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Aerobic Exercise Prescription for Pain Reduction in Fibromyalgia: A Systematic Review and Meta-Analysis

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ABSTRACT

Background and Objective: Fibromyalgia is a condition characterised by disabling levels of pain of varying intensity. Aerobic exercise may play a role in reducing pain in these patients. The aim of this review is to assess the dose of aerobic exercise needed, based on the frequency, intensity, type, time, volume and progression (FITT-VP) model, to obtain clinically relevant reductions in pain.

Databases and Data Treatment: A systematic review and meta-analysis of randomised clinical trials was conducted in the Web of Science (WoS), PEDro, PubMed and Scopus databases, the search having been conducted between July and October of 2023. Risk of bias was assessed with the Cochrane Risk of Bias assessment tool 2.

Results: Seventeen studies were included. The risk of bias varied, with six studies showing low risk; five, some concerns; and six, high risk. Aerobic exercise interventions were analysed using the FITT-VP model. Frequency ranged from 1 to 10 times per week, intensity varied from light to vigorous, and the types of exercise included music-based exercise, interval training, pool-based exercise, stationary cycling, swimming and walking. The intervention durations ranged from 3 to 24 weeks, with session lengths ranging from 10 to 45 min. Most of the studies presented significant differences, favouring aerobic exercise (MD −0.49; CI [−0.90, −0.08; $p=0.02$]), with moderate to low heterogeneity in subgroup analyses.

Conclusions: The study findings underscore the efficacy of aerobic exercise in alleviating pain among fibromyalgia patients, advocating for tailored exercise dosing to optimise adherence and outcomes.

Significance Statement: Individuals with fibromyalgia should engage in aerobic exercises two to three times weekly, for twenty-five to forty minutes in each session, aiming for more than a hundred minutes per week. They should start at low intensity, gradually increasing to higher intensities over six to twelve weeks, for optimal pain management. Exercise types should be selected in collaboration with the patient and based on personal preferences and accessibility, such as walking, and swimming, to ensure long-term adherence to the regimen.

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1 | Introduction

Fibromyalgia is a chronic condition that affects approximately 2% to 4% of the global population (Queiroz 2013) with a higher prevalence among women than in men (Wolfe et al. 2018). It is characterised by widespread musculoskeletal pain, hyperalgesia and allodynia, often accompanied by fatigue, insomnia, stiffness and psychological symptoms such as anxiety, depression and cognitive impairments (Galvez-Sánchez et al. 2020; Wolfe et al. 2010). Even so, in this population pain can be defined as a disease in and of itself (Treede et al. 2019), having been linked to disability, function and quality of life (Campos and Vázquez 2012).

Although its aetiology remains unclear, and it has traditionally been characterised as a disease of the musculoskeletal and connective tissue system (DiSantostefano 2009), its underlying pathophysiology is yet to be understood (Siracusa et al. 2021). Some studies attribute it to central sensitization (CS) processes (Häuser et al. 2015; Yunus 2007), while others associate it with inflammation (Coskun Benlidayi 2019; Kadetoff et al. 2012; Mendieta et al. 2016) or small fibre neuropathy (Martínez-Lavín 2018).

Its undefined aetiology has led to diverse treatment approaches, ranging from dietary interventions (Nadal-Nicolás et al. 2021; Pagliai et al. 2020) to pharmacological ones, with widely varying approaches, such as, for example, cannabis (Khurshid et al. 2021; Strand et al. 2023), duloxetine (Lunn, Hughes and Wiffen 2014), naltrexone (Yang et al. 2023) and amitriptyline (Moore et al. 2015). Physiotherapy also includes a wide range of treatments, such as transcutaneous electrical nerve stimulation (TENS) (Megía García et al. 2019), dry needling or acupuncture (Valera-Calero et al. 2022) and laser therapy (Yeh et al. 2019). Exercise, in particular, has been extensively studied for fibromyalgia (Couto et al. 2022; Geneen et al. 2017; Zhang et al. 2022) and has proven to be safe and cost-effective (Booth, Roberts and Laye 2012; Miyamoto et al. 2019; Pedersen and Saltin 2015).

Aerobic exercise has shown to be an effective strategy in reducing the intensity of pain and enhancing quality of life among fibromyalgia patients (Couto et al. 2022; Häuser et al. 2015; Zhang et al. 2022). In fact, some guidelines have prescribed aerobic exercise for the treatment of fibromyalgia (El Miedany et al. 2022; Häuser et al. 2008). For example the Consensus, Evidence-based, guidelines (CEG) initiative recommended graded aerobic exercise for the treatment of fibromyalgia (El Miedany et al. 2022). Though its effectiveness has been well established in this regard, the exact dose of aerobic exercise necessary to maximise pain reduction is yet to be established. This may be due to the fact that most of reviews report low-quality evidence in the papers included (Bidonde et al. 2017; Couto et al. 2022; Zhang et al. 2022).

Therefore, the aim of this systematic review and meta-analysis is to analyse the effect of different doses of aerobic exercise on the intensity of pain among fibromyalgia patients.

2 | Methodology

2.1 | Design

In accordance with PRISMA standards (Page et al. 2021), a predefined procedure, divided into search, preliminary analysis, analysis and synthesis phases, was used to carry out the systematic review. The systematic review protocol was registered in the PROSPERO (International Prospective Register of Systematic Reviews), with registration number CRD42023468534.

2.2 | Search Strategy

A search was conducted in the Web of Science (WOS), PubMed, Scopus and PEDro (Herbert et al. 2000) databases by two independent researchers (DC-R and RB-R), who modified the search strategy to suit the requirements for each individual database. The search was conducted between July and October of 2023. The Rayyan web app (Ouzzani et al. 2016) was used in order to check for duplicates and to carry on the preliminary analysis of the study.

Using Boolean operators, the through search was coupled with the following terms in all fields: 'fibromyalgia,' 'muscular rheumatism,' 'fibrositis,' 'cardiovascular training', 'cardiovascular exercise', 'endurance training', 'endurance exercise', 'aerobic training', 'aerobic exercise' and 'pain' (Data S1).

2.3 | Inclusion Criteria

The population, intervention, comparison, outcomes and study type (PICOS) (Amir-Behghadami and Janati 2020) criteria were used as the selection criteria for this systematic review and meta-analysis, which were based on methodological and clinical considerations. Therefore, the 'Population' (P) was comprised of patients with fibromyalgia, whether they were women or men, diagnosed according to American College of Rheumatology (ACR) criteria (Wolfe et al. 1990, 2010, 2016), and older than 18. As for the 'Intervention' (I) criteria, at least one of the study groups had to perform aerobic exercise, alone or with a placebo, regardless of the group of the study or kind of aerobic exercise. Moreover, the study had to provide data on the frequency, intensity, type, time, volume or progression (FITT-VP) of the exercise performed in order to be adjusted to the American College of Sport Medicine (ACSM) FITT-VP model (Pescatello et al. 2006). With reference to 'Comparison' (C), every comparison was included, and with regards to 'Outcome' (O), the study had to use some type of pain measurement in the participants, regardless of whether it was the primary or secondary outcome of the study, and had provide mean and standard deviation data. Finally, as for 'Study type' (s): only randomised clinical trials (RCT) were included.

2.4 | Selection Criteria and Data Extraction

To begin, DC-R and RB-R conducted an initial analysis of the study titles and abstracts in order to determine their relevance to the review process. If there was no agreement, or the title and abstract analysis did not provide enough information, the full text was reviewed.

Second, the full text was analysed in order to assess whether it met all the inclusion criteria or not, with any discrepancies between reviewers resolved by consensus or by a third reviewer (JMJ-C), if necessary (Page et al. 2021). A standardised process was used to extract the data, ensuring that all essential information from the study was extracted (Higgins et al. 2019).

2.5 | Assessment of Risk of Bias

To assess the risk of bias, the Cochrane Risk of Bias 2 (RoB 2) (Higgins et al. 2019; Sterne et al. 2019) tool was used. This tool evaluates the risk of bias across five domains, which are: bias arising from the randomization process, bias due to deviation from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, and bias in the selection of the results reported; as well as an overall risk of bias. These domains cover all types of bias currently understood to affect RCT, and are rated as: low risk of bias, some concerns, or high risk of bias.

2.6 | Quality of Evidence

Overall qualitative analysis was performed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system, based on five domains: study design, risk of bias, inconsistency, indirectness and imprecision (Guyatt et al. 2008). If there were serious concerns in one of these domains, the overall quality was reduced by one point, and if there were very serious concerns in one of these domains, the quality was lowered by two points (Balshem et al. 2011).

After this, evidence was classified as: high quality, expressing confidence that the actual effect is close to the estimated one; moderate quality, conveying that the actual effect is likely to be close to the estimated one, but could be substantially different; low quality, meaning that the true effect could be substantially different; and very low quality, communicating that the actual effect is likely to be substantially different (Balshem et al. 2011).

2.7 | Statistical Analysis

To conduct this meta-analysis, the effect of aerobic exercise on pain improvement was examined by comparing aerobic exercise with other interventions, or control groups were used for comparison through a subgroup analysis. Studies that featured usual physical care, or no treatment, were classified as control groups. To analyse the effect of different doses of exercise on pain management, the pre and post intervention data were compared, dividing the studies, according to the ACSM FITT-VP model (Pescatello et al. 2006), into groups by frequency, intensity, type, time, volume and progression, carrying out subgroup analysis on each of these variables. Sample size, mean and standard deviation data, presented pre and post intervention, were used, and the values were normalised to 0–10 in order to reduce the heterogeneity standardising the results.

Forest plots with mean differences (MD) and 95% confidence intervals (CI) were used to present the results of the meta-analysis, instead of standardised mean difference (SMD), due to the results of the intervention, which could be normalised (C. Andrade 2020; Tufanaru et al. 2015). Heterogeneity was also presented, which was calculated by measuring by the I^2 index, and to analyse publication bias the Egger test (Egger et al. 1997) was used. Also, a sensitivity analysis was performed to assess whether the effect size varied after eliminating each study. The overall heterogeneity was considered for the primary analysis, and subgroup-specific heterogeneity was taken into account for the dose–response analysis. The p value for heterogeneity was examined, assuming the presence of it when $p < 0.05$, which compromises the validity of the pooled estimates (Takkouche, Cadarso-Suárez and Spiegelman 1999). Furthermore, the I^2 index included low heterogeneity (0%–40%); moderate (30%–60%); considerable (50%–90%); and substantial (75%–100%) (Shamseer et al. 2015). Given that the intervention and population in this study was presumed to be heterogenous, a random effect model was selected to measure the effect of the studies included (Berlin et al. 1989; Lipsey and Wilson 2001; Shadish et al. 1994; Tufanaru et al. 2015).

To fulfil the meta-analysis, the Review Manager program (RevMan), Version 5.4, was used (The Cochrane Collaboration 2020). Statistical significance was considered when $p < 0.05$ and the results were shown in MD followed by CI.

2.8 | Clinical Relevance

The concept of minimal clinically important difference (MCID) was used to analyse the effect of different doses of exercise. MCID is the minimal difference in an outcome that is perceived as relevant by patients (Copay et al. 2007; King 2011). According to a paper by Dworkin et al. 2008 the minimally important clinical difference in pain reduction in a population suffering chronic pain, on a 0–10 scale, would be a 10%–20% decrease in the intensity of pain, with a recent paper by Fleagle et al. 2024 setting the MCID for pain during movement in musculoskeletal conditions at 1.1. Taking the mean of that interval, the MD considered relevant and, therefore, taken into account in this study, was a 15% pain reduction, equivalent to a decrease of 1.5 on a 0–10 scale.

