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The effectiveness of aerobic exercise for pain management in patients with fibromyalgia

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Abstract

The effectiveness of exercise therapy is being increasingly studied in patients with fibromyalgia. The aim of our systematic review was to determine the effectiveness of different types of aerobic exercise programs for pain management in patients with fibromyalgia. The literature search was performed by two independent researchers in the PubMed, CINAHL and PEDro databases using various combinations of the following keywords: fibromyalgia, pain and aerobic exercise. Studies were eligible if they included adults diagnosed with fibromyalgia and examined the effectiveness of at least one aerobic exercise program on pain management. A total of 14 randomized controlled trials were screened in full-text, nine of which were included in the systematic review. Overall, our results indicate that aerobic exercise is effective for pain management in patients with fibromyalgia. The results of the aerobic exercise programs were more effective for pain management than stretching exercises, but did not differ significantly from those of pilates, muscle strengthening exercises, relaxation techniques and stress management treatment. Additional high-quality studies are warranted to determine accurate clinical guidelines in terms of aerobic exercise programs for pain management in patients with fibromyalgia.

Key Words: myofascial pain syndrome; cardio-respiratory exercise; chronic pain.

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Fibromyalgia (FM) is a syndrome characterized by chronic musculoskeletal pain that can be felt in different parts of the body.[1] FM affects about 2-7% of the world's population.[2-4], and its prevalence is similar in different countries, cultures and ethnic groups.[5] The main symptoms of the disease are widespread musculoskeletal pain, muscle and joint stiffness, insomnia, fatigue, mood disorders, cognitive dysfunction, anxiety, depression, general sensitivity and inability to perform daily activities.[6,7] Although factors contributing to the development of FM include neuroendocrine disorders, genetic predisposition, oxidative stress, environmental and psychosocial changes, clear factors leading to the onset of FM are still unclear and are the subject of numerous studies.[8,9] FM seems to be triggered by central and peripheral mechanisms of excessive excitability, which can cause changes in pain perception, such as hyperalgesia and allodynia, muscle stiffness, reduced functional capacity, and sleep disturbances.[10,11] Several features of FM suggest an autoimmune component in the pathogenesis. Altered levels of inflammatory and immunoregulatory cytokines have been found in FM patients. Although these changes do not follow a consistent pattern, they may indicate that the patients' immune processes are impaired.[12] Both trauma and infections that can trigger autoimmunity are among the most common causes of FM.[13] A significantly increased prevalence of FM has been found in individuals with COVID-19, herpes simplex, hepatitis C, and Epstein-Barr viral infections, as well as in individuals with autoimmune rheumatologic diseases.[14-16]

Chronic pain may affect an individual in various ways. These often include physical, psychological, social, or economic distress.[17] Pain has a significant impact on an individual's quality of life, self-esteem and emotions. Normal participation in everyday and work activities is often limited for the patient. Research of chronic pain usually begins with the assumption that the patients' primary goal is to reduce pain and increase control over their condition.[18] However, complete and/or permanent pain relief is rarely achieved, nor does it lead to better functioning and quality of life for patients with FM.[19,20] Sometimes, the goal of reducing pain can have the opposite effect if coping methods are perceived as pain avoidance.[21] Avoidance is associated with increased pain intensity, greater anxiety and depression, as well as mental and work disability.[22] Therefore, accepting pain is

particularly important, defined as the willingness to constantly experience pain without efforts to reduce, avoid, or otherwise change it.[21] The authors found that a higher level of pain acceptance is associated with better daily functioning and less disability and symptoms.[23] A multidisciplinary approach is recommended for the treatment of FM, based on the management of physical, psychological, and social factors.[19,24] The treatment of FM involves the use of pharmacological and non-pharmacological therapy. Several pharmacological interventions have solid evidence of efficacy in treating FM symptoms, including tricyclic antidepressants, gabapentinoids, and serotonin - noradrenaline reuptake inhibitors.[25-28] However, no pharmacological intervention is effective in managing all FM symptoms, as they can only alleviate individual symptoms.[29] Accordingly, authors suggest that non-pharmacological interventions may be more effective in increasing the quality of life as they relieve pain, improve physical function and the overall status of patients with FM.[30,31] Non-pharmacological therapy includes patient education, exercise therapy, and cognitive-behavioral therapy. Exercise therapy is an important part of treatment, as patients often report impaired everyday function due to poor cardiovascular fitness, muscle strength and endurance.[32] Aerobic exercise is one of the most common type of exercise intervention used for pain management in patients with FM, as it has many positive effects when dealing with chronic pain conditions. [29,32,33] During aerobic exercise, the hypothalamus releases an increased level of neurotransmitters, including endorphins, which lead to reduced pain. Furthermore, a higher level of neurotransmitters is linked to improvements in mood and sleep quality. Aerobic exercise is also effective in reducing the inflammatory process and oxidative stress in the body, resulting in reduced anxiety, depression, and stress responses.[32] A recent systematic review of 18 studies concluded that aerobic exercise, resistance training, and stretching exercise have positive effects on pain, depression, and quality of life in adults with FM.[34] Although aerobic exercise is associated with pain reduction, the effectiveness of different aerobic exercise protocols for pain management in FM patients, compared to other exercise interventions, has not been thoroughly investigated. Therefore, we conducted a systematic review that combines previous findings and provides the latest clinical guidelines for the use of aerobic exercise in patients with FM.

