difference

✉ Guilherme T. Vilarino
guilhermevilarino@hotmail.com

1 Department of Sport Sciences, University of Beira Interior, Covilhã, Portugal

2 Research Center in Sports Sciences, Health Sciences and Human Development, CIDESD, Covilhã, Portugal

3 ESECS—Polytechnique of Leiria, Leiria, Portugal

4 Laboratory of Sport and Exercise Psychology, Human Movement Sciences Graduate Program, College of Health and Sport Science, Santa Catarina State University (UDESC), Pascoal Simone, 358, Coqueiros, Florianópolis, Santa Catarina CEP 88080-350, Brazil

5 Life Quality Research Centre, CIEQV, 2400-901, Leiria, Portugal

Introduction

Fibromyalgia is defined as a chronic rheumatological disease that causes sensory changes and musculoskeletal pain [1]. Different aspects are presented regarding the origin of the pathology, with some authors defending the hyperexcitability of the central nervous system, while others point to the imbalance of neurotransmitters [2–4].

Although a vast number of symptoms are related to fibromyalgia, widespread pain, fatigue, and muscle weakness are the primary symptoms [5–7]. As the exact cause of the origin of fibromyalgia is not known, although there is a clinical diagnosis for this condition, there is a possibility of bias during the performance of tests or of underestimated diagnoses [8]. Treatment for this syndrome aims to reduce the signs and symptoms presented by the individual in different domains (e.g., neurological, rheumatological) [7–9].

Physical exercise has frequently been used as a form of non-pharmacological treatment [10–12]. Besides it being a low-cost intervention, exercise has come to be described as one of the best allies in reducing symptoms, in addition to promoting health [12–15]. Reducing the number of tender points, and the impact of the disease on daily activities and pain, as well as improving sleep and functional capacity, are just some of the benefits of exercise in individuals with fibromyalgia [16–18]. In addition to the aforementioned physical factors, physical exercise is effective in improving pain perception and modulation, in addition to improving vitality, depression, and quality of life [19–23].

In the literature, it is possible to find several studies that aim to evaluate the effects of aerobic exercises [24–27], strength exercises [10, 15, 28–30], flexibility [31, 32], and combined exercises [33, 34]. Some recently published systematic reviews demonstrate that exercise practice is efficient in reducing common physical and psychological symptoms among individuals with fibromyalgia, however, the results indicate the need for further investigations on the effect of exercise on different symptoms [15, 35]. Furthermore, investigations into the prescription of physical exercise and its implications are essential both for patients who need treatment and for health professionals who can use evidence-based clinical practice to make the best decisions during treatment.

Therefore, given the known benefits of physical exercise in the population with fibromyalgia and the lack of indicators regarding the type, duration, and intensity of exercise, the present study aims to synthesize and analyse the effects of different physical exercise protocols in individuals with fibromyalgia, through seeking to investigate the effectiveness of the interventions performed and their effects on the main symptoms.

Methods

Search strategy

The literature search was carried out in the Web of Science, Medline, and Scopus platforms, using the PICO (population, intervention, control, and outcome) research strategy. Literature published up to 14 April 2022 was included. Two reviewers (MLLA and HPN) independently performed the search and assessed the eligibility of each article. Doubts regarding the inclusion or exclusion of studies were resolved by discussion between the two independent researchers. To guarantee the quality of the study the protocols established by PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) were used [36]. The search terms used in the database search were: "fibromyalgia", "Physical Activity", "Exercise", "Strength", "flexibility", "Aerobic Exercise", "Resistance Exercise", "Randomized Controlled Trial", using the search expression Fibromyalgia) AND (Exercise) OR (strength) OR (flexibility) OR (aerobic) OR (resistance) OR (randomized controlled trial). Although there was no restriction in the search period, there was a specification as to the type of document and language, with scientific articles written in English being selected. This review was registered with the international prospective register of systematic reviews PROSPERO (registration no. CRD42020198151).

Eligibility criteria

The inclusion criteria for this systematic review were: (i) randomized clinical trials (RCT); (ii) a study population over the age of eighteen; (iii) a diagnosis of fibromyalgia following the criteria established by the American College of Rheumatology (ACR) [1, 37]; (iv) an intervention protocol for a minimum period of four weeks; (v) aimed to evaluate the effects of a presential protocol consisting of physical exercise; (vi) use assessment instruments that analyse at least one of the symptoms presented by typical fibromyalgia patients (e.g., pain, depression, sleep, anxiety …); and (vii) present at least one intervention group and a control group without any type of intervention. The following documents were excluded from this systematic review: (i) literature reviews of any kind; ii) theses and dissertations (master's and doctorate); (iii) articles composed of multidisciplinary/interdisciplinary interventions; (iv) educational or cognitive-behavioural therapies; (v) articles that presented subjects with more than one medical diagnosis in addition to fibromyalgia; vi) investigations without a control group and physical exercise programs specific to a single modality or therapy.

Selection of studies

The selection of articles was carried out following the PRISMA recommendations [36]. Reference software (Endnote, Clarivate Analytics, Philadelphia, USA) was used to unify articles from different databases and then exclude duplicates. After the exclusion of duplicates, the title was read and then the abstracts were read, with non-relevant articles excluded. The articles eligible for the qualitative analysis were selected after complete reading of the remaining articles according to the inclusion and exclusion criteria previously mentioned in this study. This process was carried out by two reviewers (MLLA and HN) to reduce the risk of bias.

Data extraction

After defining the articles for inclusion in this study, data were extracted related to the parameters evaluated by each article and their respective analysis instruments, intervention period, number of sessions, details of the interventions, and their effects compared to control groups. The respective variables analysed in the articles were also extracted (e.g., pain, anxiety, depression). All extracted variables are detailed in the results. The authors of the articles that did not provide the necessary data for the meta-analysis were contacted by e-mail to acquire the information. For those who did not respond, the necessary information was acquired through old systematic reviews.

Bias risk assessment

The analysis of the risk of bias was performed by two researchers, separately (MLLA and HPN) and was carried out according to the methods recommended by Cochrane [38], bias according to, the following criteria: (1) generation of random sequence; (2) concealment of allocation; (3) blinding of participants and professionals; (4) blinding of outcome evaluators; (5) incomplete outcomes; (6) report of selective outcome; (7) other sources of bias. For these criteria, the following classifications were used: high risk of bias, low risk of bias, and uncertain risk of bias (the latter case when there was a lack of information or when there was any kind of doubt about the information found in the articles). For the creation of graphics referring to the risk of bias, Review Manager Software (RevMan, The Nordic Cochrane Center, Copenhagen, Denmark), version 5.4 was used.