3 | Results

3.1 | Studies Selected

An initial number of 2432 papers were identified from all the databases, with 1454 remaining after duplicates were eliminated. Following title and abstract checking, 76 full-text articles were assessed for eligibility with 17 (S. C. D. Andrade et al. 2008; Bircan et al. 2008; Fernandes et al. 2016; Franco et al. 2023; Gómez-Hernández et al. 2020; Hernando-Garijo et al. 2021; Hooten et al. 2012; Kolak, Ardıç and Fındıkoğlu 2022; Mannerkorpi et al. 2010; Medeiros et al. 2020; Mendonca et al. 2016; Rooks et al. 2007; Sanudo et al. 2015; Schachter et al. 2003; Sencan et al. 2004; Valim et al. 2003; Wigers, Stiles and Vogel 1996) of then eventually being included in the quantitative analysis after inclusion and exclusion criteria were applied (Figure 1).

3.2 | Description and Characteristics of the Studies Selected

A total of 1095 patients were analysed in 17 studies, with only seven of them being male and 1088 being female, all diagnosed using the ACR criteria. Eleven studies used the 1990 criteria (S. C. D. Andrade et al. 2008; Bircan et al. 2008; Fernandes et al. 2016; Hernando-Garijo et al. 2021; Hooten et al. 2012; Mannerkorpi et al. 2010; Rooks et al. 2007; Sanudo et al. 2015; Schachter et al. 2003; Sencan et al. 2004; Valim et al. 2003; Wigers, Stiles and Vogel 1996), three studies used the 2010 criteria (Franco et al. 2023; Medeiros et al. 2020; Mendonca et al. 2016), one study used both the 1990 and the 2010 criteria (Gómez-Hernández et al. 2020) and two studies used the 2016 criteria (Hernando-Garijo et al. 2021; Kolak, Ardıç and Fındıkoğlu 2022). Pain was recorded in every study, whether it was the main outcome or not, with the Visual Analogue Scale (VAS) being used in twelve studies (S. C. D. Andrade et al. 2008; Bircan et al. 2008; Fernandes et al. 2016; Gómez-Hernández et al. 2020; Hernando-Garijo et al. 2021; Kolak, Ardıç and Fındıkoğlu 2022; Medeiros et al. 2020; Sanudo et al. 2015; Schachter et al. 2003; Sencan et al. 2004; Valim et al. 2003; Wigers, Stiles and Vogel 1996), the Numerical Rating Scale (NRS) being used in one study (Franco et al. 2023), the Pain Severity subscale of the Multidimensional Pain Inventory being used in one study (Hooten et al. 2012), the Fibromyalgia Impact Questionnaire Pain subscale (FIQ Pain) being used in two studies (Mannerkorpi et al. 2010; Rooks et al. 2007), and the Visual Numerical Scale being used in one study (Mendonca et al. 2016) (Table 1).

3.3 | Risk of Bias

Overall, six papers featured low risk of bias (Fernandes et al. 2016; Franco et al. 2023; Gómez-Hernández et al. 2020; Hernando-Garijo et al. 2021; Mannerkorpi et al. 2010; Medeiros et al. 2020), five papers presented some concerns (Hooten et al. 2012; Mendonca et al. 2016; Rooks et al. 2007; Sanudo et al. 2015; Wigers, Stiles and Vogel 1996) and six presented a high risk of bias (S. C. D. Andrade et al. 2008; Bircan

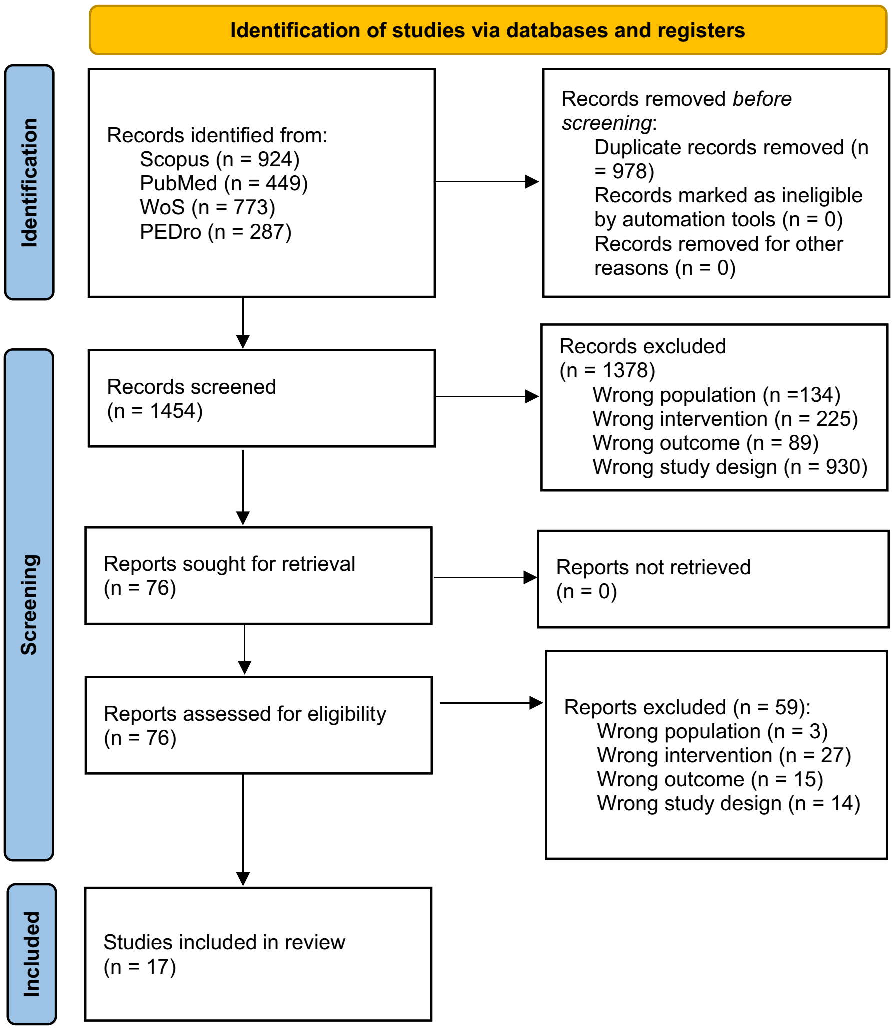


FIGURE 1 | Prisma flow chart.

TABLE 1 | Characteristic of selected studies.

Authors (year)	ACR diagnostic criteria	Sample size (AE/CO), Sex (F/M), Age (AE/CO)	Aerobic group	Comparison group	Pain measurement	Follow-up	Results and conclusions
Bircan et al. (2008)	1990	13/13 All F 48′3 ± 5′3/46 ± 8,5	AE	SE	VAS	Not performed	Aerobic exercise and strength training significantly improved symptoms, tender point count, fitness, depression and quality of life in fibromyalgia without differences between both groups of exercise.
Andrade et al. (2008)	1990	23/23 All F 48′8 ± 9′9/48′3 ± 8′9	Two AE groups	None	VAS	Not performed	Aerobic exercise program performed in water (pool or sea) was significantly effective reducing pain for patients with fibromyalgia. However, sea water exercises have been shown to bring more advantages related to emotional aspects.
Medeiros et al. (2020)	2010	21/21 All F 50′7 ± 9′7/45′5 ± 10′6	AE	Modified Pilates	VAS	Not performed	Significant improvements were observed in the two groups in relation to the disease symptoms and no differences were observed between mat Pilates and aquatic aerobic exercise in any of the measured variables.
Fernandes et al. (2016)	1990	39/36 All F 48′3 ± 8′9/49′3 ± 9′2	Two AE groups	None	VAS	Not performed	Swimming, like walking, is an effective method for significantly reducing pain and improving both functional capacity and quality of life in patients with fibromyalgia.
Franco et al. (2023)	2010	49/48 All F/47F and 1 M 48′5 ± 10/51′4 ± 10′1	AE	Modified Pilates	NRS	Twelve months	There was no significant difference between groups for the impact of fibromyalgia. Pilates was not cost-effective compared to aerobic exercise for the impact of fibromyalgia. However, Pilates seemed to be the preferred option of treatment although it depends on the willingness-to-pay threshold
Gómez-Hernández et al. (2020)	1990 and 2010	32/32 All F 54′8 ± 8′52/53′97 ± 5	AE	AE + Stretching	VAS	Not performed	Adding stretching to a moderate-intensity aerobic exercise program significantly increased sleep quality, decreased the impact of fibromyalgia on the quality of life and reduce pain compared with just a moderate-intensity aerobic exercise program.

(Continues)

TABLE 1 | (Continued)

Authors (year)	ACR diagnostic criteria	Sample size (AE/CO), Sex (F/M), Age (AE/CO)	Aerobic group	Comparison group	Pain measurement	Follow-up	Results and conclusions
Hernando-Garijo et al. (2021)	2016	17/17 All F 51′81 ± 9′05/55′06 ± 8′51	AE	Control group	VAS	Not performed	A telerehabilitation program based on aerobic exercise achieved significant improvements on pain intensity, mechanical pain sensitivity and psychological distress compared to a control group during the lockdown declared in Spain due to COVID-19 pandemic.
Hooten et al. (2012)	1990	36/36 All F 45′8 ± 11′5/47′3 ± 10′1	AE	SE	Pain Severity subscale of the Multidimensional Pain inventory	Not performed	Strength and aerobic exercise had equivalent effects, both significantly reducing pain severity among patients with fibromyalgia.
Kolak, Ardıç and Fındıkoğlu (2022)	2016	13/13/15 All F 48′3 ± 10/46 ± 11′2/4′9 ± 7′6	AE	SE Stretching	VAS	Not performed	Supervised aerobic/muscle strengthening combined with stretching exercises reduce pain and FM severity more than a home stretching exercise alone.
Mannerkorpi et al. (2010)	1990	34/33 All F 48 ± 7′8/50 ± 7′6	Two AE groups	None	FIQ Pain	Six months	Moderate-to-high intensity aerobic exercise by means of Nordic walking twice a week for 15 weeks was found to be a feasible mode of exercise, resulting in a significantly improved functional capacity and a decreased level of activity limitations. Pain severity did not change over time during the exercise period.
Mendonca et al. (2016)	2010	15/15/15 All F/ All F/ 14F and 1 M 48 ± 11′8/49′9 ± 10′6/44′5 ± 14	AE	tDCS tDCS + AE	VNS	Two months	The combination of tDCS with aerobic exercise is superior compared with each individual intervention (cohen's d effect sizes > 0.55). The combination intervention had a significant effect on pain, anxiety and mood while AE or tDCS alone could reach significant differences between each other.

(Continues)

TABLE 1 | (Continued)

Authors (year)	ACR diagnostic criteria	Sample size (AE/CO), Sex (F/M), Age (AE/CO)	Aerobic group	Comparison group	Pain measurement	Follow-up	Results and conclusions
Rooks et al. (2007)	1990	35/35/27/38 All F 48 ± 11/50 ± 11/51 ± 12/0 ± 11	AE	SE SE + Education	FIQ Pain	Six months	Progressive walking, simple strength training movements and stretching activities significantly improved functional status, key symptoms and self-efficacy in women with fibromyalgia actively being treated with medication. The benefits of exercise are enhanced when combined with targeted self-management education.
Sanudo et al. (2015)	1990	16/12 All F 55 ± 2/58 ± 2	AE	Control group	VAS	Not performed	Aerobic exercise training induces changes in cardiac autonomic nervous system modulation in fibromyalgia and suggest that these changes in heart rate variability parameters were accompanied by changes in anxiety and depression.
Schachter et al. (2003)	1990	56/51/36 All F 41′9 ± 8′57/41′3 ± 8′67/42′5 ± 6′69	Two AE groups	Control group	VAS	Not performed	Progressive, home-based, low-impact aerobics improved physical function and fibromyalgia symptoms minimally in participants who completed at least two thirds of the recommended exercise. Fractionation of exercise training provide no advantage in terms of exercise adherence, improvements in fibromyalgia symptoms or physical function.
Sencan et al. (2004)	1990	20/20/20 All F 35′4 ± 9′62/35′55 ± 7′86/32′65 ± 9′39	AE	Control group Paroxetine	VAS	Six months	Paroxetine and aerobic exercises have significantly better therapeutic effect when compared to placebo group on long-term follow-up with no significant difference on evaluation parameters.
Valim et al. (2003)	1990	32/28 All F	AE	Stretching	VAS	Not performed	Aerobic exercise is beneficial to patients with fibromyalgia, but the cardiorespiratory fitness gain is not related to improvement of fibromyalgia symptoms.