Materials and Methods

Information sources and search strategy

The search for relevant studies was conducted in March 2023. We searched the PubMed, CINAHL and PEDro databases for all papers published in English language, regardless of the year of publication. We used the following search strategy: fibromyalgia AND pain AND ("aerobic exercise" OR "aerobic training"). The search was conducted by two reviewers independently and the results were combined. The search strategy was carried out in two phases: 1) the assessment of eligible articles based on title and abstract, and 2) the assessment of eligible articles based on the full text.

Eligibility criteria

The eligibility criteria were structured according to the PICOS tool:[35]

- Population (P): The population included both women and men of all age groups who had been diagnosed with FM. Studies with less than 40 subjects were excluded, as were studies that examined other pathologies.
- Intervention (I): Studies were included if at least one experimental group was included in an aerobic exercise program. No exclusion criteria were established based on the intensity of aerobic exercise. However, studies where the intervention lasted less than three weeks were excluded. Studies were also excluded if aerobic exercise was performed in combination with other types of exercise programs and the effectiveness of the aerobic exercise program could not be clearly determined.
- Comparison (C): Studies were included if they assessed the effectiveness of aerobic exercise compared to a control group that received other forms of therapeutic or exercise intervention or received no intervention at all.
- Outcomes (O): Studies were included if they assessed pain intensity according to the Visual Analogue Scale (VAS), number of painful regions, number of tender points, pain pressure thresholds at all 18 specified sites measured with an electronic algometer, Short Form-36 Health Survey (pain category), pain severity subscale of the Multidimensional Pain Inventory (MPI), Fibromyalgia Impact Questionnaire Pain scale (FIQ Pain) and short form McGill pain questionnaire (MPQ) as an outcome measure.
- Study Design (S): Randomized controlled trials including at least one experimental and control group were included.

Study extraction and analysis

Data extraction included the following items: sample characteristics (gender and age range of participants), intervention characteristics (treatment groups, type of intervention, total weeks, duration, frequency), outcome variables and main findings. Data collection was carried out by one researcher, with the supervision of the second researcher.

Methodological quality

The quality of the included studies was assessed independently by two researchers, using the PEDro scale, which rates the quality of studies from 0 to 10.[31] Studies scoring from 9-10 were considered as “excellent”, 6-8 as “good,” 4-5 as “fair,” and <4 as “poor” quality. The average quality of the studies was rated as “good” (mean = 6.33). Four studies were rated as being of “fair” quality,

Table 1. *Assessment of the methodological quality of the included studies by the PEDro scale.*[36]

N	Criteria	de Medeiros et al.[11]	Sevimli et al.[37]	Hooten et al.[38]	Mannerkorpi et al.[39]	Assis et al.[40]	Valim et al.[41]	Schachter et al.[42]	Richards and Scott[43]	Wigers et al.[44]
1	Random allocation	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2	Concealed allocation	Yes	No	Yes	Yes	Yes	No	No	No	No
3	Groups similar at baseline	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes
4	Subject blinding	No	No	No	No	No	No	No	No	No
5	Therapist blinding	No	No	No	No	No	No	No	No	No
6	Assessor blinding	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes
7	Adequate follow-up	Yes	Yes	Yes	Yes	Yes	No	No	No	No
8	Intention-to-treat analysis	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes
9	Between-groups comparisons	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10	Point estimates and variability	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	PEDro scale scoring	8	5	7	8	8	5	5	5	6

whereas the remaining five were rated as being of "good" quality.
Results from the PEDro scale are summarized in Table 1.

Results

With the initial search strategy, we found 289 potential articles, of which 159 were in the PubMed database, 80 in CINAHL and 50 in PEDro databases. After removing the duplicates, a total of 188 studies were exported to MS Excel (Microsoft, Redmond, USA) where key information about the studies were recorded. All studies were screened by title and abstract in order to exclude those not meeting the inclusion criteria. Finally, 18 studies were reviewed in full text and nine of them were excluded due to inappropriate content. Thus, a total of nine appropriate studies were included in the systematic review. The literature search process is presented in Figure 1.
Basic information of the nine studies included in the systematic review are presented in the Table 1 of Supplementary Materials. It was found that gymnastic-based aerobic exercise program and pool-based aquatic aerobic exercise program provides better results for pain management compared to isometric strength and stretching exercise program.[37] Aerobic exercise was also superior to stretching exercise in terms of reducing the number of tender points and pain during palpation of the tender point.[41] However, four studies have reported that aerobic exercise is effective in reducing pain, although the results did not significantly differ compared to mat pilates, strengthening exercise, relaxation techniques, and stress management treatment.[11,38,40,43,44] On the other hand, pain intensity did not significantly decrease over time in the Nordic walking and low-intensity walking group.[39] It was also found that there was no reduction in pain, number of painful regions and increase in pain pressure threshold in the progressive aerobic exercise group.[42]