Data analysis

The results of the studies were recalculated to determine the magnitude of the differences in the studied variables between the control and experimental groups. The percentage difference between the experimental group and the control group ([experimental group – control group/control group) × 100]) was calculated considering the average values presented by the studies that provided this information. To identify the gains or losses from the exercise, symbols were used to compare the control group with the experimental group, specifically ">" (higher than) and "<" (lower than). The meta-analysis was performed with RevMan 5.4 to determine the effects of the different types of exercises (i.e., aerobic, strength, and combined) and exercise durations (intervention period and time per session) on pain and on the FIQ domains. These variables were the most commonly used outcomes in the included studies, and thus considered the most relevant for further analysis. To assess the differences between the exercise interventions and the control group, the means and respective standard deviations were used as effect measures. Only articles that provided this information were included in the meta-analysis. The I^2 was used to measure the heterogeneity of the RCTs, considering the classification established by Higgins et al. [39] ($I^2 < 25\%$ low; $I^2 = 50–75\%$ moderate; $I^2 > 75\%$ high).To classify the magnitude of the effect size of the SMD the category of Cohen was selected (d values between 0.2 and 0.5 represent a small effect size; between 0.5 and 0.8 a medium effect size; greater than 0.8 a large effect size) [40]. Negative values of effect size in this meta-analysis favour the exercise intervention, while positive values favour the control group. All articles classified as combined interventions performed two different exercise modalities (e.g., aerobic and strength) in their intervention protocols. Aerobic interventions were considered those exercise programs aiming to increase cardiovascular response to exercise (e.g., increased heart rate, oxygen uptake) by performing specific activities such as walking, running, aquatic exercise, cycling, while the strength interventions included exercises aiming to improve muscular fitness by exercising a muscle or a muscle group against an external resistance or using bodyweight resistance.

Results

After the exclusion of duplicates, a total of 420 articles were eligible for this review. Following the analysis of the titles, 193 articles were read in full to check the criteria, resulting in 18 articles to be included in the quality review and 16 articles for the meta-analysis. Figure 1 shows the PRISMA flow diagram.

Table 1 presents the characteristics of the included studies, specifically participants, duration, intervention, and main outcomes. Among the different evaluated variables, pain was the most analysed parameter (77.8% of the articles). The second and third most investigated variables were the FIQ and strength with 61.1% and 55.6% of the manuscripts, respectively. The minimum intervention period presented by one of the articles was 8 weeks [26, 41], while the maximum period lasted 8 months [42]. Regarding the frequency and duration of each session, 55.6% of the articles had a frequency of two sessions per week and 44.4% included three sessions per week. The shortest session duration, in one study, was 30 min[43] and the maximum session time ranged from 60 to 90 min [44].

Regarding the exercise protocols used, only one study evaluated a stretching protocol (4.7%) [19], six addressed strength exercises (28.6%) [10, 19, 45, 46, 51, 54], and six

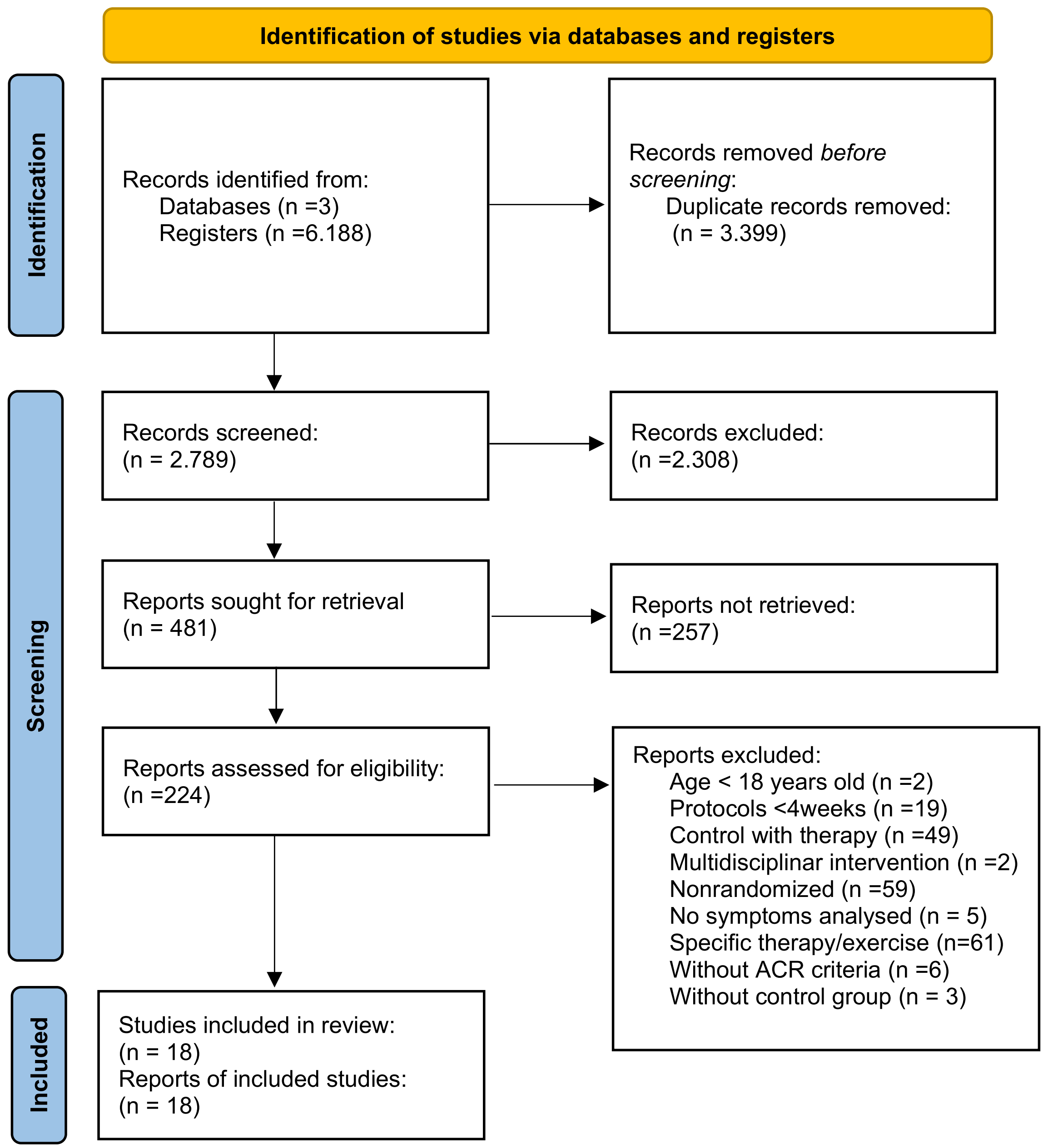


Fig. 1 Flowchart of the selection and steps to identify articles according to PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)

focused on aerobic exercise (28.6%) [26, 34, 43, 46, 48, 52]. The strength programs were carried out on the ground in four studies and one study combined aquatic and ground exercise. The aerobic exercise was implemented on the ground ($n=5$) and combining aquatic and ground exercise ($n=1$). Most studies (38.1%) carried out a combined protocol. Of the eight articles with combined therapies, 50% were performed in water and 50% used the ground. From the total of 18 articles, approximately 39% used water as a means of intervention and 61% used the ground to perform the exercises.

Regarding the intensity, while some studies started with 40–50% RM and progressed up to 80% RM, for strength gain most articles used 60–65% RM as a starting point. Eight (44.5%) articles created a protocol for the progression of exercise intensity each week, while others performed the adjustment at each session depending on the participant's tolerance.