(Continues)

TABLE 1 | (Continued)

Authors (year)	ACR diagnostic criteria	Sample size (AE/CO), Sex (F/M), Age (AE/CO)	Aerobic group	Comparison group	Pain measurement	Follow-up	Results and conclusions
Wigers, Stiles and Vogel (1996)	1990	20/20/20 18F and 2M/18F and 2M/19F and 1M 43/44/46	AE	Stress management Control group	VAS	Four years	Both Aerobic exercise and stress management showed positive short-term effects. Aerobic exercise was significantly most effective at follow up, despite being subject to the most sceptical patient attitude prior to the study.

Abbreviations: ACR, American College of Rheumatology; AE, aerobic exercise; CO, comparator; F, female; FIQ, Fibromyalgia Impact Questionnaire; M, male; NRS, Numeric Rating Scale; SE, strength exercise; VAS, Visual Analogue Scale; VNS, Verbal Numeric Scale.

et al. 2008; Kolak, Ardıç and Fındıkoğlu 2022; Schachter et al. 2003; Sencan et al. 2004; Valim et al. 2003). The domain with the least risk of bias was the fourth, with only one study (Sencan et al. 2004) showing a high risk of bias in it (Data S2 and S3).

3.4 | Characteristics of the Aerobic Exercise Prescription

To summarise the characteristics of the intervention studied, the FITT-VP model (Pescatello et al. 2006) was used (Table 2).

In terms of frequency, the studies selected ranged from one to ten times per week, with one of them featuring training one time per week (Mannerkorpi et al. 2010), six of them, two times per week (Franco et al. 2023; Hernando-Garijo et al. 2021; Mannerkorpi et al. 2010; Medeiros et al. 2020; Rooks et al. 2007; Sanudo et al. 2015), nine of them, three times per week (S. C. D. Andrade et al. 2008; Bircan et al. 2008; Fernandes et al. 2016; Gómez-Hernández et al. 2020; Kolak, Ardıç and Fındıkoğlu 2022; Mendonca et al. 2016; Sencan et al. 2004; Valim et al. 2003; Wigers, Stiles and Vogel 1996); one study, three to five and six to ten times per week (Schachter et al. 2003); and another study, five times per week (Hooten et al. 2012).

Several ways of prescribing intensity were use in the studies selected, ranging from a percentage of maximum heart rate (Bircan et al. 2008; Fernandes et al. 2016; Franco et al. 2023; Gómez-Hernández et al. 2020; Hooten et al. 2012; Mendonca et al. 2016; Sanudo et al. 2015; Schachter et al. 2003; Valim et al. 2003; Wigers, Stiles and Vogel 1996), to VO_{2max} (S. C. D. Andrade et al. 2008; Kolak, Ardıç and Fındıkoğlu 2022), to Borg's rate of perceived exertion (RPE) (G. Borg 1998; G. A. V. Borg 1982), both modified (Hernando-Garijo et al. 2021; Medeiros et al. 2020) and non-modified (Mannerkorpi et al. 2010). Two studies did not report on the intensity of the exercise (Rooks et al. 2007; Sencan et al. 2004). In order to summarise intensity, mean intensity was calculated using the intensity reported in each study, and synthetized into light, moderate or vigorous intensity, according to ACSM criteria (Garber et al. 2011). Therefore, four studies were classified as light intensity (S. C. D. Andrade et al. 2008; Gómez-Hernández et al. 2020; Mannerkorpi et al. 2010; Schachter et al. 2003), seven studies, as moderate intensity (Bircan et al. 2008; Franco et al. 2023; Hooten et al. 2012; Kolak, Ardıç and Fındıkoğlu 2022; Mendonca et al. 2016; Sanudo et al. 2015; Wigers, Stiles and Vogel 1996); and four were labelled as vigorous intensity (Fernandes et al. 2016; Hernando-Garijo et al. 2021; Mannerkorpi et al. 2010; Valim et al. 2003).

Three studies used music-based exercise classes as its intervention (Hernando-Garijo et al. 2021; Schachter et al. 2003; Wigers, Stiles and Vogel 1996), two used interval training (Mannerkorpi et al. 2010; Sanudo et al. 2015), two used pool-based exercise (S. C. D. Andrade et al. 2008; Medeiros et al. 2020), three used stationary bikes (Gómez-Hernández et al. 2020; Hooten et al. 2012; Sencan et al. 2004), one used swimming (Fernandes et al. 2016), another used treadmills or stationary bikes, according to the patient's preference (Franco et al. 2023); four used treadmills

TABLE 2 | Characteristics of the aerobic exercise intervention.

Authors (year)	Frequency	Intensity	Type	Time	Volume	Progression
Bircan et al. (2008)	3 times per week	60%–70% MHR	Walking on treadmill	8 weeks	20–30 min	No progression
Andrade et al. (2008)	3 times per week	50%–75% VO_{2max}	Pool-based aerobic exercise (pool)	12 weeks	40 min	No progression
	3 times per week	50%–75% VO_{2max}	Pool-based aerobic exercise (sea)	12 weeks	40 min	No progression
Medeiros et al. (2020)	2 times per week	Not reported	Pool-based aerobic exercise	12 weeks	30 min	No progression
Fernandes et al. (2016)	3 times per week	11 beats bellow anaerobic threshold	Swing group	12 weeks	40 min	No progression
	3 times per week	Anaerobic threshold	Walking group	12 weeks	40 min	No progression
Franco et al. (2023)	2 times per week	57–76 MHR	Treadmill or stationary bike	8 weeks	40 min	No progression
Gómez-Hernández et al. (2020)	3 times per week	50%–70% MHR	Stationary cycling	12 weeks	10 min	No progression
Hernando-Garijo et al. (2021)	2 times per week	4–7 Modified RPE Borg	Aerobic-type exercise	15 weeks	Not reported	No progression
Hooten et al. (2012)	5 times per week	70%–75% MHR	Stationary cycling	3 weeks	10–30 min	Time progression
Kolak, Ardıç and Fındıkoğlu (2022)	3 times per week	50%–70% VO_{2max}	Walking on treadmill	12 weeks	40 min	Intensity progression
Mannerkorpi et al. (2010)	2 times per week	13–15 RPE	Interval Nordic walking	15 weeks	20 min	No progression
	1 time per week	9–11 RPE	Walking group	15 weeks	Not reported	No progression
Mendonca et al. (2016)	3 times per week	60%–70% MHR	Walking on treadmill	4 weeks	30 min	Intensity progression
Rooks et al. (2007)	2 times per week	Not reported	Walking on treadmill	16 weeks	45 min	Time progression
Sanudo et al. (2015)	2 times per week	60%–80% MHR	Walking on treadmill	24 weeks	30–35 min	No progression
Schachter et al. (2003)	6–10 times per week	40%–75% MHR	Aerobic-type exercise	16 weeks	5–15 min	Both time and intensity progression
	3–5 times per week	40%–65% MHR	Aerobic-type exercise	16 weeks	10–30 min	
Sencan et al. (2004)	3 times per week	Not reported	Stationary cycling	6 weeks	30 min	No progression
Valim et al. (2003)	3 times per week	Anaerobic threshold	Walking group	20 weeks	30–35 min	No progression
Wigers, Stiles and Vogel (1996)	3 times per week	60%–70% MHR	Aerobic-type exercise	14 weeks	18–20 min	No progression

Abbreviations: MHR, maximum heart rate; RPE, rate of perceived exertion; VO_{2max}, maximal oxygen volume.

(Bircan et al. 2008; Kolak, Ardıç and Fındıkoğlu 2022; Mendonca et al. 2016; Rooks et al. 2007), while another three walked outside (Fernandes et al. 2016; Mannerkorpi et al. 2010; Valim et al. 2003).

The duration of the intervention ranged from three to twenty-four weeks, with three individual studies using three (Hooten et al. 2012), four (Mendonca et al. 2016) and 6 weeks (Sencan et al. 2004). Two studies were in the eight-week range (Bircan et al. 2008; Franco et al. 2023), five studies were in the twelve-week range (S. C. D. Andrade et al. 2008; Fernandes et al. 2016; Gómez-Hernández et al. 2020; Kolak, Ardıç and Fındıkoğlu 2022; Medeiros et al. 2020) one lasted fourteen weeks (Wigers, Stiles and Vogel 1996), two lasted fifteen (Hernando-Garijo et al. 2021; Mannerkorpi et al. 2010), another two ran for sixteen weeks (Rooks et al. 2007; Schachter et al. 2003) and two individuals studies spanned twenty (Valim et al. 2003) and twenty-four weeks (Sanudo et al. 2015).

Volume was measured in minutes, and ranged from ten to forty-five. In order to better synthetize the volumes of the interventions, mean times were used for the individual studies that used time ranges for their interventions. With this in mind, two studies used ten minutes (Gómez-Hernández et al. 2020; Schachter et al. 2003), one used nineteen minutes (Wigers, Stiles and Vogel 1996), three studies used twenty minutes (Hooten et al. 2012; Mannerkorpi et al. 2010; Schachter et al. 2003), one used twenty-five minutes (Bircan et al. 2008), three used thirty minutes (Medeiros et al. 2020; Mendonca et al. 2016; Sencan et al. 2004), two studies thirty-two and a half minutes (Sanudo et al. 2015; Valim et al. 2003), four studies featured exercise for forty minutes (S. C. D. Andrade et al. 2008; Fernandes et al. 2016; Franco et al. 2023; Kolak, Ardıç and Fındıkoğlu 2022) and one study involved exercise for forty-five minutes (Rooks et al. 2007). To determine the weekly volume of exercise, the daily exercise time was multiplied by its frequency, and the interventions were divided into three groups: less than sixty minutes, in three studies (Hernando-Garijo et al. 2021; Mannerkorpi et al. 2010; Wigers, Stiles and Vogel 1996); between sixty minutes and a hundred minutes, in eight studies (Bircan et al. 2008; Franco et al. 2023; Medeiros et al. 2020; Mendonca et al. 2016; Rooks et al. 2007; Sanudo et al. 2015; Schachter et al. 2003; Valim et al. 2003), and more than a hundred minutes, in four studies (S. C. D. Andrade et al. 2008; Fernandes et al. 2016; Hooten et al. 2012; Kolak, Ardıç and Fındıkoğlu 2022).

The progression was only reported in five studies (Hooten et al. 2012; Kolak, Ardıç and Fındıkoğlu 2022; Mendonca et al. 2016; Rooks et al. 2007; Schachter et al. 2003), with two of them increasing in intensity (Kolak, Ardıç and Fındıkoğlu 2022; Mendonca et al. 2016), another two, in time (Hooten et al. 2012; Rooks et al. 2007) and one individual study tracking increases in both intensity and time (Schachter et al. 2003).

3.5 | Treatment Results

Overall, a qualitative analysis was performed to summarise the quality of evidence for prescribing aerobic exercise for pain management among fibromyalgia patients (Table 3). Moreover, forest plots were generated, showcasing the effect size and confidence

TABLE 3 | Quality of the evidence (GRADE).

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ejercicio aeróbico	Comparación	Relative (95% CI)	Absolute (95% CI)		
Pain												
13	Randomised trials	Serious[a]	Serious[b]	Not serious	Not serious	None	517	470	—	MD: −0.42 CI (−0.83, −0.01)	⊕⊕○○ Low[a,b]	

Abbreviations: CI, confidence interval; MD, mean difference.
[a]Two-thirds of the studies present a high risk of bias or raise significant concerns regarding the reliability of their findings.
[b]The results vary across studies, indicating potential differences.

interval for each individual study, as well as totals. A global forest plot comparing aerobic exercise with another treatment or control group was produced, classifying each study into a subgroup depending on comparison. If one of the studies had more than one comparison, it was divided into as many subgroups as necessary. For the dose analysis, based on the FITT-VP model (Pescatello et al. 2006), an individual forest plot was also completed for each variable.