Discussion

The aim of our systematic review was to assess the effectiveness of aerobic exercise for pain management in patients with FM. Studies included in the systematic review investigated the effectiveness of aerobic exercise in comparison with various forms of exercise interventions on pain management in patients with FM.
Pain threshold has been found to increase in individuals exercising at an intensity of at least 75% of maximal aerobic capacity.[45] This is due to the activation of potent opioidergic and other pain inhibitory mechanisms controlled by the central nervous system.[46] Although regular exercise programmes can have beneficial effects in people with chronic pain, some patients report worsening of symptoms.[47,48] In chronic pain conditions characterised by central sensitization, such as FM and chronic fatigue syndrome, impairment of endogenous

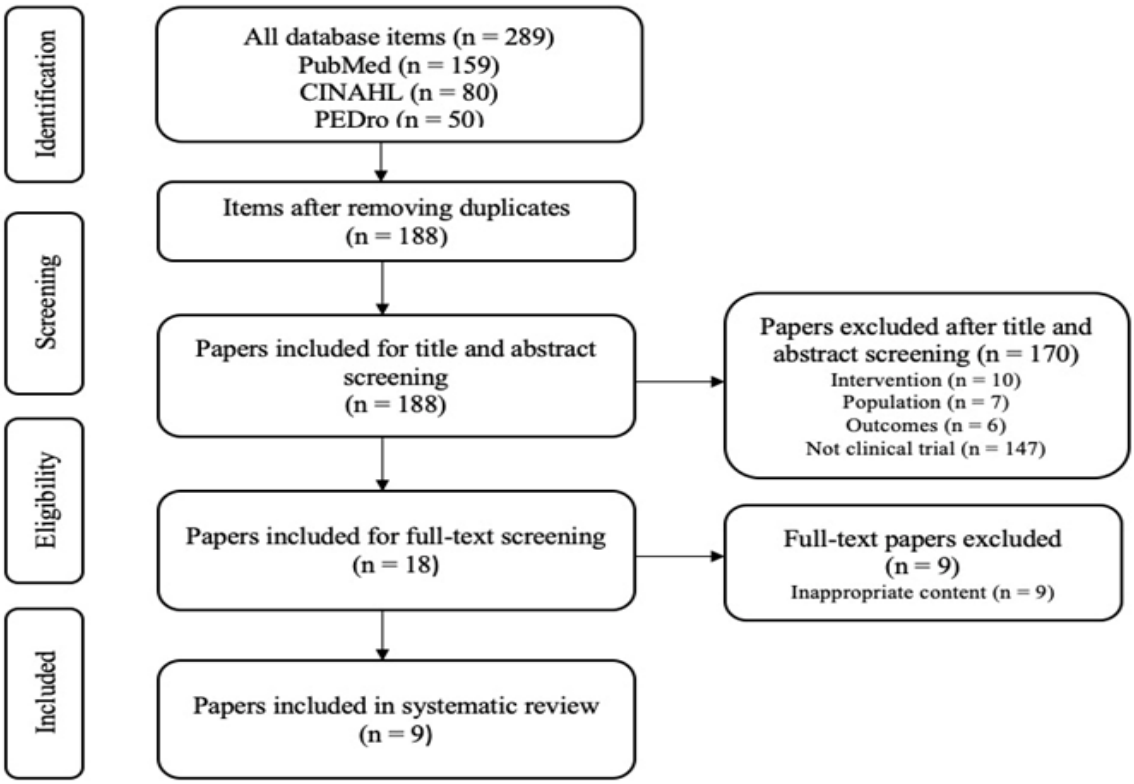

Fig 1. *PRISMA flowchart of study selection process.*

pain inhibition has been reported with excessively intense exercise and worsening of symptoms after exercise.[47-49]

Sevimli et al.[37] concluded that aquatic aerobic exercise and gymnastics are more effective methods for pain management in patients with FM compared to isometric resistance exercise and stretching exercises. Similar findings were reported by Valim et al.[41] who compared walking and stretching exercises for pain management in patients with FM. Aerobic exercise was found to be more effective than stretching exercises in pain management, number of tender points, and increasing pressure tolerance. Assis et al.[40] examined the effectiveness of water running, walking, and running on land. Authors reported that pain scores decreased in both groups, with an average reduction of 40% in water running and 30% in walking and running on land. However, it is emphasized that although walking is a practical form of exercise for most patients, it may be difficult and painful for some with concurrent diseases (e.g. arthritis). Therefore, aerobic exercise in water is particularly suitable for people with lower limb limitations.[40] It is assumed that hydrostatic pressure and higher water temperatures may increase sensory input and block nociceptors, thereby contributing to pain relief.[50] Accordingly, De Medeiros et al.[11] reported the positive effects of aerobic exercise in water on pain management, although the results did not differ significantly compared to the control group that performed mat pilates. The main finding of Hooten et al.[38] was that aerobic exercise and strength training had comparable effects on pain management and increasing pain pressure threshold. Previous studies suggest that aerobic exercise and strength training may improve muscle oxygenation, leading to a reduction in peripheral and central sensitization and thus a reduction in pain intensity.[51,52]