Some outcomes were assessed by more than one article and specific exercise protocols had a greater impact on symptom improvement in the populations evaluated, namely: reduced pain (36.9%) [46], reduced FIQ (34.9%) [46],

Table 1 General characteristics of included studies

Study	Participants	Duration	Intervention	Outcomes
Andrade et al. 2017 [24]	TG: 27 CG: 27	16 wks 2 days/week 45 min	TG: Heated pool Warm up: 10 min; Cool down: 5 min AT: 30 min (10 min each level) in 3 HR levels Level 1: 80% VAT; Level 2: 110% VAT; Level 3: 100% VAT CG: no intervention	PPT: TG < CG 21% Pain: TG > CG – 15.6% FM impact: TG < CG – 22.9% Well-being: TG > CG 46,8% VO_2 Peak: TG > CG 28.5%
Assumpção et al. 2018 [19]	TG_1: 14 TG_2: 16 CG: 14	12 wks 2 days/week 40 min	TG_1: Stretching Weeks 1 a 4: 3 rep. 30 s; Weeks 5 a 8: 4 rep. 30 s; Weeks 9 a 12: 5 rep. 30 s TG_2: Resistance Session 1 e 2: no load; Session 3 a 12: 0,5 kg each week if slightly intense on the Borg scale CG: no intervention	FM impact: TG_1 > CG 5% FM impact: TG_2 < CG – 12.1% QoL: TG_1 > CG 60.5% QoL: TG_2 > CG 30.7%
Gowans et al. 2001 [43]	CG: 23 TG: 27	23 wks 3 days/week 30 min	TG: heated pool and gym Week 1–6: heated pool; week 7–23: 1 session heated pool and 2 gym Warm-up: 5 min—stretching AT: 20 min—60–75% MHR Cool down: 5 min—stretching CG: no intervention	Depression: TG < CG – 20.6% FM impact: TG < CG – 11.5% Anxiety: TG < CG – 20.1% Physical function: TG > CG 17% General mental health: TG > CG 38.3% Auto-efficacy: TG > CG 29.4%
Häkkinen et al. 2001 [10]	TG: 11 CG: 10 HG: 12	21 wks 2 days/week	TG e HG: Strength training Warm-up and cool down: bicycle ergometer and muscle stretching ST: 6–8 exercises; Week 1–3: 15–20 rep. (40–60% RM); Week 4 a 7: 10–12 rep. (60–70% RM); Week 8 a 14: 8–12 rep. (60–80% RM); Week 15 a 21: 5–10 rep. (70–80% RM) CG: no intervention	Muscle strength: TG > CG 2400% Cervical Pain: TG > CG – 56.9% Depression: TG > CG – 52% EMG: ND
Häkkinen et al. 2002 [45]	TG: 11 CG: 10 HG: 12	21 wks 2 days/week	TG e HG: Warm-up and cool down: bicycle ergometer and muscle stretching ST: 4–5 exercises; Week 1–7: 3–4 sets, 10–20 rep. (40–70% RM); week 11: 3–4 set, 10–20 rep. (40–60%/60%-70% RM); Week 14: 3–4 set, 10–20 rep. (40–60%/60%-80% RM); 2 leg extensor exercises: Week 1–7: 3–5 set, 8–12 rep. (low loads); 5–8 rep. (high loads) CG: no intervention	Intergroups results: ND

Table 1 (continued)

Study	Participants	Duration	Intervention	Outcomes
Izquierdo-Alventosa et al. 2020 [41]	TG: 16	8 wks	TG: Low-intensity physical exercise	Pain catastrophizing: TG < CG – 26.1%
	CG: 16	2 days/week	Warm up: walking slow pace and moving the main joint structures	Anxiety: TG < CG – 11.2%
		60 min	TG: Sessions 1 to 4: 15 min -walking at a comfortable speed, 25 min 10-exercise circuit and cooling down for 20 min; 1-kg and velocity 60 beats. Sessions 5 to 16: many repetitions as possible in 1 min of the exercises of the 10-exercise circuit for 40 min, loads 0.5–2 kg for the upper limbs, 1–3 kg for the lower limbs	Depression: TG < CG – 14.8% Stress: TG < CG -7.6% Pain acceptance: TG > CG 5.2% PPT: TG > CG 38% QoL: TG > CG – 8.3% SPFC: TG > CG – 10%
			Cool down: walking slow pace, trunk stretching, and breathing deeply, while lying on the floor	
			CG: no intervention	
Kayo et al. 2012 [46]	TG1: 30	16 wks	TG_1: Walking program	Pain: TG1 < CG – 21.2% Pain: TG2 < CG – 26.9% FM impact: TG1 < CG – 34.9% FM impact: TG2 < CG – 23.8% QoL: TG1 > CG 52.6% QoL: TG2 > CG 34.9%
	TG2: 30	3 days/week	Warm-up: 5–10 min, cool down: 5 min—stretching	
	CG: 30	60 min	WP: 25–30 min a 50 min (Week 16); Week 1: 40–50% HRR; Week 16: 60–70% HRR	
			TG_2: Strength training	
			ST: Week 1–3: 3 set, 10 rep; Week 4–16: 3 set, 15 rep; Week 5–16: with load	
			CG: no intervention	
Letieri et al. 2013 [47]	TG: 33	15 wks	TG: heated pool	FM impact: TG < CG – 32.4% Depression: TG < CG – 35.4% Pain: TG < CG – 28.2%
	CG: 31	2 days/week	Warm up and cool down: 5 min—stretching and relaxation	
		45 min	Exercises: 35 min—strength, mobility, balance, coordination, and agility	
Mengshoel, Komnaes e Førre, 1992 [48]	TG: 11	20 wks	TG:	Static endurance UE: TG > CG 11.5%
	CG:14	2 days/week	AT: low impact exercises (120-150 bpm) focused lower extremities and upper extremities exercises between periods of rest	
		60 min	CG: no intervention	

Table 1 (continued)