3.5.1 | Overall Qualitative Analysis and Meta-Analysis

Included in this analysis were thirteen studies (Bircan et al. 2008; Franco et al. 2023; Hernando-Garijo et al. 2021; Hooten et al. 2012; Kolak, Ardıç and Fındıkoğlu 2022; Medeiros et al. 2020; Mendonca et al. 2016; Rooks et al. 2007; Sanudo et al. 2015; Schachter et al. 2003; Sencan et al. 2004; Valim et al. 2003; Wigers, Stiles and Vogel 1996), with nine different subgroups, and nineteen individual data entries, comparing, against a control group (Hernando-Garijo et al. 2021; Sanudo et al. 2015; Schachter et al. 2003; Sencan et al. 2004; Wigers, Stiles and Vogel 1996), resistance training (Bircan et al. 2008; Hooten et al. 2012; Kolak, Ardıç and Fındıkoğlu 2022; Rooks et al. 2007), stretching (Kolak, Ardıç and Fındıkoğlu 2022; Valim et al. 2003), Pilates (Franco et al. 2023; Medeiros et al. 2020), transcranial direct current stimulation (tDCS) (Mendonca et al. 2016), paroxetine (Sencan et al. 2004), education (Rooks et al. 2007), education combined with resistance training (Rooks et al. 2007) and stress management techniques (Wigers, Stiles and Vogel 1996). The Quality of the evidence was moderate, and the general results favoured aerobic exercise, with a statistically significant difference (MD −0.49; CI [−0.90, −0.08; $p = 0.02$]), and considerable heterogeneity ($I^2 = 62\%$). In the analysis by subgroups, aerobic exercise only presented differences with the control group (MD −1.14; CI [−1.76, −0.52]; $p < 0.001$) and the stretching group (MD −1.41; CI [−2.21, −0.62]; $p < 0.001$), with low heterogeneity ($I^2 = 37\%$), and none ($I^2 = 0\%$), respectively. Comparison of the effects of resistance training, Pilates, paroxetine, education, education plus resistance training, and stress management techniques, found no significant differences, with no heterogeneity for resistance training ($I^2 = 0\%$) and substantial heterogeneity for the comparison with Pilates ($I^2 = 79\%$). For the comparisons with tDCS, paroxetine, education, education plus resistance training, and stress management techniques, the analysis could not be applied, as there was only one study in each group (Figure 2). Publication bias was analysed through visual inspection of the funnel plot (Data S4), and a sensitivity analysis was performed excluding articles with possible bias, but this did not alter the overall results.

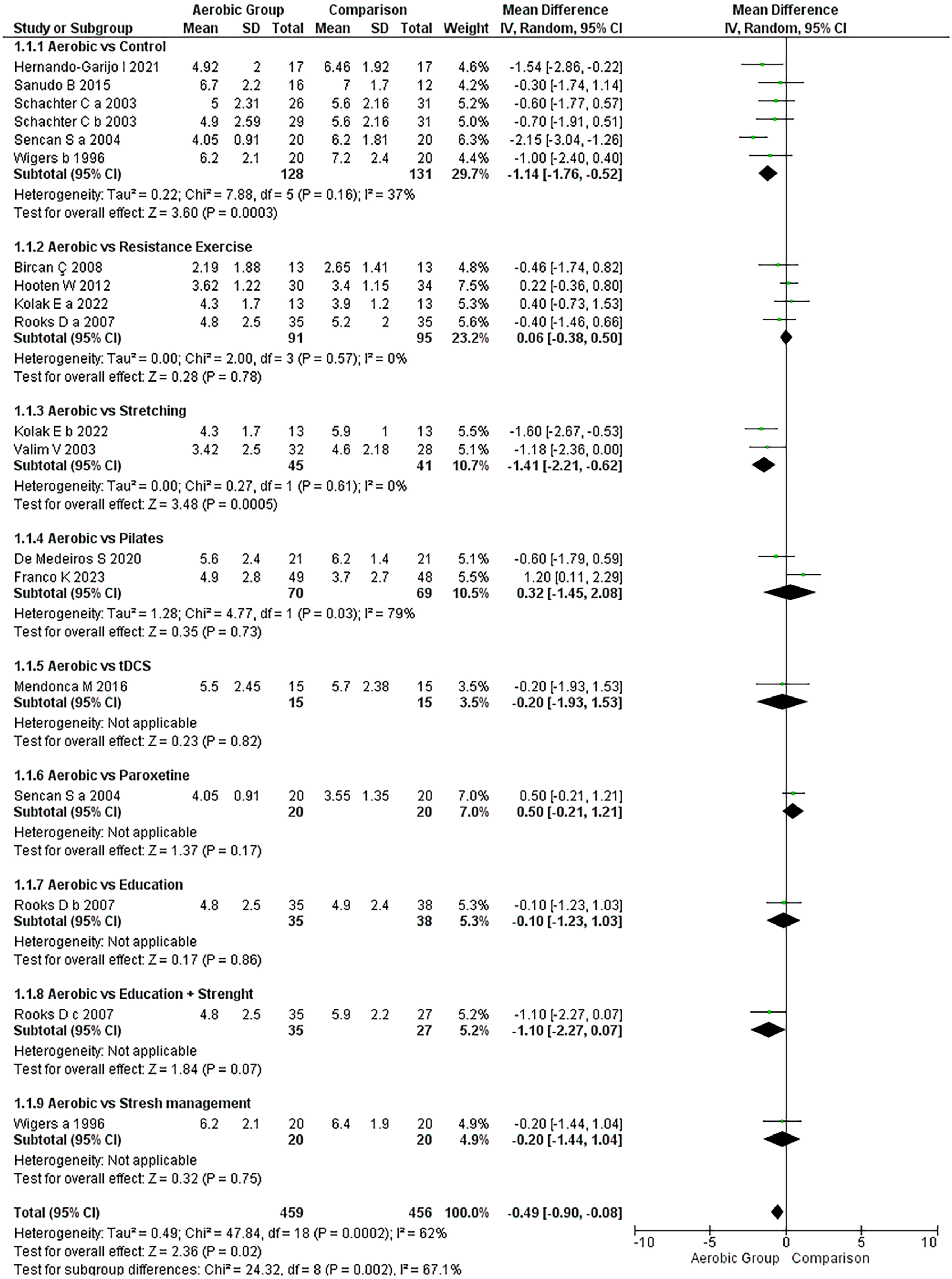
3.5.2 | Dose Analysis

The dose analysis was divided into six different groups, based on the FITT-VP model (Pescatello et al. 2006), with independent subgroups analysis in each variable using the mean difference between pre and post treatment.

3.5.2.1 | Frequency. For this examination fifteen different studies (S. C. D. Andrade et al. 2008; Bircan et al. 2008; Fernandes et al. 2016; Franco et al. 2023; Hernando-Garijo et al. 2021; Hooten et al. 2012; Kolak, Ardıç and Fındıkoğlu 2022; Mannerkorpi et al. 2010; Medeiros et al. 2020; Mendonca et al. 2016; Rooks et al. 2007; Sanudo et al. 2015; Schachter et al. 2003; Sencan et al. 2004; Valim et al. 2003), with eighteen separated interventions, were utilised and organised into six subgroups based on the frequency of exercise per week: one (Mannerkorpi et al. 2010), two (Franco et al. 2023; Hernando-Garijo et al. 2021; Medeiros et al. 2020; Rooks et al. 2007; Sanudo et al. 2015), three (S. C. D. Andrade et al. 2008; Bircan et al. 2008; Fernandes et al. 2016; Kolak, Ardıç and Fındıkoğlu 2022; Mendonca et al. 2016; Sencan et al. 2004; Valim et al. 2003), three to five (Schachter et al. 2003), five (Hooten et al. 2012) and six to ten (Schachter et al. 2003) times per week. Differences were observed in the two (MD 1.84; CI [1.13, 2.54]; $p < 0.001$), three (MD 3.02; CI [2.61, 3.43]; $p < 0.001$) and five (MD 1.24; CI [0.75, 1.73]; $p < 0.001$) times per week subgroups, without significant heterogeneity within the subgroups (Figure 3).

3.5.2.2 | Intensity. In this examination, eleven (S. C. D. Andrade et al. 2008; Fernandes et al. 2016; Gómez-Hernández et al. 2020; Hernando-Garijo et al. 2021; Hooten et al. 2012; Kolak, Ardıç and Fındıkoğlu 2022; Mannerkorpi, Burckhardt and Bjelle 1994; Medeiros et al. 2020; Mendonca et al. 2016; Rooks et al. 2007; Sanudo et al. 2015; Schachter et al. 2003; Valim et al. 2003; Wigers, Stiles and Vogel 1996) distinct studies, with thirteen interventions, were separate, utilised and classified, based on the mean intensity of exercise, applying the ACSM classification (Garber et al. 2011) to establish three subgroups: light (Gómez-Hernández et al. 2020; Mannerkorpi et al. 2010; Schachter et al. 2003), moderate (Hooten et al. 2012; Kolak, Ardıç and Fındıkoğlu 2022; Mendonca et al. 2016; Sanudo et al. 2015; Wigers, Stiles and Vogel 1996) and vigorous (Fernandes et al. 2016; Hernando-Garijo et al. 2021; Valim et al. 2003) exercise. Differences were found through all subgroup analyses of light (MD 0.82; CI [0251, 1.38]; $p = 0.004$), moderate (MD 1.35; CI [0.83, 1.86]; $p < 0.001$) and vigorous (MD 2.77; CI [2.25, 3.29]; $p < 0.001$) exercise, without significant heterogeneity within the subgroups (Figure 4).

3.5.2.3 | Type. In this analysis, fourteen (S. C. D. Andrade et al. 2008; Bircan et al. 2008; Fernandes et al. 2016; Gómez-Hernández et al. 2020; Hernando-Garijo et al. 2021; Hooten et al. 2012; Kolak, Ardıç and Fındıkoğlu 2022; Mannerkorpi et al. 2010; Medeiros et al. 2020; Mendonca et al. 2016; Rooks et al. 2007; Sanudo et al. 2015; Sencan et al. 2004; Valim et al. 2003) studies, with seventeen interventions, were separated, incorporated and categorised based on the type of exercise included in the respective exercise programs, divided into music-based exercise (Hernando-Garijo et al. 2021; Schachter et al. 2003; Wigers, Stiles and Vogel 1996), interval training (Mannerkorpi, Burckhardt and Bjelle 1994; Sanudo et al. 2015), pool-based exercise (S. C. D. Andrade et al. 2008; Medeiros et al. 2020), stationary cycling (Gómez-Hernández et al. 2020; Hooten et al. 2012), swimming (Fernandes et al. 2016), walking outside (Fernandes et al. 2016; Valim et al. 2003) and walking on a treadmill (Kolak, Ardıç and Fındıkoğlu 2022; Mendonca et al. 2016; Rooks et al. 2007) The study conducted by Franco et al. 2023, although it reported the type of intervention, was excluded due to the incorporation of two different kinds of cardiovascular exercises in its group. Differences were observed