Richards and Scott[43] compared the results of aerobic exercise and relaxation techniques and found that both methods were equally effective for pain management and in reducing the number of painful points three months after the conclusion of the intervention. At the one year follow up, the reduction in the number of painful points was maintained in both groups, although the difference was greater and in patients that were included in the aerobic exercise program. Wigers et al.[44] found that both aerobic exercise and stress management treatment were short-term effective methods for pain management, number of painful regions, and increasing pain pressure threshold, but no significant long-term changes were observed in symptom severity. Mannerkorpi et al.[39] investigated the effectiveness of moderate-to-high-intensity Nordic walking and low-intensity walking program. Surprisingly, some patients in the Nordic walking group as well as in the low-intensity walking group reported temporary increases in pain, which could be due to dysfunctions in peripheral and central pain mechanisms in FM.[39] In a study that evaluated the effectiveness of aerobic dance, it was found that there

was a worsening of FM symptoms, particularly an increase in pain intensity.[53] Van Santen et al.[54] also concluded that pain intensity increased in the group that performed high-intensity aerobic exercise compared to the control group that underwent low-intensity exercise. Within high-intensity walking, the use of poles was advised, which facilitates walking and relieves the lower extremities. Walking in short intervals, allowing for a short rest after each intense interval, can also be beneficial in reducing the risk of pain.[39] Schachter et al.[42] compared the effectiveness of progressive low-intensity aerobics with a control group that did not receive any intervention. They found that pain intensity, the number of painful regions, and pain pressure threshold did not significantly change between groups. This could be attributed to the lack of supervision during the exercise program, as patients performed exercises independently at home. Therefore, it was not possible to verify the reported data on exercise duration and whether patients exercised at the targeted intensity.[42]

Despite the lack of agreement on the most effective form of exercise, authors assume that combined exercise with two to three moderate-intensity training sessions per week lasting 30-45 minutes, is most effective in reducing FM symptoms.[33] It is important to adjust the type, duration, frequency, and exercise intensity according to the individual's goals and abilities.

Our systematic review has several limitations. Firstly, it is difficult to determine clear clinical recommendations because of the high heterogeneity of the included studies in terms of the aerobic exercise type, duration of the program, differences in volume (number of repetitions, sets or exercises) and the intensity of aerobic exercise. Therefore, further studies are needed to limit the high variability of exercise programs. Secondly, most of the included studies did not directly investigate the effectiveness of aerobic exercise for pain management in FM patients, but instead compared the effectiveness of different intervention on both physical and psychological parameters. Additionally, in none of the included studies was the therapist or the subject blinded to group allocation. One of the limitations is also the lack of studies comparing the effectiveness of aerobic exercise with a control group that did not receive the intervention. Finally, the findings of most studies were based on short-term measurements and further studies are needed to clarify the long-term effectiveness of aerobic exercise for pain management in patients with FM. In conclusion, our systematic review indicate that aerobic exercise is effective for pain management in patients with FM. The results indicate that aerobic exercise programs are more effective for pain management in patients with FM compared to stretching exercises. However, the results showed no significant difference between aerobic exercise and pilates, muscle strength training, relaxation techniques or stress management treatment in terms of pain management in patients with FM. Due to the favorable effects on pain, aerobic exercise programs are warranted to be included in daily clinical practice when treating patients with FM. However, high-quality studies with large numbers of participants and long-term follow-up are needed to clearly determine clinical guidelines for implementing aerobic exercise program for pain management in patients with FM.

List of acronyms

CINAHL - cumulative index to nursing and allied health literature
FIQ Pain - fibromyalgia impact questionnaire pain scale
FM - Fibromyalgia
MPI - multidimensional pain inventory
MPQ - McGill pain questionnaire
PEDro - physiotherapy evidence database
PRISMA - preferred reporting items for systematic reviews and meta-analyses
SF-36 - short form-36 health survey
VAS - visual analogue scale

Contributions of Authors

EIK: Substantial contributions to the conception and design of the work; EIK, DM: acquisition, analysis, or interpretation of data for the work, drafting the work and revising it critically for important intellectual content; EIK, DM: 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.

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Conflict of Interest

The authors have no conflict of interest to declare.

Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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References