Study	Participants	Duration	Intervention	Outcomes
Munguia-Izquierdo et al. 2007 [49]	TG: 35	16 wks	TG: heated pool	PPT: ND
	CG:25	3 days/week	Warm up: 10 min—Mobility and walking; Cool down: 10 min—relaxation	
		50–70 min	ST: 10-20 min; Week 1–2: 8 exercises, 1 set, 10–15 rep.; Week 3–4: 8–10 exercises, 1–2 set 10–15 rep.; Week 5–8: 8–10 exercises, 1–2 set 10–12 rep.; Week 9–12: 8–10 exercises, 2–3 set 10–12 rep.; Week 13–16: 8–10 exercises, 2–3 set 8–10 rep	
			AT: 20–30 min; Week 1–2: 50–60% MHR; Week 3 a 4: 55–65% MHR; Week 5–8: 60–70% MHR; Week 9–12: 65–75% MHR; Week 13–16: 70–80% MHR	
			CG: no intervention	
Munguia-Izquierdo et al. 2008 [50]	TG: 29	16 wks	TG: heated pool	Nº TP: TG < CG − 26% Sleep Quality: TG < CG − 13% Cognitive function: TG > CG 23% Endurance strength: TG > CG 201.3%
	CG: 24	3 days/week	Warm up: 10 min—Mobility and walking; Cool down: 10 min—relaxation	
	HG: 25	50–70 min	ST: 10-20 min; Week 1–2: 8 exercises, 1 set, 10–15 rep.; Week 3–4: 8–10 exercises, 1–2 set 10–15 rep.; Week 5–8: 8–10 exercises, 1–2 set 10–12 rep.; Week 9–12: 8–10 exercises, 2–3 set 10–12 rep.; Week 13–16: 8–10 exercises, 2–3 set 8–10 rep	
			AT: 20–30 min; Week 1–2: 50–60% MHR; Week 3 a 4: 55–65% MHR; Week 5–8: 60–70% MHR; Week 9–12: 65–75% MHR; Week 13–16: 70–80% MHR	
			CG: no intervention	
Nichols e Glenn 1994 [26]	TG: 10	8 wks	TG:	Psychological profile: TG < CG − 6.5% Disability: TG > CG 61.4%
	CG: 9	3 days/week	Warm up and cool down: Stretching and Walking	
			AT: 20 min—Walking (60–70% MHR)	
			CG: no intervention	
Roman et al. 2015 [51]	TG: 20	18 wks	TG: 2 sessions heated pool and 1 on-land	Strength: TG > CG 29.4% Balance: TG > CG 57.2% FM impact: TG < CG − 14.3% PPT: TG > CG 86,4% No. TP: TG < CG − 35.7% Pain: TG < CG 26%
	CG:19	2 days/week	Warm up and cool down: 5 min—Stretching and Walking	
		60 min	ST and balance: 40 min—circuit training, 1–3 set, 8–12 rep., 0.5–2 kg	
			CG: no intervention	
Sañudo et al. 2015 [52]	TG: 16	24 wks	TG:	HRV: TG > CG 2.8% Anxiety: TG < CG − 24%
	CG: 12	3 days/week	Warm up: 10 min; cool down: 5–10 min—easy movements	
		45–60 min	and slow walking	
			AT: 15–20 min (60–65% MHR)	
			IT: 15 min, 75–80% MHR, six repetitions of 1.5 min, with 1 min interpolated rest intervals	
			CG: no intervention	

Table 1 (continued)

Study	Participants	Duration	Intervention	Outcomes
Sañudo et al. 2011 [53]	TG.: 18	24 wks	TG:	FM impact: TG < CG − 14.9% QoL: TG > CG 30.4%
	CG: 20	2 days/week	Warm up/cool down: 10 min, flexibility exercises	
		45–55 min	AT: 10–15 min (65–70% MHR)	
			ST: 15–20 min, circuit training, 8 exercises, 1 set, 8–10 rep., 1–3 kg	
			CG: no intervention	
Sañudo et al. 2010 [34]	TG1: 18	24 wks	TG_1: Aerobic Training	Intergroups results: ND
	TG2: 17	2 days/week	Warm up and cool down: 10 min—easy movements and slow walking	
	CG: 20	45–60 min	AT: 15–20 min (60–65% MHR)	
			IT: 15 min, 75–80% MHR, six repetitions of 1.5 min, with 1 min interpolated rest intervals	
			TG_2: Aerobic Training + Strength training	
			Warm up and cool down: 10 min, stretching	
			AT: 10–15 min (65–70% MHR)	
			ST and Stretching: 15–20 min, 8 exercises, 1 set, 8–10 rep., 1–3 kg; Flexibility—10 min, 8–9 exercises, 1 set, 3 rep. (30 s)	
			CG: no intervention	
Tomás-Carus et al. 2008 [42]	TG: 15	8 months	TG: heated pool	FM impact: TG < CG − 20% Anxiety: TG < CG − 15.5% Functional capacity: TG > CG − 10.60%
	CG:15	3 days/week	Warm up and cool down: 10 min -slow walks and easy movements	
		60 min	PT: aerobic exercises—10 min (60–65% MHR); strength exercises—20 min, 4 sets, 10 rep.; aerobic exercises—10 min (60–65% MHR)	
			CG: no intervention	
Valkeinen et al. 2008 [44]	TG: 13	21 wks	TG: strength and endurance training (2:1 and 1:2 alternate weeks)	MAC: TG > CG 2.8% MMS TG > CG 2.6% Fatigue TG < CG − 33.9%
	CG: 11	3 days/week	ST: week 1–4: 2 set 40–60% RM; week 5–7: 2 set 50–70% RM; week 8–11: 2 set 60–70% RM; week 12–14: 2 set 60–80% RM; week 15–18: 2 set 60–80% RM; week 19–21: 2 set 70–80% RM	
		60–90 min	AT: Week 1–7: 30 min heart rate < aerobic threshold; week 8 a 4: heart rate < aerobic threshold, between aerobic and anaerobic thresholds and > anaerobic threshold; week 15 a 21: alternating thresholds	

TG treatment group, *CG* control group, *wks* weeks, *AT* aerobic training, *VAT* ventilatory anaerobic threshold, *PPT* pressure pain threshold, *FM* fibromyalgia, *rep*. repetitions, *QoL* quality of life, *HG* health group, *ST* strength training, *EMG* electromyographic activity, *ND* non defined, *WP* walking program, *HRR* heart rate reserve, *SPFC* self-perceived functional capacity, FC functional capacity, UE upper extremity, *MHR* Maximum heart rate, *TP* tender points, *IT* interval training, *HRV* heart rate variability, *PT* physical training, *MAC* maximal aerobic capacity, *MMS* maximal muscle strength improved quality of life (60.5%) [19], increased pressure pain threshold (86.4%) [51], reduced depression (52%) [10] and anxiety (24%) [52], and increased balance (57.2%) [51].

Regarding the risks of bias, although all the articles included were RCTs, 55.6% of the studies demonstrated a low risk of bias for generation of random sequence and 61.1% an uncertain risk of bias for allocation concealment (Fig. 2). Only 38.9% of the articles had a low risk of bias for blinding of participants and professionals.

The meta-analysis presented in Fig. 3 provides a comparison of exercise and a control group for the FIQ because of different types of exercise intervention. All exercise interventions were shown to have a beneficial effect on reducing the FIQ (SMD − 0.98; 95% CI − 1.49 to − 0.48). As for the analysis of the subgroups, the aerobic training demonstrated a high effect size while the strength intervention had a moderate effect. Despite the high heterogeneity presented by the combined intervention groups, the effect size (SMD − 1.34; 95% CI − 2.2 to − 0.06) also favoured the practice of exercise to reduce the FIQ.

Considering the pain outcome as one of the most relevant variables for the individual with fibromyalgia, a deeper analysis of the intervention period (Fig. 4) and session time (Fig. 5) was performed. No significant results were found for protocols with a duration lower than 12 weeks or greater than 24 weeks. Protocols between 13 and 24 weeks, on the other hand, had a high effect size, but with a high heterogeneity index.