Study or Subgroup	Aerobic Group Mean	Aerobic Group SD	Aerobic Group Total	Comparison Mean	Comparison SD	Comparison Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 Aerobic vs Control								
Hernando-Garijo I 2021	4.92	2	17	6.46	1.92	17	4.6%	-1.54 [-2.86, -0.22]
Sanudo B 2015	6.7	2.2	16	7	1.7	12	4.2%	-0.30 [-1.74, 1.14]
Schachter C a 2003	5	2.31	26	5.6	2.16	31	5.2%	-0.60 [-1.77, 0.57]
Schachter C b 2003	4.9	2.59	29	5.6	2.16	31	5.0%	-0.70 [-1.91, 0.51]
Sencan S a 2004	4.05	0.91	20	6.2	1.81	20	6.3%	-2.15 [-3.04, -1.26]
Wigers b 1996	6.2	2.1	20	7.2	2.4	20	4.4%	-1.00 [-2.40, 0.40]
Subtotal (95% CI)			**128**			**131**	**29.7%**	**-1.14 [-1.76, -0.52]**
Heterogeneity: Tau² = 0.22; Chi² = 7.88, df = 5 (P = 0.16); I² = 37%								
Test for overall effect: Z = 3.60 (P = 0.0003)								
1.1.2 Aerobic vs Resistance Exercise								
Bircan Ç 2008	2.19	1.88	13	2.65	1.41	13	4.8%	-0.46 [-1.74, 0.82]
Hooten W 2012	3.62	1.22	30	3.4	1.15	34	7.5%	0.22 [-0.36, 0.80]
Kolak E a 2022	4.3	1.7	13	3.9	1.2	13	5.3%	0.40 [-0.73, 1.53]
Rooks D a 2007	4.8	2.5	35	5.2	2	35	5.6%	-0.40 [-1.46, 0.66]
Subtotal (95% CI)			**91**			**95**	**23.2%**	**0.06 [-0.38, 0.50]**
Heterogeneity: Tau² = 0.00; Chi² = 2.00, df = 3 (P = 0.57); I² = 0%								
Test for overall effect: Z = 0.28 (P = 0.78)								
1.1.3 Aerobic vs Stretching								
Kolak E b 2022	4.3	1.7	13	5.9	1	13	5.5%	-1.60 [-2.67, -0.53]
Valim V 2003	3.42	2.5	32	4.6	2.18	28	5.1%	-1.18 [-2.36, 0.00]
Subtotal (95% CI)			**45**			**41**	**10.7%**	**-1.41 [-2.21, -0.62]**
Heterogeneity: Tau² = 0.00; Chi² = 0.27, df = 1 (P = 0.61); I² = 0%								
Test for overall effect: Z = 3.48 (P = 0.0005)								
1.1.4 Aerobic vs Pilates								
De Medeiros S 2020	5.6	2.4	21	6.2	1.4	21	5.1%	-0.60 [-1.79, 0.59]
Franco K 2023	4.9	2.8	49	3.7	2.7	48	5.5%	1.20 [0.11, 2.29]
Subtotal (95% CI)			**70**			**69**	**10.5%**	**0.32 [-1.45, 2.08]**
Heterogeneity: Tau² = 1.28; Chi² = 4.77, df = 1 (P = 0.03); I² = 79%								
Test for overall effect: Z = 0.35 (P = 0.73)								
1.1.5 Aerobic vs tDCS								
Mendonca M 2016	5.5	2.45	15	5.7	2.38	15	3.5%	-0.20 [-1.93, 1.53]
Subtotal (95% CI)			**15**			**15**	**3.5%**	**-0.20 [-1.93, 1.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.23 (P = 0.82)								
1.1.6 Aerobic vs Paroxetine								
Sencan S a 2004	4.05	0.91	20	3.55	1.35	20	7.0%	0.50 [-0.21, 1.21]
Subtotal (95% CI)			**20**			**20**	**7.0%**	**0.50 [-0.21, 1.21]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.37 (P = 0.17)								
1.1.7 Aerobic vs Education								
Rooks D b 2007	4.8	2.5	35	4.9	2.4	38	5.3%	-0.10 [-1.23, 1.03]
Subtotal (95% CI)			**35**			**38**	**5.3%**	**-0.10 [-1.23, 1.03]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.17 (P = 0.86)								
1.1.8 Aerobic vs Education + Strenght								
Rooks D c 2007	4.8	2.5	35	5.9	2.2	27	5.2%	-1.10 [-2.27, 0.07]
Subtotal (95% CI)			**35**			**27**	**5.2%**	**-1.10 [-2.27, 0.07]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.84 (P = 0.07)								
1.1.9 Aerobic vs Stresh management								
Wigers a 1996	6.2	2.1	20	6.4	1.9	20	4.9%	-0.20 [-1.44, 1.04]
Subtotal (95% CI)			**20**			**20**	**4.9%**	**-0.20 [-1.44, 1.04]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.32 (P = 0.75)								
Total (95% CI)			**459**			**456**	**100.0%**	**-0.49 [-0.90, -0.08]**
Heterogeneity: Tau² = 0.49; Chi² = 47.84, df = 18 (P = 0.0002); I² = 62%								
Test for overall effect: Z = 2.36 (P = 0.02)								
Test for subgroup differences: Chi² = 24.32, df = 8 (P = 0.002), I² = 67.1%								

FIGURE 2 | Aerobic exercise versus comparation. A minus sign signifies an effect in favour of the aerobic intervention.

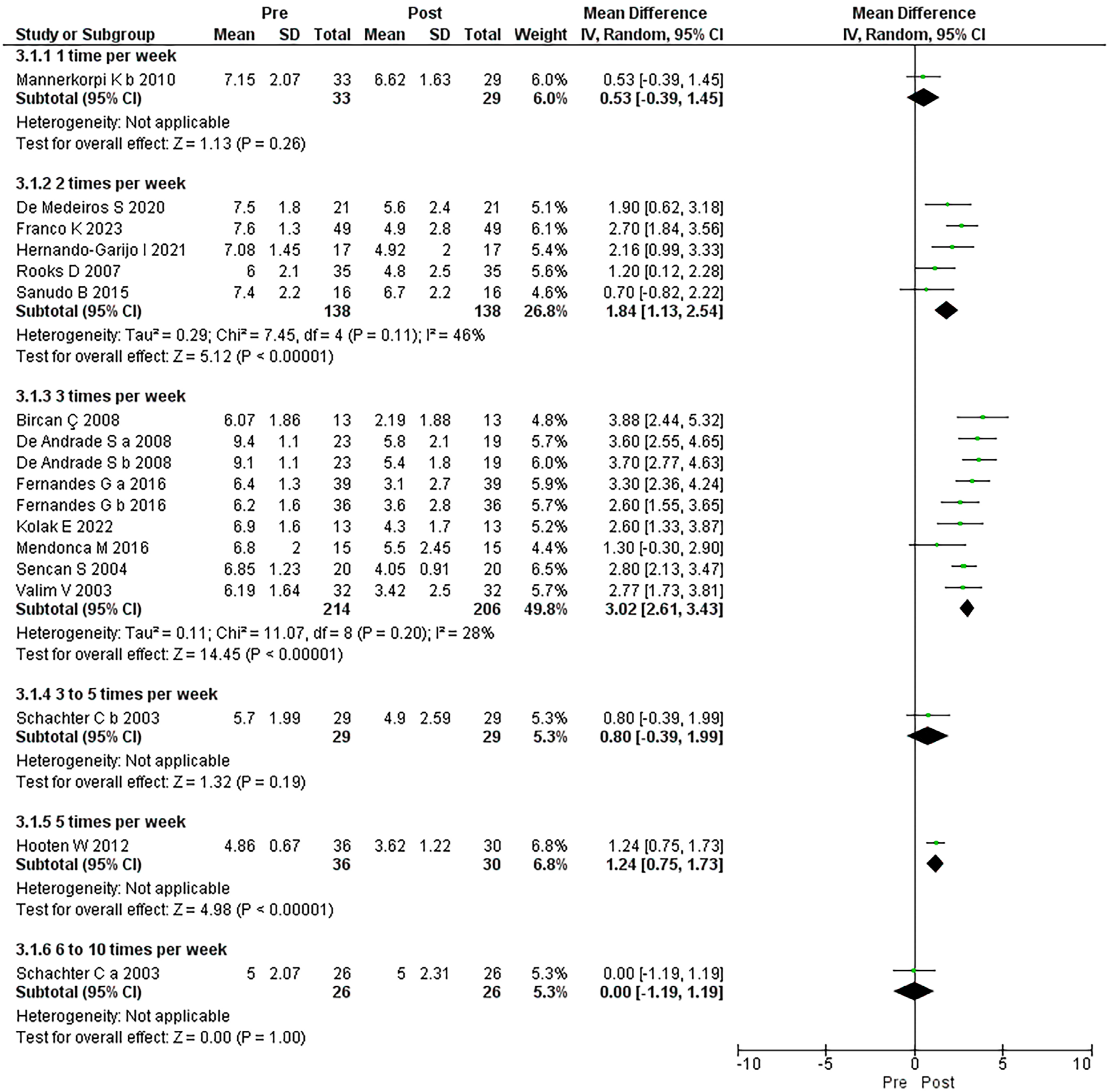


FIGURE 3 | Pre/Post comparison of the frequency domain. A positive sign signifies an effect of favour of post intervention.

between music-based exercise (MD 0.99; CI [0.11, 1.88]; $p < 0.03$), pool-based exercise (MD 3.14; CI [2.10, 4.18]; $p < 0.001$), stationary cycling (MD 1.21; CI [1.04, 1.38]; $p < 0.001$), swimming (MD 3.30; CI [2.36, 4.24]; $p < 0.001$), walking outside (MD 2.69; CI [1.95, 3.43]; $p < 0.001$) and walking on a treadmill (MD 1.70; CI [0.79, 2.61]; $p < 0.001$) without significant heterogeneity within the subgroups (Figure 5).

3.5.2.4 | **Time.** In this analysis, fifteen (S. C. D. Andrade et al. 2008; Bircan et al. 2008; Fernandes et al. 2016; Franco et al. 2023; Hooten et al. 2012; Kolak, Ardıç and Fındıkoğlu 2022; Mannerkorpi, Burckhardt and Bjelle 1994; Medeiros et al. 2020; Mendonca et al. 2016; Rooks et al. 2007; Sanudo et al. 2015; Schachter et al. 2003; Sencan et al. 2004; Valim et al. 2003; Wigers, Stiles and Vogel 1996) studies were included, with nineteen interventions separated and categorised based on the length of the intervention, in weeks, into 3 weeks (Hooten et al. 2012), 4 weeks (Mendonca et al. 2016), 6 weeks (Sencan et al. 2004), 8 weeks (Bircan et al. 2008; Franco et al. 2023), twelve weeks S. C. D. (Andrade et al. 2008; Fernandes et al. 2016; Kolak, Ardıç and Fındıkoğlu 2022; Medeiros et al. 2020), fourteen weeks (Wigers, Stiles and Vogel 1996), fifteen weeks (Mannerkorpi, Burckhardt and Bjelle 1994), sixteen weeks (Rooks et al. 2007; Schachter et al. 2003), twenty weeks (Valim et al. 2003). Differences were observed between three (MD 1.24; CI [0.75, 1.73]; $p < 0.001$), six (Sencan et al. 2004) (MD 2.80; CI [2.13, 3.47]; $p < 0.001$), eight (MD 3.14; CI [2.02, 4.27]; $p < 0.001$), twelve (MD 3.04; CI [2.51, 3.57]; $p < 0.001$), sixteen (MD 0.70; CI [0.01,

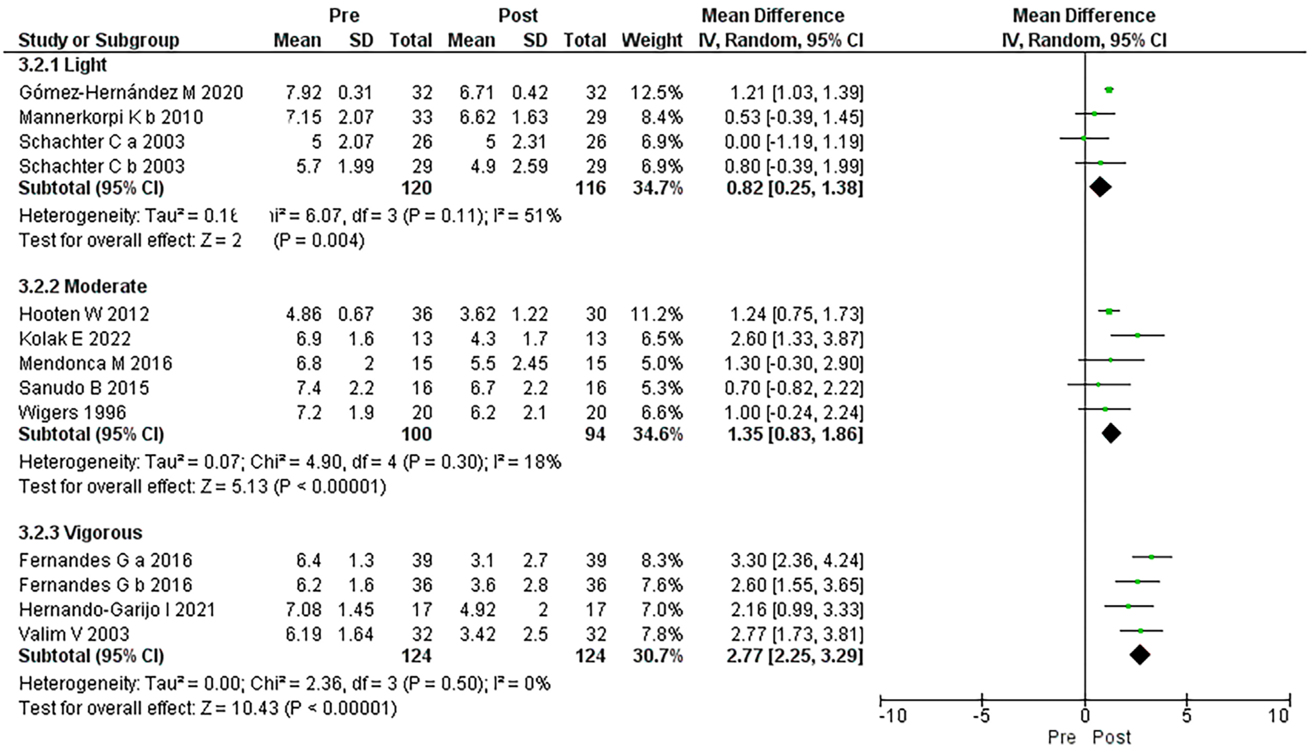


FIGURE 4 | Pre/Post comparison of the intensity domain. A positive sign signifies an effect of favour of post intervention.