1. Siracusa R, Paola RD, Cuzzocrea S, Impellizzeri D. Fibromyalgia: Pathogenesis, Mechanisms, Diagnosis and Treatment Options Update. Int J Mol Sci. 2021 Apr 9;22(8):3891. doi: 10.3390/ijms22083891. PMID: 33918736; PMCID: PMC8068842.
2. Vincent A, Lahr BD, Wolfe F, Clauw DJ, Whipple MO, Oh TH, Barton DL, St Sauver J. Prevalence of fibromyalgia: a population-based study in Olmsted County, Minnesota, utilizing the Rochester Epidemiology Project. Arthritis Care Res (Hoboken). 2013 May;65(5):786-92. doi: 10.1002/acr.21896. PMID: 23203795; PMCID: PMC3935235.
3. Branco JC, Bannwarth B, Failde I, Abello Carbonell J, Blotman F, Spaeth M, Saraiva F, Nacci F, Thomas E, Caubère JP, Le Lay K, Taieb C, Matucci-Cerinic M. Prevalence of fibromyalgia: a survey in five European countries. Semin Arthritis Rheum. 2010 Jun;39(6):448-53. doi: 10.1016/j.semarthrit.2008.12.003. Epub 2009 Feb 27. PMID: 19250656.
4. Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum. 1995 Jan;38(1):19-28. doi: 10.1002/art.1780380104. PMID: 7818567.
5. McBeth J, Jones K. Epidemiology of chronic musculoskeletal pain. Best Pract Res Clin Rheumatol. 2007 Jun;21(3):403-25. doi: 10.1016/j.berh.2007.03.003. PMID: 17602991.
6. Gerdle B, Björk J, Cöster L, Henriksson K, Henriksson C, Bengtsson A. Prevalence of widespread pain and associations with work status: a population study. BMC Musculoskelet Disord. 2008 Jul 15;9:102. doi: 10.1186/1471-2474-9-102. PMID: 18627605; PMCID: PMC2488345.
7. Bennett RM, Jones J, Turk DC, Russell IJ, Matallana L. An internet survey of 2,596 people with fibromyalgia. BMC Musculoskelet Disord. 2007 Mar 9;8:27. doi: 10.1186/1471-2474-8-27. PMID: 17349056; PMCID: PMC1829161.
8. Bradley LA. Pathophysiology of fibromyalgia. Am J Med. 2009 Dec;122(12 Suppl):S22-30. doi: 10.1016/j.amjmed.2009.09.008. PMID: 19962493; PMCID: PMC2821819.
9. Yunus MB, Khan MA, Rawlings KK, Green JR, Olson JM, Shah S. Genetic linkage analysis of multicase families with fibromyalgia syndrome. J Rheumatol. 1999 Feb;26(2):408-12. PMID: 9972977.
10. Bhargava J, Hurley JA. Fibromyalgia. 2022 Oct 10. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–. PMID: 31082018.
11. de Medeiros SA, de Almeida Silva HJ, do Nascimento RM, da Silva Maia JB, de Almeida Lins CA, de Souza MC. Mat Pilates is as effective as aquatic aerobic exercise in treating women with fibromyalgia: a clinical, randomized and blind trial. Adv Rheumatol. 2020 Apr 6;60(1):21. doi: 10.1186/s42358-020-0124-2. PMID: 32252822.
12. Andrés-Rodríguez L, Borràs X, Feliu-Soler A, Pérez-Aranda A, Angarita-Osorio N, Moreno-Peral P, Montero-Marin J, García-Campayo J, Carvalho AF, Maes M, Luciano JV. Peripheral immune aberrations in fibromyalgia: A systematic review, meta-analysis and meta-regression. Brain Behav Immun. 2020 Jul;87:881-889. doi: 10.1016/j.bbi.2019.12.020. Epub 2019 Dec 27. PMID: 31887417.
13. Buskila D, Atzeni F, Sarzi-Puttini P. Etiology of fibromyalgia: the possible role of infection and vaccination. Autoimmun Rev. 2008 Oct;8(1):41-3. doi: 10.1016/j.autrev.2008.07.023. Epub 2008 Aug 13. PMID: 18706528.
14. Kocyigit BF, Akyol A. The relationship between COVID-19 and fibromyalgia syndrome: prevalence, pandemic effects, symptom mechanisms, and COVID-19 vaccines. Clin Rheumatol. 2022 Oct;41(10):3245-3252. doi: 10.1007/s10067-022-06279-9. Epub 2022 Jul 8. PMID: 35804273.
15. Reshkova V, Kalinova D, Milanov I. Evaluation of antiviral antibodies against Epstein-Barr Virus and neurotransmitters in patients with fibromyalgia. J. Neurol Neurosci. 2015;6 doi: 10.21767/2171-6625.100035.
16. Lichtenstein A, Tiosano S, Amital H. The complexities of fibromyalgia and its comorbidities. Curr Opin Rheumatol. 2018 Jan;30(1):94-100. doi: 10.1097/BOR.0000000000000464. PMID: 29040155.
17. White KP, Harth M. The occurrence and impact of generalized pain. Baillieres Best Pract Res Clin Rheumatol. 1999 Sep;13(3):379-89. doi: 10.1053/berh.1999.0027. PMID: 10562368.
18. Kratz AL, Davis MC, Zautra AJ. Pain acceptance moderates the relation between pain and negative affect in female osteoarthritis and fibromyalgia patients. Ann Behav Med. 2007 Jun;33(3):291-301. doi: 10.1007/BF02879911. PMID: 17600456; PMCID: PMC2593934.
19. Macfarlane GJ, Kronisch C, Dean LE, Atzeni F, Häuser W, Fluß E, Choy E, Kosek E, Amris K, Branco J, Dincer F, Leino-Arjas P, Longley K, McCarthy GM, Makri S, Perrot S, Sarzi-Puttini P, Taylor A, Jones GT. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis. 2017 Feb;76(2):318-328. doi: 10.1136/annrheumdis-2016-209724. Epub 2016 Jul 4. PMID: 27377815.
20. Turk DC. Customizing treatment for chronic pain patients: who, what, and why. Clin J Pain. 1990