Regarding the session duration, only one study performed sessions with a duration equal to or lower than 30 min, with moderate effects on pain relief. There was a reduction in pain in the intervention subgroups with interventions between 30 and 60 min, despite high heterogeneity observed between the studies. When the intervention lasted for more than 60 min, the result was not significant (Fig. 5).

Discussion

The main objective of this systematic review with meta-analysis was to investigate the influence of physical exercise programs in individuals diagnosed with fibromyalgia and to summarize the respective effects. Results showed that strength training, aerobic training, and combined exercise programs resulted in favourable effects on fibromyalgia symptoms. Among these, the aerobic and combined interventions presented the highest effects on reducing the FIQ. Flexibility interventions, however, were not significant for reducing it. Greater improvements in pain relief seemed to occur in exercise programs that lasted between 13 and 24 weeks and using training sessions that lasted no more than 60 min. Although the physical and psychosocial status impact the response to the treatment of fibromyalgia, and the progression of exercise depends on the symptoms presented by the individual [55], the training protocols that followed a gradual progression of intensity, specifically monitoring heart rate or % of maximal load, seemed to more consistently reduce symptomatology [10, 19, 41, 46, 50].

Analyzing the results included in this review, almost all articles had a beneficial effect on at least one of the evaluated parameters. The training programs that had the most positive effects on a greater number of symptoms were in the studies of Roman et al. [51], Gowans et al. [43] and Munguia-Izquierdo and Legaz-Arrese [50], during strength training, aerobic, and combined interventions, respectively. In line with these results, Geneen et al. [56] showed that aerobic activities and strength exercises proved to be beneficial for this population and Bidonde et al. [57] suggested an effect of combined interventions.

The literature presents different training methods (i.e., aerobic, strength, flexibility and combined interventions), but a common factor among them is the use of aquatic exercises, either alone or alternating with land-based exercise. The properties of water and the physical activity performed in a heated swimming pool seemed to positively affect different systems of the human body [58, 59]. As a consequence, these physiological changes can assist in the relaxation of body muscles, improve blood flow, and allow muscle strengthening due to the resistance generated by the water [58, 59]. Given the benefits, the practice of physical exercise in water has been strongly indicated to reduce common symptoms in this specific population, such as pain, anxiety, and depression as well as being effective for increasing the physical capacity of these individuals [25, 60, 61].

The meta-analysis allowed us to further understand the effects of exercise in reducing the impact of fibromyalgia assessed by the FIQ. The three different types of exercises were able to improve the indicators associated with the FIQ and consequently reduce the fibromyalgia symptoms. The aerobic and strength protocols showed a moderate and high effect size; however, the combined protocols presented the greatest effect size. The high heterogeneity reveals a trend towards the need for further investigations on combined interventions with a better focus on methodological quality. Although blinding of intervention between evaluators and participants is desirable, blinding is difficult in intervention trials [62]. These results can be corroborated by Bidonde et al. [57] who presented low to moderate evidence of combined exercise in the different parameters related to fibromyalgia.

To facilitate the analysis of the intervention period and frequency, the articles were divided into categories: (i) < 12 weeks (3 months); (ii) 13–24 weeks (between 3 and 5 months); and (iii) > 24 weeks (> 6 months). All the aerobic

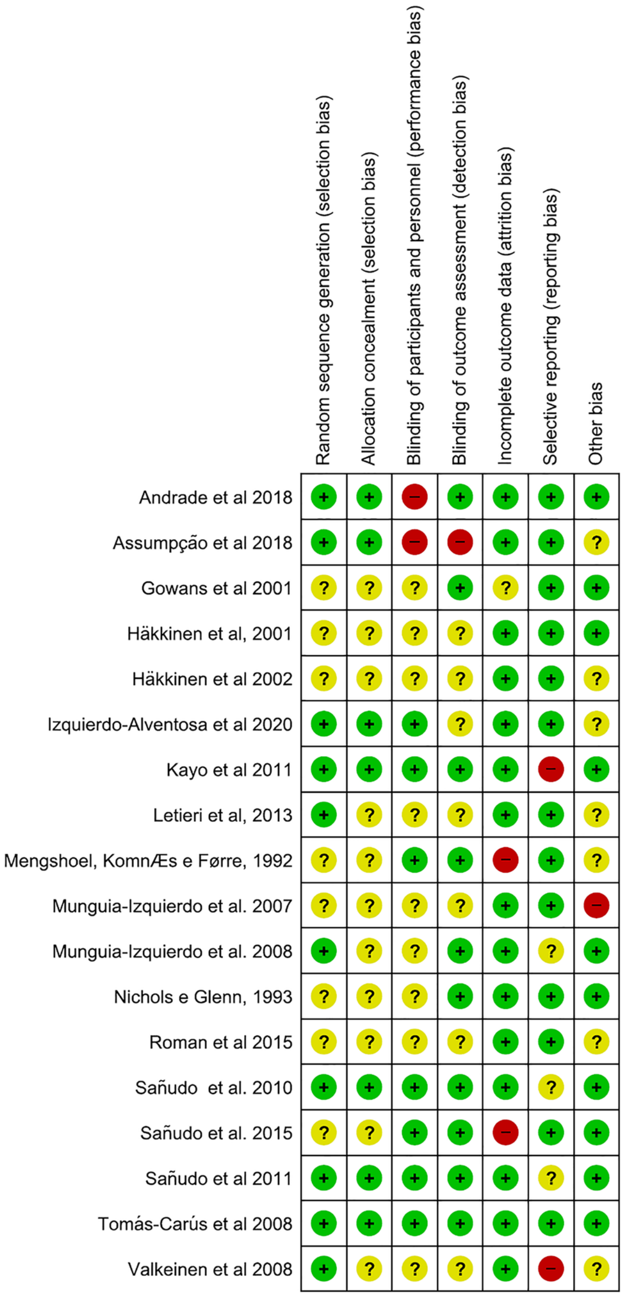


Fig. 2 Summary of the risk of bias for each item for each article included in the study (+ low risk, ? unclear risk, − high risk.)

exercise programs included in the meta-analysis had a duration of over 13 weeks. To promote positive effects, it is suggested that an aerobic protocol should have a frequency of two to three sessions per week and an intervention period composed of at least 4–6 weeks [63]. These results are supported by a recent study that also emphasized the importance of strength training in addition to aerobic training with 30–60 min per session [14]. In addition to this information, specifically for the pain outcome, protocols below 12 weeks and above 24 weeks did not demonstrate significant effects between the treatment group and control. Although these results favour the period of 13–24 weeks, it is essential to critically analyze these results, due to the heterogeneity between the protocols. This difference may exist due to differences in intensities and environment (aquatic or ground), among other factors, in addition to the methodological quality of each study. One can speculate that short durations are not enough to provide adaptations in pain, and very long interventions might lead to some reduced efficacy. However, we should be aware that only two studies focused on interventions that lasted 12 weeks or less [19, 42], and only one study focused on interventions longer than 24 weeks [43]. It would be expected that longer durations would result in greater improvements, but the low and steady intensity throughout the training program, the limited recovery of the patients' condition, and/or the few participants (decreasing the statistical power to detect some changes) may have influenced the results [43]. Nevertheless, from a qualitative perspective, all articles showed benefits in at least one of the assessed symptoms, reinforcing the results of Busch et al. [64] For the articles classified in the second classification (13–24 weeks), there was a predominance of interventions with a frequency of two training sessions per week, including aerobic, strength, or combined protocols.