1.39]; $p = 0.05$) and twenty (MD 2.77; CI [1.73, 3.81]; $p < 0.001$) weeks, without significant heterogeneity within the subgroups (Figure 6).

3.5.2.5 | Volume. In this analysis, sixteen (S. C. D. Andrade et al. 2008; Bircan et al. 2008; Fernandes et al. 2016; Franco et al. 2023; Gómez-Hernández et al. 2020; Hooten et al. 2012; Kolak, Ardıç and Fındıkoğlu 2022; Mannerkorpi et al. 2010; Medeiros et al. 2020; Mendonca et al. 2016; Rooks et al. 2007; Sanudo et al. 2015; Schachter et al. 2003; Sencan et al. 2004; Valim et al. 2003; Wigers, Stiles and Vogel 1996) studies were included, with nineteen interventions separated and categorised based on two different approaches.

The first was the mean duration of every exercise session, measured in minutes, being subclassified into ten minutes (Gómez-Hernández et al. 2020; Schachter et al. 2003), twenty minutes (Hooten et al. 2012; Mannerkorpi, Burckhardt and Bjelle 1994; Schachter et al. 2003; Wigers, Stiles and Vogel 1996), twenty-five minutes (Bircan et al. 2008), thirty minutes (Medeiros et al. 2020; Mendonca et al. 2016; Sanudo et al. 2015; Sencan et al. 2004; Valim et al. 2003), forty minutes (S. C. D. Andrade et al. 2008; Fernandes et al. 2016; Franco et al. 2023; Kolak, Ardıç and Fındıkoğlu 2022) and forty-five minutes (Rooks et al. 2007). Differences were found between twenty (MD 1.01; CI [0.63, 1.40]; $p < 0.001$), twenty-five (MD 3.88; CI [2.44, 5.32]; $p < 0.001$), thirty (MD 2.22; CI [1.33, 3.11]; $p < 0.001$) and forty (MD 3.14; CI [2.71, 3.52]; $p < 0.001$) and forty-five (MD 1.20; CI [0.12, 2.28]; $p = 0.03$) minutes, without significant heterogeneity within the subgroups (Figure 7).

The second approach was the total duration of exercise per week, which was subclassified into three different groups: less than 60 min (Gómez-Hernández et al. 2020; Mannerkorpi et al. 2010; Wigers, Stiles and Vogel 1996), between 60 and 100 min (Medeiros et al. 2020; Mendonca et al. 2016; Rooks et al. 2007; Sanudo et al. 2015; Schachter et al. 2003), and more than 100 min (S. C. D. Andrade et al. 2008; Fernandes et al. 2016; Kolak, Ardıç and Fındıkoğlu 2022). Differences were found between less than 60 min (MD, 1.01; CI [0.53, 1.49]; $p < 0.001$), between 60 and 100 min (MD 0.96; CI [0.44, 1.49]; $p < 0.001$) and more than 100 min (MD 3.23; CI [2.77, 3.69]; $p < 0.001$) per week, without significant heterogeneity within the subgroups (Figure 8).

3.5.2.6 | Progression. In this analysis, five (Hooten et al. 2012; Kolak, Ardıç and Fındıkoğlu 2022; Mendonca et al. 2016; Rooks et al. 2007; Schachter et al. 2003) studies were included, with six interventions separated and categorised, based on how the exercise progressed during the time of the intervention, into three separate groups: intensity (Kolak, Ardıç and Fındıkoğlu 2022; Mendonca et al. 2016), volume (Hooten et al. 2012; Rooks et al. 2007) and intensity & volume (Schachter et al. 2003). Differences were found between the progression in intensity (MD 2.05; CI [0.79, 3.31]; $p = 0.001$) and volume (MD 1.23; CI [0.79, 1.68]; $p < 0.001$), without significant heterogeneity within the subgroups (Figure 9).

3.6 | Clinical Relevance

The MCID was achieved under several conditions related to the characteristics of the exercise. In terms of frequency, interventions conducted two or three times per week were effective (Figure 3), while only vigorous-intensity exercises reached

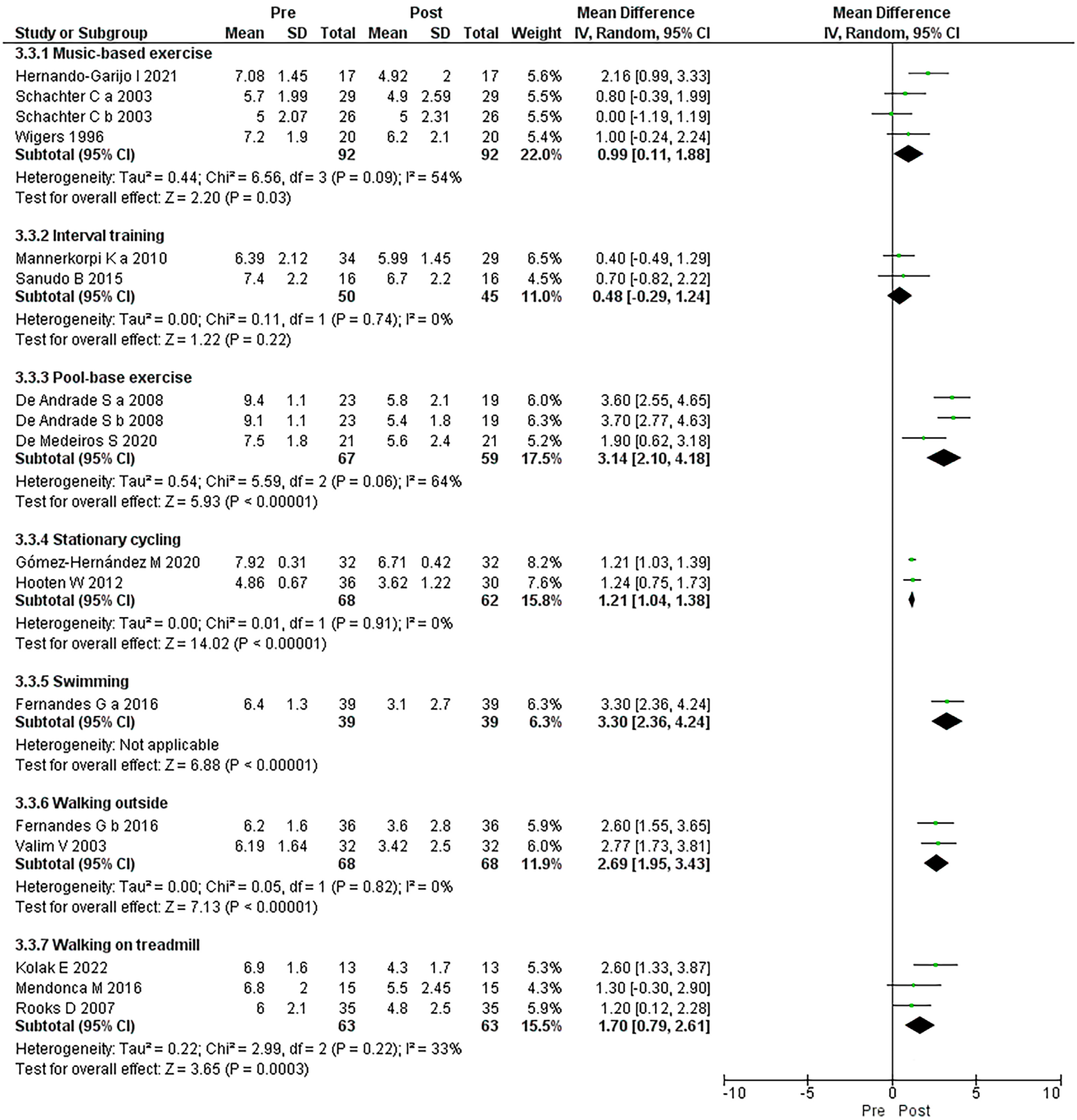


FIGURE 5 | Pre/Post comparison of the type domain. A positive sign signifies an effect of favour of post intervention.

the MCID in terms of intensity (Figure 4). Regarding exercise type, MCID was attained from pool-based exercises, swimming and walking, whether performed outdoors or on a treadmill (Figure 5). Concerning intervention duration, MCID was achieved after periods of six, eight, twelve and twenty weeks (Figure 6). Additionally, the MCID was reached with sessions lasting twenty-five, thirty and forty minutes (Figure 7). In terms of weekly volume, interventions exceeding one hundred minutes per week were required (Figure 8). Notably, the only progression method that produced the MCID was intensity (Figure 9).

4 | Discussion

The aim of this systematic review and meta-analysis was to analyse the effect of different doses of aerobic exercise on the pain of patients with fibromyalgia.