Dec;6(4):255-70. doi: 10.1097/00002508-199012000-00002. PMID: 2135025.
21. McCracken LM. Learning to live with the pain: acceptance of pain predicts adjustment in persons with chronic pain. Pain. 1998 Jan;74(1):21-27. doi: 10.1016/S0304-3959(97)00146-2. PMID: 9514556.
22. Vlaeyen JWS, Linton SJ. Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. Pain. 2000 Apr;85(3):317-332. doi: 10.1016/S0304-3959(99)00242-0. PMID: 10781906.
23. Tangen SF, Helvik AS, Eide H, Fors EA. Pain acceptance and its impact on function and symptoms in fibromyalgia. Scand J Pain. 2020 Oct 25;20(4):727-736. doi: 10.1515/sjpain-2020-0049. PMID: 32759409.
24. Booth J, Moseley GL, Schiltenwolf M, Cashin A, Davies M, Hübscher M. Exercise for chronic musculoskeletal pain: A biopsychosocial approach. Musculoskeletal Care. 2017 Dec;15(4):413-421. doi: 10.1002/msc.1191. Epub 2017 Mar 30. PMID: 28371175.
25. Häuser W, Thieme K, Turk DC. Guidelines on the management of fibromyalgia syndrome - a systematic review. Eur J Pain. 2010 Jan;14(1):5-10. doi: 10.1016/j.ejpain.2009.01.006. Epub 2009 Mar 4. PMID: 19264521.
26. Tzellos TG, Toulis KA, Goulis DG, Papazisis G, Zampeli VA, Vakfari A, Kouvelas D. Gabapentin and pregabalin in the treatment of fibromyalgia: a systematic review and a meta-analysis. J Clin Pharm Ther. 2010 Dec;35(6):639-56. doi: 10.1111/j.1365-2710.2009.01144.x. PMID: 21054455.
27. Arnold LM, Clauw DJ, Wohlreich MM, Wang F, Ahl J, Gaynor PJ, Chappell AS. Efficacy of duloxetine in patients with fibromyalgia: pooled analysis of 4 placebo-controlled clinical trials. Prim Care Companion J Clin Psychiatry. 2009;11(5):237-44. doi: 10.4088/PCC.08m00680. PMID: 19956462; PMCID: PMC2781036.
28. Arnold LM. Duloxetine and other antidepressants in the treatment of patients with fibromyalgia. Pain Med. 2007 Sep;8 Suppl 2:S63-74. doi: 10.1111/j.1526-4637.2006.00178.x. PMID: 17714117.
29. Chen J, Han B, Wu C. On the superiority of a combination of aerobic and resistance exercise for fibromyalgia syndrome: A network meta-analysis. Front Psychol. 2022 Sep 28;13:949256. doi: 10.3389/fpsyg.2022.949256. PMID: 36248603; PMCID: PMC9554347.
30. Jones KD, Adams D, Winters-Stone K, Burckhardt CS. A comprehensive review of 46 exercise treatment studies in fibromyalgia (1988-2005). Health Qual Life Outcomes. 2006 Sep 25;4:67. doi: 10.1186/1477-7525-4-67. PMID: 16999856; PMCID: PMC1590013.
31. Busch AJ, Barber KA, Overend TJ, Peloso PM, Schachter CL. Exercise for treating fibromyalgia syndrome. Cochrane Database Syst Rev. 2007 Oct 17;(4):CD003786. doi: 10.1002/14651858.CD003786.pub2. PMID: 17943797.
32. Bidonde J, Busch AJ, Schachter CL, Overend TJ, Kim SY, Góes SM, Boden C, Foulds HJ. Aerobic exercise training for adults with fibromyalgia. Cochrane Database Syst Rev. 2017 Jun 21;6(6):CD012700. doi: 10.1002/14651858.CD012700. PMID: 28636204; PMCID: PMC6481524.
33. Sosa-Reina MD, Nunez-Nagy S, Gallego-Izquierdo T, Pecos-Martín D, Monserrat J, Álvarez-Mon M. Effectiveness of Therapeutic Exercise in Fibromyalgia Syndrome: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. Biomed Res Int. 2017;2017:2356346. doi: 10.1155/2017/2356346. Epub 2017 Sep 20. PMID: 29291206; PMCID: PMC5632473.
34. Couto N, Monteiro D, Cid L, Bento T. Effect of different types of exercise in adult subjects with fibromyalgia: a systematic review and meta-analysis of randomised clinical trials. Sci Rep. 2022 Jun 20;12(1):10391. doi: 10.1038/s41598-022-14213-x. PMID: 35725780; PMCID: PMC9209512.
35. Methley AM, Campbell S, Chew-Graham C, McNally R, Cheraghi-Sohi S. PICO, PICOS and SPIDER: a comparison study of specificity and sensitivity in three search tools for qualitative systematic reviews. BMC Health Serv Res. 2014 Nov 21;14:579. doi: 10.1186/s12913-014-0579-0. PMID: 25413154; PMCID: PMC4310146.
36. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. Phys Ther. 2003 Aug;83(8):713-21. PMID: 12882612.
37. Sevimli D, Kozanoglu E, Guzel R, Doganay A. The effects of aquatic, isometric strength-stretching and aerobic exercise on physical and psychological parameters of female patients with fibromyalgia syndrome. J Phys Ther Sci. 2015 Jun;27(6):1781-6. doi: 10.1589/jpts.27.1781. Epub 2015 Jun 30. PMID: 26180320; PMCID: PMC4499983.
38. Hooten MW, Qu W, Townsend CO, Judd JW. Effects of strength vs aerobic exercise on pain severity in adults with fibromyalgia: a randomized equivalence trial. Pain. 2012 Apr;153(4):915-923. doi: 10.1016/j.pain.2012.01.020. Epub 2012 Feb 15. PMID: 22341565.
39. Mannerkorpi K, Nordeman L, Cider A, Jonsson G. Does moderate-to-high intensity Nordic walking improve functional capacity and pain in fibromyalgia? A prospective randomized controlled