The frequency and intensity of symptoms can incapacitate individuals diagnosed with fibromyalgia. One way to interrupt the vicious circle of fibromyalgia is to replace 30 min of physical inactivity with light to moderate physical activity [20]. The results of this meta-analysis revealed that greater effects were observed after exercises performed for 30–60 min. To ensure the benefits of interventions lasting up to 30 min, further studies are needed.

In relation to strength training and despite the differences found in the articles regarding the intensity adopted at the beginning of the exercises performed, it is suggested that the intervention start with low intensity (40% of 1RM) and gradually increase the intensity [30]. With an aerobic focus, the most common intensity used was approximately 40–65% of maximum heart rate (MHR) in the initial phase of the exercise programs and then progression was made up to 80% MHR. Interventions should follow a well-structured protocol, that respects the individual's evolution. Each exercise should be performed with the appropriate intensity to reduce the risk of symptom increase. Otherwise, there will be a risk of worsening symptoms [65, 66].

Several studies reported the benefits of aerobic exercise for reducing the signs and symptoms presented by patients with fibromyalgia [27, 67, 68]. Six articles had the objective of evaluating the effects of an aerobic intervention protocol, but only four studies used instruments to assess cardiovascular parameters or performed analysis of aerobic capacity. The other studies chose to evaluate mainly the subjective

Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Aerobic Intervention								
Andrade et al 2018	49.2	14.7	27	63.8	9.2	27	9.4%	-1.17 [-1.75, -0.59]
Gowans et al 2001	48.6	16.2	27	54.9	13	23	9.4%	-0.42 [-0.98, 0.14]
Kayo et al 2011	36.7	22.5	30	55.6	14.1	30	9.5%	-0.99 [-1.53, -0.46]
Sañudo et al. 2010	52.1	18.1	18	63.7	17.1	20	9.1%	-0.65 [-1.30, 0.01]
Subtotal (95% CI)			**102**			**100**	**37.4%**	**-0.82 [-1.15, -0.48]**
Heterogeneity: Tau² = 0.03; Chi² = 4.05, df = 3 (P = 0.26); I² = 26%								
Test for overall effect: Z = 4.73 (P < 0.00001)								
Strength Intervention								
Kayo et al 2011	42.4	22.3	30	55.6	14.1	30	9.6%	-0.70 [-1.22, -0.18]
Roman et al 2015	54.7	14.7	20	63.8	15.4	19	9.1%	-0.59 [-1.24, 0.05]
Subtotal (95% CI)			**50**			**49**	**18.7%**	**-0.66 [-1.06, -0.25]**
Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P = 0.80); I² = 0%								
Test for overall effect: Z = 3.17 (P = 0.002)								
Combined Intervention								
Letieri et al, 2013	53.07	6.36	33	77.52	4.09	31	7.8%	-4.49 [-5.43, -3.55]
Munguia-Izquierdo et al. 2007	63.1	10.3	29	62.7	14.1	24	9.5%	0.03 [-0.51, 0.57]
Sañudo et al. 2010	52.9	13.2	17	63.7	17.1	20	9.0%	-0.68 [-1.35, -0.02]
Sañudo et al 2011	54.9	12.5	18	64.5	11.4	20	9.0%	-0.79 [-1.45, -0.12]
Tomás-Carús et al 2008	5.2	1.6	15	6.5	1	15	8.6%	-0.95 [-1.71, -0.19]
Subtotal (95% CI)			**112**			**110**	**44.0%**	**-1.34 [-2.62, -0.06]**
Heterogeneity: Tau² = 1.98; Chi² = 67.83, df = 4 (P < 0.00001); I² = 94%								
Test for overall effect: Z = 2.05 (P = 0.04)								
Total (95% CI)			**264**			**259**	**100.0%**	**-0.98 [-1.49, -0.48]**
Heterogeneity: Tau² = 0.63; Chi² = 72.98, df = 10 (P < 0.00001); I² = 86%								
Test for overall effect: Z = 3.80 (P = 0.0001)								
Test for subgroup differences: Chi² = 1.13, df = 2 (P = 0.57), I² = 0%								

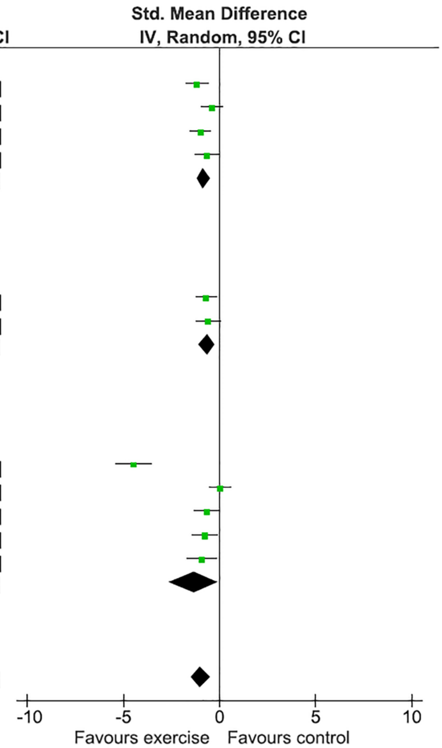


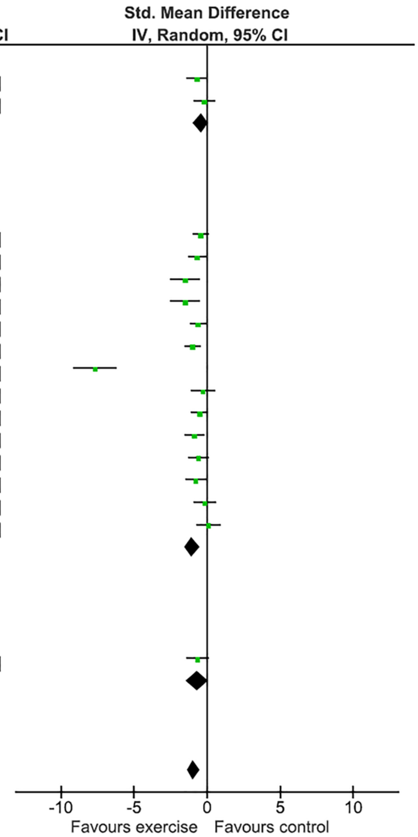
Fig. 3 Effectiveness of exercise on the impact of fibromyalgia

effects of the applied training program, with positive results on pain, depression, quality of life, the FIQ, and the pressure pain threshold. Although aerobic exercise is widely indicated, different factors can create barriers and consequently affect the results expected. For instance, aerobic exercise programs with high intensities can be directly related to the individual's non-adherence to training [69]. All aerobic exercise protocols were performed with a maximum time of 60 min, with the Gowans et al.[43] study having the shortest aerobic intervention time, consisting of 30 min with significant results. As it is known that individuals with fibromyalgia have a low level of physical condition and consequently low tolerance to exercise, some authors suggested a reduction in the duration of the sessions and an increase in the frequency of exercises for the population with fibromyalgia [17, 70, 71]. Moreover, professionals should prioritize lower intensities to favour adherence to the activities and maintenance of the frequency throughout the program [17, 70, 71].