Starting with frequency of exercise, the findings of this review indicate that only exercising two or 3 days per week of exercise produced MCID in terms of pain improvement in fibromyalgia patients. Prior studies have linked sedentary behaviours with the onset of chronic pain and chronic disease (Bontrup

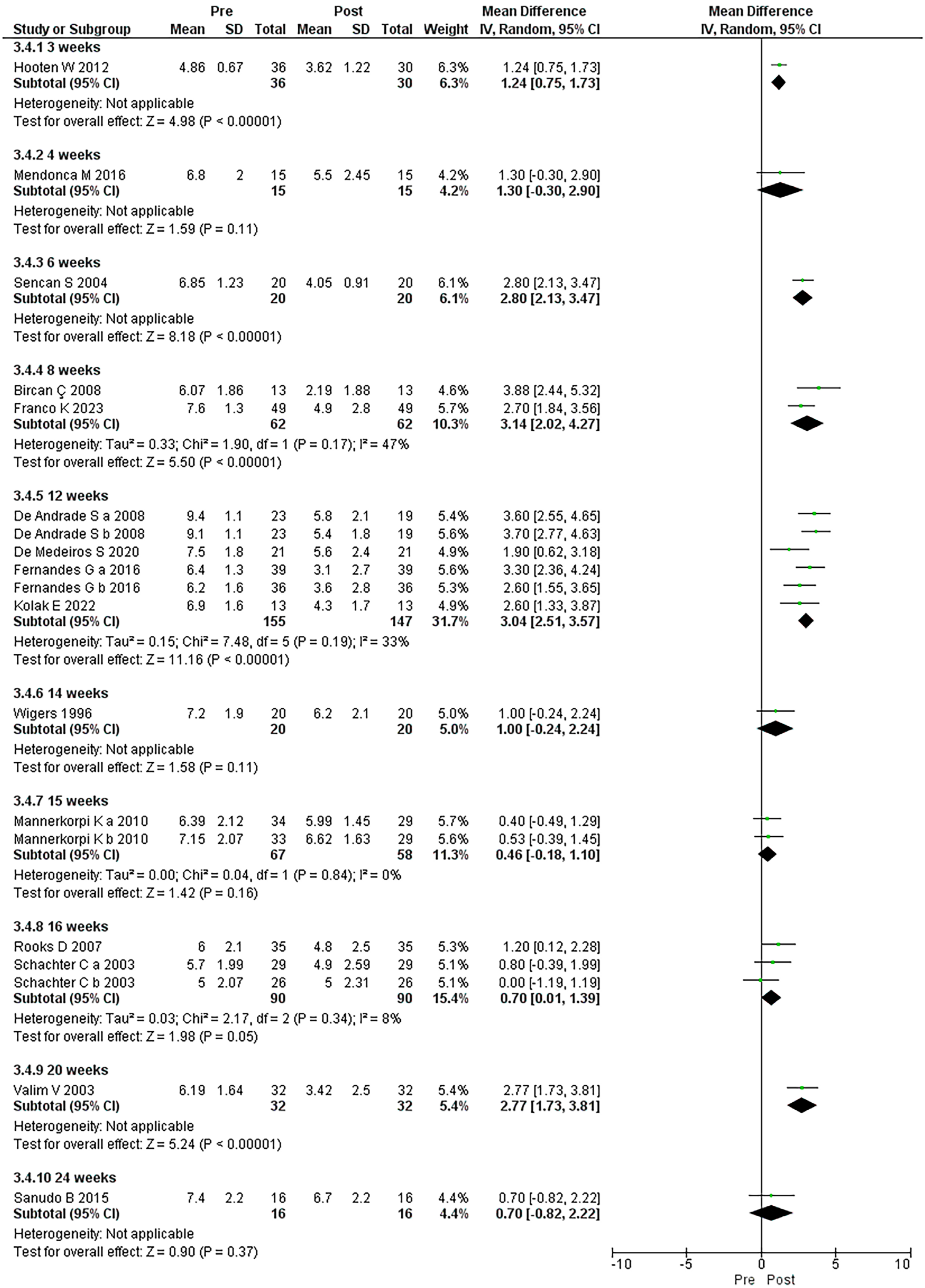


FIGURE 6 | Pre/Post comparison of the time domain. A positive sign signifies an effect of favour of post intervention.

Study or Subgroup	Pre Mean	Pre SD	Pre Total	Post Mean	Post SD	Post Total	Weight	Mean Difference IV, Random, 95% CI
3.5.1 10 minutes								
Gómez-Hernández M 2020	7.92	0.31	32	6.71	0.42	32	6.9%	1.21 [1.03, 1.39]
Schachter C a 2003	5	2.07	26	5	2.31	26	4.9%	0.00 [-1.19, 1.19]
Subtotal (95% CI)			**58**			**58**	**11.9%**	**0.75 [-0.39, 1.90]**
Heterogeneity: Tau² = 0.54; Chi² = 3.87, df = 1 (P = 0.05); I² = 74%								
Test for overall effect: Z = 1.29 (P = 0.20)								
3.5.2 20 minutes								
Hooten W 2012	4.86	0.67	36	3.62	1.22	30	6.5%	1.24 [0.75, 1.73]
Mannerkorpi K a 2010	6.39	2.12	34	5.99	1.45	29	5.7%	0.40 [-0.49, 1.29]
Schachter C b 2003	5.7	1.99	29	4.9	2.59	29	4.9%	0.80 [-0.39, 1.99]
Wigers 1996	7.2	1.9	20	6.2	2.1	20	4.8%	1.00 [-0.24, 2.24]
Subtotal (95% CI)			**119**			**108**	**22.0%**	**1.01 [0.63, 1.40]**
Heterogeneity: Tau² = 0.00; Chi² = 2.79, df = 3 (P = 0.43); I² = 0%								
Test for overall effect: Z = 5.20 (P < 0.00001)								
3.5.3 25 minutes								
Bircan Ç 2008	6.07	1.86	13	2.19	1.88	13	4.4%	3.88 [2.44, 5.32]
Subtotal (95% CI)			**13**			**13**	**4.4%**	**3.88 [2.44, 5.32]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.29 (P < 0.00001)								
3.5.4 30 minutes								
De Medeiros S 2020	7.5	1.8	21	5.6	2.4	21	4.7%	1.90 [0.62, 3.18]
Mendonca M 2016	6.8	2	15	5.5	2.45	15	4.0%	1.30 [-0.30, 2.90]
Sanudo B 2015	7.4	2.2	16	6.7	2.2	16	4.2%	0.70 [-0.82, 2.22]
Sencan S 2004	6.85	1.23	20	4.05	0.91	20	6.2%	2.80 [2.13, 3.47]
Valim V 2003	6.19	1.64	32	3.42	2.5	32	5.3%	2.77 [1.73, 3.81]
Subtotal (95% CI)			**104**			**104**	**24.4%**	**2.09 [1.32, 2.86]**
Heterogeneity: Tau² = 0.41; Chi² = 8.99, df = 4 (P = 0.06); I² = 55%								
Test for overall effect: Z = 5.31 (P < 0.00001)								
3.5.6 40 minutes								
De Andrade S a 2008	9.4	1.1	23	5.8	2.1	19	5.3%	3.60 [2.55, 4.65]
De Andrade S b 2008	9.1	1.1	23	5.4	1.8	19	5.6%	3.70 [2.77, 4.63]
Fernandes G a 2016	6.4	1.3	39	3.1	2.7	39	5.6%	3.30 [2.36, 4.24]
Fernandes G b 2016	6.2	1.6	36	3.6	2.8	36	5.3%	2.60 [1.55, 3.65]
Franco K 2023	7.6	1.3	49	4.9	2.8	49	5.7%	2.70 [1.84, 3.56]
Kolak E 2022	6.9	1.6	13	4.3	1.7	13	4.8%	2.60 [1.33, 3.87]
Subtotal (95% CI)			**183**			**175**	**32.2%**	**3.11 [2.71, 3.52]**
Heterogeneity: Tau² = 0.00; Chi² = 4.94, df = 5 (P = 0.42); I² = 0%								
Test for overall effect: Z = 15.04 (P < 0.00001)								
3.5.7 45 minutes								
Rooks D 2007	6	2.1	35	4.8	2.5	35	5.2%	1.20 [0.12, 2.28]
Subtotal (95% CI)			**35**			**35**	**5.2%**	**1.20 [0.12, 2.28]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.17 (P = 0.03)								

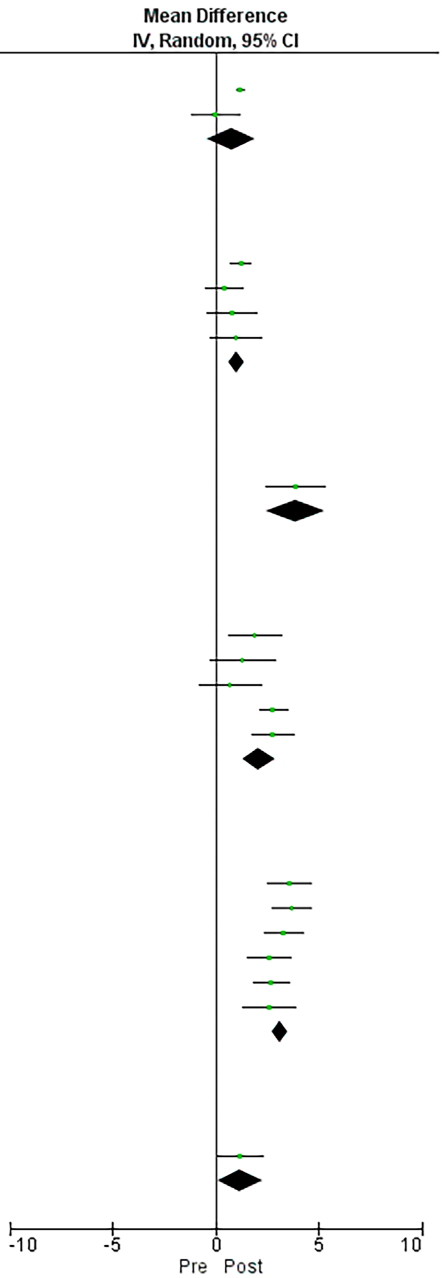


FIGURE 7 | Pre/Post comparison of the daily volume domain. A positive sign signifies an effect of favour of post intervention.

et al. 2019; Booth, Roberts and Laye 2012; Zhaoyang and Martire 2019). In this regard, in pain-free populations even a single session of aerobic exercise has demonstrated acute hypoalgesia (Niwa et al. 2022; Rice et al. 2019), while patients with chronic pain, exhibit more heterogeneous responses to exercise (Lannersten and Kosek 2010; Meeus et al. 2015; Rice et al. 2019; Staud, Robinson and Price 2005). This could be for various reasons, such us impaired exercise-induced hypoalgesia (EIH) (Meeus et al. 2015; Wewege and Jones 2021). Despite this, a metanalysis by Polaski et al. 2019 concluded that increasing the frequency of exercise among patients with chronic pain should increase its effects, while another study, by KRAMER et al. 2020 found that a daily treatment approach had better results than 3 days of treatment. Taking into account that only the studies by Schachter et al. 2003 and Hooten et al. 2012 featured patients who exercised more than 3 days per week, and only one group, in the study by Mannerkorpi et al. 2010, featured patients who exercised just 1 day per week, (facts which could limit the results of this review), and moreover, taking into account the general recommendation of three to 5 days of aerobic exercise per week for general health (Bull et al. 2020; Garber et al. 2011; Pescatello et al. 2006), these results should be taken with caution, and more trials should study the association between higher or lower frequencies of exercise and reductions in pain among patients with fibromyalgia.

Regarding the intensity of the exercise, only the vigorous intensity group achieved the MCID. Although these results are in line with a substantial body of scientific evidence on healthy individuals (Hiura et al. 2017; Naugle et al. 2014), and could be explained by the activity of the endogenous opioid

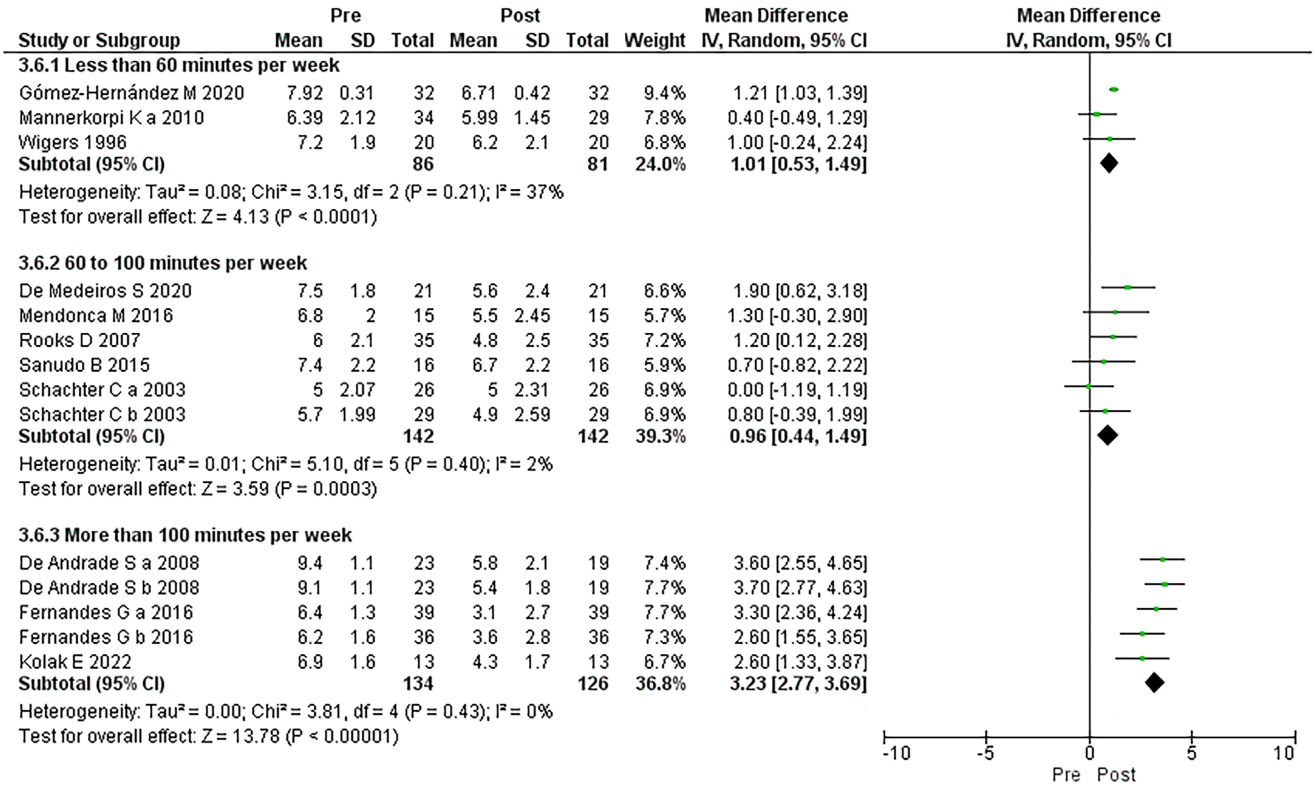


FIGURE 8 | Pre/Post comparison of the weekly volume domain. A positive sign signifies an effect of favour of post intervention.