trial. Arthritis Res Ther. 2010;12(5):R189. doi: 10.1186/ar3159. Epub 2010 Oct 13. PMID: 20942911; PMCID: PMC2991024.
40. Assis MR, Silva LE, Alves AM, Pessanha AP, Valim V, Feldman D, Neto TL, Natour J. A randomized controlled trial of deep water running: clinical effectiveness of aquatic exercise to treat fibromyalgia. Arthritis Rheum. 2006 Feb 15;55(1):57-65. doi: 10.1002/art.21693. PMID: 16463414.
41. Valim V, Oliveira L, Suda A, Silva L, de Assis M, Barros Neto T, Feldman D, Natour J. Aerobic fitness effects in fibromyalgia. J Rheumatol. 2003 May;30(5):1060-9. PMID: 12734907.
42. Schachter CL, Busch AJ, Peloso PM, Sheppard MS. Effects of short versus long bouts of aerobic exercise in sedentary women with fibromyalgia: a randomized controlled trial. Phys Ther. 2003 Apr;83(4):340-58. PMID: 12665405.
43. Richards SC, Scott DL. Prescribed exercise in people with fibromyalgia: parallel group randomised controlled trial. BMJ. 2002 Jul 27;325(7357):185. doi: 10.1136/bmj.325.7357.185. PMID: 12142304; PMCID: PMC117444.
44. Wigers SH, Stiles TC, Vogel PA. Effects of aerobic exercise versus stress management treatment in fibromyalgia. A 4.5 year prospective study. Scand J Rheumatol. 1996;25(2):77-86. doi: 10.3109/03009749609069212. PMID: 8614771.
45. Hoffman MD, Shepanski MA, Ruble SB, Valic Z, Buckwalter JB, Clifford PS. Intensity and duration threshold for aerobic exercise-induced analgesia to pressure pain. Arch Phys Med Rehabil. 2004 Jul;85(7):1183-7. doi: 10.1016/j.apmr.2003.09.010. PMID: 15241771.
46. Millan MJ. Descending control of pain. Prog Neurobiol. 2002 Apr;66(6):355-474. doi: 10.1016/s0301-0082(02)00009-6. PMID: 12034378.
47. Van Oosterwijck J, Nijs J, Meeus M, Van Loo M, Paul L. Lack of endogenous pain inhibition during exercise in people with chronic whiplash associated disorders: an experimental study. J Pain. 2012 Mar;13(3):242-54. doi: 10.1016/j.jpain.2011.11.006. Epub 2012 Jan 24. PMID: 22277322.
48. Meeus M, Roussel NA, Truijen S, Nijs J. Reduced pressure pain thresholds in response to exercise in chronic fatigue syndrome but not in chronic low back pain: an experimental study. J Rehabil Med. 2010 Oct;42(9):884-90. doi: 10.2340/16501977-0595. PMID: 20878051.
49. Lannersten L, Kosek E. Dysfunction of endogenous pain inhibition during exercise with painful muscles in patients with shoulder myalgia and fibromyalgia. Pain. 2010 Oct;151(1):77-86. doi: 10.1016/j.pain.2010.06.021. PMID: 20621420.
50. Bender T, Karagülle Z, Bálint GP, Gutenbrunner C, Bálint PV, Sukenik S. Hydrotherapy, balneotherapy, and spa treatment in pain management. Rheumatol Int. 2005 Apr;25(3):220-4. doi: 10.1007/s00296-004-0487-4. Epub 2004 Jul 15. PMID: 15257412.
51. Sedlock DA, Lee MG, Flynn MG, Park KS, Kamimori GH. Excess postexercise oxygen consumption after aerobic exercise training. Int J Sport Nutr Exerc Metab. 2010 Aug;20(4):336-49. doi: 10.1123/ijsnem.20.4.336. PMID: 20739722.
52. Imamura H, Shibuya S, Uchida K, Teshima K, Masuda R, Miyamoto N. Effect of moderate exercise on excess post-exercise oxygen consumption and catecholamines in young women. J Sports Med Phys Fitness. 2004 Mar;44(1):23-9. PMID: 15181386.
53. Nørregaard J, Bülow PM, Lykkegaard JJ, Mehlsen J, Danneskiold-Samsøoe B. Muscle strength, working capacity and effort in patients with fibromyalgia. Scand J Rehabil Med. 1997 Jun;29(2):97-102. PMID: 9198259.
54. van Santen M, Bolwijn P, Landewé R, Verstappen F, Bakker C, Hidding A, van Der Kemp D, Houben H, van der Linden S. High or low intensity aerobic fitness training in fibromyalgia: does it matter? J Rheumatol. 2002 Mar;29(3):582-7. PMID: 11908577.