When focusing on the strength training programs, studies showed a moderate effect size on the FIQ. The literature suggests that these protocols can reduce the number of tender points, improve balance, and reduce depression [15, 30]. These results are corroborated by the Busch et al. [64] study. Forty-three percent of the studies that presented a session time between 30 and 60 min included a strength protocol as the intervention and the higher percentages of strength gain occurred in medium intervention programs [10]. Among the studies that assessed the effects of strength training, the study by Hakkinen et al. [10] obtained the highest percentage strength gain, despite the lower number of sessions during the intervention period when compared to the study of Roman et al. [51]. Roman et al. [51] achieved good strength gains and positive results in other subjective parameters, such as the FIQ and a reduction in the pain threshold. The good results in the study of Hakkinen et al. [10] could be caused by the clearly defined progression of loads every 3 weeks and consequent adjustments that were made repeatedly to guarantee progression and adaptations. On the contrary, the study of Roman et al. [51] consisted of a strength intervention, carried out on the ground and in water, with variations in intensity and no clear description of load progression, perhaps leading to lower positive results related to strength gain. These differences between the types of training, in addition to the alternation in training environments, may justify the different gains between studies since exercises performed in a heated aquatic environment bring more benefits when compared to the ground [25].

The combined protocols demonstrated a high effect, specifically in reducing the FIQ. Busch et al. [64] found some limitations regarding the combined exercise protocols performed, which culminated in a lack of data regarding this exercise type. In a recent study carried out by

Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
≤ 12 weeks								
Assumpção et al 2018	4.4	3	16	6.4	2.7	14	5.9%	-0.68 [-1.42, 0.06]
Izquierdo-Alventosa et al 2020	-42.94	7.96	16	-40.81	13.54	16	6.0%	-0.19 [-0.88, 0.51]
Subtotal (95% CI)			**32**			**30**	**11.9%**	**-0.42 [-0.92, 0.09]**
Heterogeneity: Tau² = 0.00; Chi² = 0.90, df = 1 (P = 0.34); I² = 0%								
Test for overall effect: Z = 1.61 (P = 0.11)								
13 to 24 weeks								
Andrade et al 2018	5.4	2.4	27	6.4	2.1	27	6.4%	-0.44 [-0.98, 0.10]
Gowans et al 2001	-56	26.1	23	-39.7	20.9	27	6.4%	-0.68 [-1.26, -0.11]
Häkkinen et al 2002	24	19	11	60	27	10	5.2%	-1.49 [-2.49, -0.50]
Häkkinen et al, 2001	24	19	11	60	27	10	5.2%	-1.49 [-2.49, -0.50]
Kayo et al 2011 (1)	-3.27	1.92	30	-2.15	1.56	30	6.5%	-0.63 [-1.15, -0.11]
Kayo et al 2011 (2)	-3.94	2.02	30	-2.15	1.56	30	6.4%	-0.98 [-1.52, -0.44]
Letieri et al, 2013	44.22	2.76	33	63.73	2.21	31	3.9%	-7.68 [-9.14, -6.22]
Mengshoel, KomnÆs e Førre, 1992	60	21.6	11	66	21.6	14	5.8%	-0.27 [-1.06, 0.53]
Munguia-Izquierdo et al. 2007	66.9	14.7	29	75.8	20	24	6.4%	-0.51 [-1.06, 0.04]
Roman et al 2015	6.47	3.1	20	8.75	1.73	19	6.1%	-0.88 [-1.54, -0.22]
Sañudo et al. 2010 (3)	69.7	17.4	17	80.5	18.1	20	6.1%	-0.59 [-1.26, 0.07]
Sañudo et al. 2010 (4)	67.2	15.6	18	80.5	18.1	20	6.1%	-0.77 [-1.43, -0.11]
Sañudo et al. 2015	6.7	2.2	16	7	1.7	12	5.9%	-0.15 [-0.89, 0.60]
Valkeinen et al 2008	34.15	24.57	13	31.74	19.6	11	5.7%	0.10 [-0.70, 0.91]
Subtotal (95% CI)			**289**			**285**	**82.2%**	**-1.02 [-1.53, -0.50]**
Heterogeneity: Tau² = 0.82; Chi² = 102.68, df = 13 (P < 0.00001); I² = 87%								
Test for overall effect: Z = 3.87 (P = 0.0001)								
> 24 weeks								
Tomás-Carús et al 2008	4.6	2.6	14	6.4	2.7	14	5.8%	-0.66 [-1.42, 0.10]
Subtotal (95% CI)			**14**			**14**	**5.8%**	**-0.66 [-1.42, 0.10]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.69 (P = 0.09)								
Total (95% CI)			**335**			**329**	**100.0%**	**-0.91 [-1.34, -0.48]**
Heterogeneity: Tau² = 0.68; Chi² = 105.03, df = 16 (P < 0.00001); I² = 85%								
Test for overall effect: Z = 4.14 (P < 0.0001)								
Test for subgroup differences: Chi² = 2.67, df = 2 (P = 0.26), I² = 25.1%								



Footnotes
(1) Aerobic intervention
(2) Strength intervention
(3) Combined intervention
(4) Aerobic intervention

Fig. 4 Effectiveness of protocol period on pain outcome

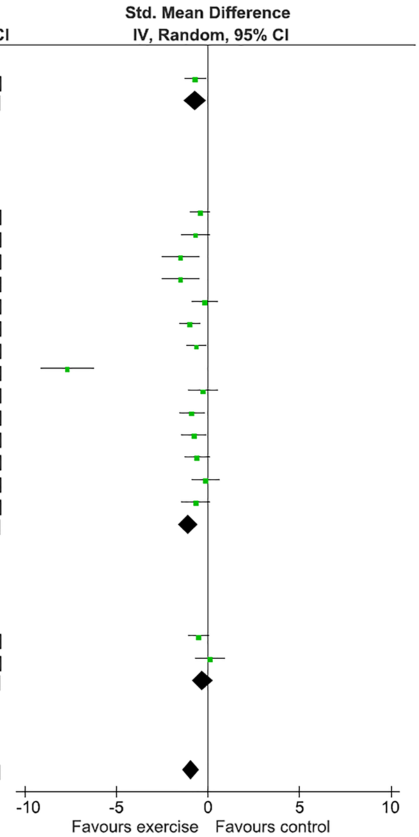
Bidonde et al. [57] the effects of the combined practice were clear, despite the low evidence and great heterogeneity found, a factor that corroborates the findings of the present study. The high rate of heterogeneity in these exercise programs could be justified by the existence of variation in session time (45–90 min), total intervention time (15–24 weeks), and different types of intervention. The environment in which the intervention was carried out (aquatic environment and others) could also be a factor that increases the heterogeneity between studies. In addition to these factors, the methodological quality of the studies must be taken into account. Thus, in a qualitative analysis of the findings, we should highlight that combined training showed promising results, such as reducing the FIQ [70], and depression [42], and improving aerobic capacity [72] and muscle strength [48]. To achieve these benefits in this population, it is suggested that the exercises should start lightly and there should be a gradual increase in intensity over time, always within what is bearable by the individual, to obtain the desired positive effects [17].