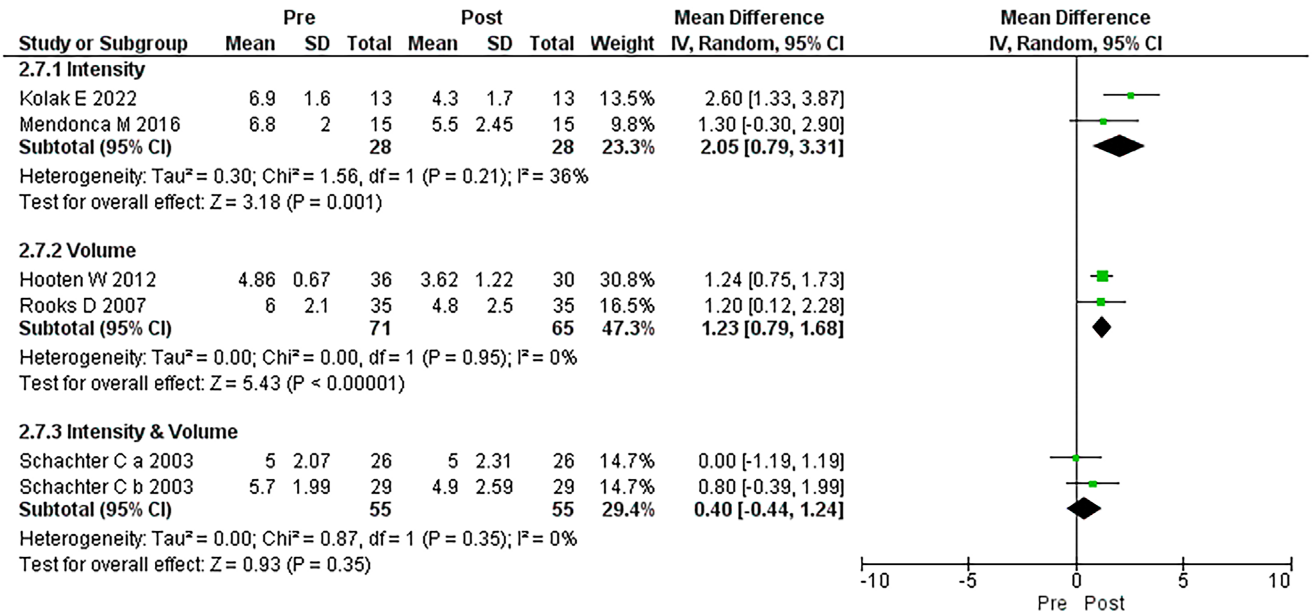


FIGURE 9 | Pre/Post comparison of the progression domain. A positive sign signifies an effect of favour of post intervention.

system (Hiura et al. 2017; Saanijoki et al. 2018), EIH (Naugle et al. 2014; Vaegter, Handberg and Graven-Nielsen 2014) or the release of endocannabinoids (Gupta et al. 2024) a study by Vierck et al. 2001 found that exercising at high intensity did not change clinical ratings of pain; and a metanalysis by Naugle, Fillingim and Riley (2012) found that high-intensity exercise actually increased the pain experienced, with both studies including patients with fibromyalgia. These findings correlate with those of Newcomb et al. (2011), where exercising at preferred intensity, even though this intensity was usually light, yielded better results than exercising at moderate intensity among patients with fibromyalgia. These results could be due to the fact that those studies used single sessions of aerobic exercise, while this study focuses on whole training periods, which could elicit training-induced hypoalgesia (Song et al. 2022). This, coupled with the results on exercise progression, indicating that only greater intensity yields MCIDs, and the fact that patients with fibromyalgia have difficulty adhering to moderate- and high-intensity exercise programs (Busch et al. 2011; Sarmento et al. 2023), highlights the importance of clinicians emphasising adherence to the exercise regimen, as a sustained commitment in an structured and progressive training would allow patients to engage in higher exercise intensities over time, which is crucial for achieving pain reduction and improving overall outcomes. (Song et al. 2023).

Subsequently, regarding the type of exercise, pool-based exercise, swimming and walking, both on a treadmill or outdoors, achieved both statistical differences and MCID, while interval training did not produce either. This discrepancy in the results with reference to interval training could be attributed to what was previously mentioned about the intensity of the exercise and the need for progress in terms of intensity. However, as it was only studied in two papers (Mannerkorpi et al. 2010; Sanudo et al. 2015), further research is needed on this aspect, as well as the impact of group vs. solo exercise. Some studies emphasise the equivalence between different modalities of exercise for the reduction of pain among fibromyalgia patients (Busch et al. 2011; Couto et al. 2022; Hooten et al. 2012; Rebollo-Salas et al. 2024; Rodríguez-Almagro et al. 2023). Therefore, the primary goal when selecting the type of exercise should be to enhance the patient's adherence and consequent health benefits. Water-based exercises provide buoyancy, which reduces joint stress and muscle impact (Kutzner et al. 2017). In addition, depending on water temperature, water-based exercise could produce competing stimuli on nerve endings and therefore, increase the hypoalgesic effects of exercise, or even trigger a pain response in some patients (Mooventhan and Nivethitha 2014). Meanwhile load-bearing exercises, such as walking, involve the mechanical loading of the musculoskeletal system, which can enhance bone density (Olmedillas et al. 2012; Simas et al. 2017). With this in mind, and although the swimming group showed the most differences pre- and post-intervention, this finding was only present in one study (Fernandes et al. 2016), so other factors, such as the patient's preferences, the feasibility of engaging in the activity, and the possibility of practicing it collectively, should be taken into account when prescribing the initial type of exercise, although it would be advisable to progress to a load-bearing exercise, such as walking.

The results of the time interaction in this meta-analysis showcase that statistical differences can be found among patients exercising for three to twenty weeks, although the MCID was only reached by those patients completing six to twenty weeks of exercise. It is important to note, however, that the three (Hooten et al. 2012) and twenty-week (Valim et al. 2003) data are based on only one study, with some concerns and high risk of bias, so this should be approached with some reservation. Therefore, patients should exercise for at least 6 weeks to improve their symptomatology, with more studies being needed in this regard. Patients with fibromyalgia have been seen to undergo diverse changes in their central nervous systems (Čeko et al. 2020; Harris et al. 2007; Ichesco et al. 2014; Napadow et al. 2010) and peripheral nervous systems (Behnoush et al. 2023; Caro and Winter 2014; Doppler et al. 2015; Martínez-Lavín 2018), which could be related to the maintenance of pain or their inability to produce EIH. Aerobic exercise could potentially enhance brain function and neuroplasticity by reducing neuro-inflammation and regulating neurotrophic factors (Gondoh et al. 2009; Jia et al. 2022). Even so, the link between changes over time in brain connectivity and pain requires further studies, due to contradictory results in this field (Flodin et al. 2015; Kan et al. 2023; Leon-Llamas et al. 2020) and the fact that the results varied greatly between studies, with the study by Wigers, Stiles and Vogel (1996), following the patient for 4 years showing the most reduction in pain among patients who continued exercising for this period.

In terms of the volume of aerobic exercise per session, exercising for twenty-five, thirty or forty minutes yielded both statistical differences and the MCID, although only one study used twenty-five minutes (Bircan et al. 2008) and forty-five minutes (Rooks et al. 2007). Thus these results should be approached with caution. These findings correlate with two independent papers that found no changes in clinical pain after just ten minutes of exercise (Staud et al. 2010; Vierck et al. 2001), suggesting that a minimal amount of exercise may be needed to achieve EIH. Considering the weekly volume of aerobic exercise, only the groups that exercised for more than 100 min per week achieved MCID. Patients with fibromyalgia tend to have reduced physical fitness compared to the healthy population (Mannerkorpi, Burckhardt and Bjelle 1994). In this regard, aerobic exercise could improve their general fitness levels and overall quality of life while reducing the intensity of pain (García-Correa et al. 2021). For this, the relationship between the weekly volume, frequency and intensity of exercise should be considered. The general recommendation for general aerobic fitness is to exercise at moderate intensity for approximately thirty to sixty minutes per day, or one hundred and fifty minutes per week; or at vigorous intensity for twenty to sixty minutes per day, or seventy-five minutes per week; or a combination of both (Garber et al. 2011; Pescatello et al. 2006). Thus, the goal should be to ensure that patients with fibromyalgia adhere to an exercise routine and reach the minimum recommended exercise volume to achieve meaningful health benefits.

To our knowledge, this is the first systematic review and meta-analysis to analyse the dose–response relationship in aerobic exercise taking into account the MCID and prescription FITT-VP model, although there are meta-analyses that have analysed some of these aspects separately (Haeuser et al. 2010). Although some limitations had been already highlighted, other limitations should be considered, such as heterogeneity, risk of bias among the studies included, the fact that the overall analysis did not consider the different types of aerobic exercise, and the limited sample size of the studies included. Therefore the results of this study should be taken with caution, and more studies are needed in this field.

5 | Conclusions

Based on a moderate quality of evidence, the findings of this study underscore the benefits of aerobic exercise for treating pain in patients with fibromyalgia. A comprehensive examination of

FITT-VP exercise parameters using the MCID was conducted, resulting in several recommendations for implementing an aerobic exercise program in patients with fibromyalgia. Patients with fibromyalgia should start with a feasible type of exercise to enhance their long-term adherence to the protocol, of an initially low intensity, which should be increased over the course of six to twelve weeks. They should aim for at least 100 min per week, distributed between two to three sessions of twenty-five to forty minutes each. However, it is important to tailor the dose of exercise according to each patient's capabilities and needs so as to maximise their adherence to the program and overall results.

Author Contributions

Conceptualization, D.C.R., A.R.S., J.M.J.C.; Data Curation, D.C.R., J.M.J.C.; Formal analysis, D.C.R.; Funding, A.R.S.; Acquisition and resources, D.C.R., A.R.S., J.M.J.C.; Methodology, D.C.R., A.R.S., J.M.J.C.; Project administration, A.R.S., J.M.J.C.; Supervision, A.R.S., J.M.J.C.; Validation, A.R.S., J.M.J.C.; Writing – Original Draft Preparation, D.C.R., R.B.R.; Writing Review and editing, D.C.R., A.R.S., R.B.R., J.M.J.C.

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The authors have nothing to report.

Ethics Statement

The authors have nothing to report.

Consent

All authors have approved and consent to the publication of this paper.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors have nothing to report.

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Supporting Information

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