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Supplementary Materials Table 1. *Overview of the studies included in the systematic review.*

Authors	Population	Intervention	Outcome measures for pain	Findings
de Medeiros et al.[11]	N=42 F (48,1 ± 10,2y)	EG: Aquatic aerobic exercise (n=21); 12 weeks, twice a week, each session lasted 40 min CG: Mat pilates (n=21); 12 weeks, twice a week; each session lasted 40 min	VAS; SF-36	There was a statistically significant reduction in pain in EG and CG ($p < 0.05$). The measurements showed no statistically significant differences between the groups ($p > 0.05$).
Sevimli et al.[37]	N=75 F (35 ± 8,8y)	EG: Group 1: Gymnastic-based aerobic exercise program (n=25); 3 months, twice a week, each session lasted 40-50 min Group 2: Pool-based aquatic aerobic exercise program (n=25); 3 months, twice a week, each session lasted 40-50 min CG: Home-based isometric strength and stretching exercise program (n=25); 3 months, once a day, each session lasted 15 min	VAS	There was a statistically significant reduction in pain in EG ($p < 0.001$) compared to CG ($p > 0.05$). No statistically significant difference was found between EG ($p > 0.05$).
Hooten et al.[38]	N=72 (65 F, 7 M) (46,6 ± 10,8y)	EG: Aerobic exercise – stationary bicycle (n=36); 3 weeks, 10 min daily during week 1; 15 min daily during week 2; 20-30 min daily during week 3 CG: Strengthening exercise (n=36); 3 weeks, once a day, each session lasted 25-30 min	MPI; Pain pressure threshold	There was a statistically significant reduction in pain and increase in pain pressure threshold in EG and CG ($p < 0.01$). There were no statistically significant differences between between the groups ($p > 0.05$).

Mannerkorpi et al.[39]	N=67 F (49 ± 7,7y)	EG: Moderate-to-high intensity Nordic walking (n=34); 15 weeks, twice a week, each session lasted 40-45 min CG: Low-intensity walking (n=33); 15 weeks, once a week, each session lasted 40-45 min	FIQ Pain	No statistically significant reduction in pain was found in EG and CG ($p > 0.05$).
Assis et al.[40]	N=52 F (40 ± 9,6y)	EG: Deep water running (n=26); 15 weeks, 3 times a week, each session lasted 60 min CG: Land-based exercises (walking or jogging) (n=26); 15 weeks, 3 times a week, each session lasted 60 min	VAS	There was a statistically significant reduction in pain in EG and CG ($p < 0.01$). There were no statistically significant differences between the groups ($p > 0.05$).
Valim et al.[41]	N=60 F (45,5 ± 10,5y)	EG: Aerobic exercise – walking (n=32); 20 weeks, 3 times a week, each session lasted 45 min CS: Stretching exercise (n=28); 20 weeks, 3 times a week, each session lasted 45 min	VAS; Number of tender points; Pain score during palpation of the tender point SF-36	The reduction of pain, number of tender points and pain during palpation of the tender point was statistically significant in EG ($p < 0.05$). There was a statistically significant difference between the groups ($p < 0.05$).
Schachter et al.[42]	N=143 F (41,9 ± 7,97y)	EG: Progressive low-impact aerobic program; 16 weeks, progressed from 3 to 5 times a week and 10 to 30 min Group 1: Long bouts of exercise – once daily (n=56) Group 2: Short bouts of exercise – twice daily (n=51) CG: No exercise (n=36)	VAS; Pain distribution; Pain pressure threshold	There was no statistically significant reduction in pain, number of painful regions and increase in pain pressure threshold in EG ($p > 0.05$). In the CG, pain was statistically significantly reduced ($p > 0.05$). There were no statistically significant differences between EG and CG ($p > 0.05$).

Richards and Scott[43]	N=136 (126 F, 10 M) (46,5y)	EG: Aerobic exercise – walking on a treadmill or stationary bicycle (n=69); 12 weeks, twice a week, each session lasted 60 min CG: Relaxation techniques and stretching exercise (n=67); 12 weeks, twice a week, each session lasted 60 min	Number of tender points; MPQ	There was a statistically significant reduction in pain ($p < 0.05$) and number of tender points ($p < 0.001$) in the EG and CG at three months. The reduction in number of tender points persisted for 12 months ($p < 0.001$), though by then the difference between the two groups was greater and favoured the exercise group ($p < 0.05$)
Wigers et al.[44]	N=60 (55 F, 5 M) (44y)	EG: Aerobic exercise (n=20); 14 weeks, 3 times a week, each session lasted 45 min CG: Group 1: Stress management treatment (n=20); 6 weeks – 2 times a week, 8 weeks – once a week, each session lasted 90 min Group 2: Treatment-as-usual (n=20); Aquatic therapy, psychomotor treatment, tricyclic antidepressants, analgesics, muscle relaxants, hypnotics, tranquilizers	VAS; Pain distribution; Pain pressure threshold	In EG, there was a statistically significant reduction in pain ($p < 0.05$), number of painful regions ($0 < 0.01$) and increase in pain pressure threshold ($p < 0.001$). Results also showed a statistically significant reduction in pain ($p < 0.05$), number of painful regions ($p < 0.05$) and increase in pain pressure threshold ($p < 0.01$) in CG.

Legend: CG = control group; EG = experimental group; F = female; FIQ = Fibromyalgia Impact Questionaire); M = male; MPI = Multidimensional Pain Inventory; MPQ = McGill Pain Questionnaire); n = number of participants; SF-36 = Short Form-36 Health Survey; VAS = Visual analogue scale.