The intervention consisting of flexibility exercises did not provide evidence of a significant reduction in the symptoms of fibromyalgia assessed by the FIQ. Although some authors suggested the prescription of stretches to improve the symptoms associated with fibromyalgia, there is still a scarcity of studies on the effects of this type of exercise in this population [32, 73].

Limitations and future perspectives

Despite the important contributions of this systematic review to fibromyalgia, especially regarding interventions performed using physical exercise and their effects on subjects diagnosed with fibromyalgia, some limitations should be mentioned. Limitations in the studies themselves might have influenced the results, such as the lack of information regarding the training program, namely load progressions (intensity and volume) during the intervention period, or incomplete information that made it impossible to analyse some variables. For example, not all articles evaluated in

Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
≤30 minutes								
Gowans et al 2001	-56	26.1	23	-39.7	20.9	27	6.4%	-0.68 [-1.26, -0.11]
Subtotal (95% CI)			**23**			**27**	**6.4%**	**-0.68 [-1.26, -0.11]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.34 (P = 0.02)								
>30 and ≤ 60minutes								
Andrade et al 2018	5.4	2.4	27	6.4	2.1	27	6.4%	-0.44 [-0.98, 0.10]
Assumpção et al 2018	4.4	3	16	6.4	2.7	14	5.9%	-0.68 [-1.42, 0.06]
Häkkinen et al 2002	24	19	11	60	27	10	5.2%	-1.49 [-2.49, -0.50]
Häkkinen et al, 2001	24	19	11	60	27	10	5.2%	-1.49 [-2.49, -0.50]
Izquierdo-Alventosa et al 2020	-42.94	7.96	16	-40.81	13.54	16	6.0%	-0.19 [-0.88, 0.51]
Kayo et al 2011 (1)	-3.94	2.02	30	-2.15	1.56	30	6.4%	-0.98 [-1.52, -0.44]
Kayo et al 2011 (2)	-3.27	1.92	30	-2.15	1.56	30	6.5%	-0.63 [-1.15, -0.11]
Letieri et al, 2013	44.22	2.76	33	63.73	2.21	31	3.9%	-7.68 [-9.14, -6.22]
Mengshoel, KomnÆs e Førre, 1992	60	21.6	11	66	21.6	14	5.8%	-0.27 [-1.06, 0.53]
Roman et al 2015	6.47	3.1	20	8.75	1.73	19	6.1%	-0.88 [-1.54, -0.22]
Sañudo et al. 2010 (3)	67.2	15.6	18	80.5	18.1	20	6.1%	-0.77 [-1.43, -0.11]
Sañudo et al. 2010 (4)	69.7	17.4	17	80.5	18.1	20	6.1%	-0.59 [-1.26, 0.07]
Sañudo et al. 2015	6.7	2.2	16	7	1.7	12	5.9%	-0.15 [-0.89, 0.60]
Tomás-Carús et al 2008	4.6	2.6	14	6.4	2.7	14	5.8%	-0.66 [-1.42, 0.10]
Subtotal (95% CI)			**270**			**267**	**81.5%**	**-1.06 [-1.58, -0.53]**
Heterogeneity: Tau² = 0.86; Chi² = 100.08, df = 13 (P < 0.00001); I² = 87%								
Test for overall effect: Z = 3.92 (P < 0.0001)								
>60 minutes								
Munguia-Izquierdo et al. 2007	66.9	14.7	29	75.8	20	24	6.4%	-0.51 [-1.06, 0.04]
Valkeinen et al 2008	34.15	24.57	13	31.74	19.6	11	5.7%	0.10 [-0.70, 0.91]
Subtotal (95% CI)			**42**			**35**	**12.1%**	**-0.27 [-0.86, 0.31]**
Heterogeneity: Tau² = 0.06; Chi² = 1.51, df = 1 (P = 0.22); I² = 34%								
Test for overall effect: Z = 0.93 (P = 0.35)								
Total (95% CI)			**335**			**329**	**100.0%**	**-0.91 [-1.34, -0.48]**
Heterogeneity: Tau² = 0.68; Chi² = 105.03, df = 16 (P < 0.00001); I² = 85%								
Test for overall effect: Z = 4.14 (P < 0.0001)								
Test for subgroup differences: Chi² = 3.81, df = 2 (P = 0.15), I² = 47.4%								



Footnotes
(1) Kayo (2) Strength intervention
(2) Kayo (1) Aerobic intervention
(3) (4) Aerobic intervention
(4) (3) Combined intervention

Fig. 5 Effectiveness of exercise session time on fibromyalgia for the pain outcome

this review described complete data about the duration of the sessions and/or the intensity of the exercises performed, or the gains between the groups analysed, and this hindered the possibility of determining changes in all variables. Due to the difference in methodological quality presented by the studies included in this systematic review, the risk of bias presented in some protocols, and the heterogeneity of the exercise protocols (e.g., different durations, intensities, and activities performed), the results found should be carefully considered and analysed. Future investigations should be carefully designed to have greater methodological rigour and thus reduce the risk of bias. In addition, further research should focus on different exercise programs, such as understanding the effects of stretching on the symptoms of fibromyalgia.

Conclusion

The results confirmed that the practice of physical exercise seems to be beneficial for the improvement in symptoms and physical fitness of individuals diagnosed with fibromyalgia. Thus, intervention protocols that have a more global positive effect on the main symptoms found in these individuals are suitable and can be used as a possible adjunctive treatment tool. Physical exercise in general (aerobic, strength, or combined) has been shown to be beneficial for individuals with fibromyalgia, but greater results were found after combined training protocols and aerobic exercises. Strength interventions presented a moderate effect on FIQ. Literature findings suggested that exercise programs lasting 13–24 weeks should be used to reduce pain, and each session should last between 30 and 60 min. Furthermore, it is recommended that each training program should start at light intensity with gradually increasing intensity over time. Otherwise, it may have a reverse effect, which could aggravate the symptoms of the affected individuals.

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Author contributions Conception or design of the work: MLLA, DM, DAM and HPN. Data acquisition: MLLA and HPN. Analysis: MLA, DM, DAM, GTV, AA and HN. Interpretation of data for the work: MLLA, DM, GTV, AA and HPN. All authors drafted the work or revised it critically for important intellectual content. All authors gave final approval of the version to be published. All authors had agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors take full responsibility for the integrity of the study and the final manuscript.

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Availability of data and materials The data supporting the conclusions of this article will be made available by the authors.

Declarations

Conflict of interest None declared.

Ethics approval and consent to participate Not applicable.

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