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Prescription of exercises for the treatment of chronic pain along the continuum of nociplastic pain: a systematic review with meta-analysis

Running title: Prescription of exercises for chronic pain

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Significance: The pain mechanism must be considered to optimize exercise prescription in patients with different chronic pain profiles. The main message of this article is that low to moderate intensity global exercises performed for a long period of treatment should be performed in patients with nociplastic pain predominance. Additionally, focused and intense exercises for a short period of treatment can be prescribed for patients with nociceptive pain predominance.

ABSTRACT

Background and Objective: To compare different exercise prescriptions for patients with chronic pain along the continuum of nociplastic pain: fibromyalgia, chronic whiplash-associated disorders (CWAD), and chronic idiopathic neck pain (CINP). **Databases and Data Treatment:** Randomized controlled trials comparing different exercise parameters were included. The search was performed in the databases Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, CINAHL, and PEDro. Data on the parameters for the physical exercise programs for pain management were extracted for analysis. **Results:** Fifty studies with 3,562 participants were included. For fibromyalgia, both aerobic or strengthening exercises were similar and better than stretching exercises alone. Exercises could be performed in 50- to 60-minute supervised sessions, 2 to 3 times a week, for 13 weeks or more. For CWAD, body awareness exercises were similar to combined exercises, and there was no difference in adding sling exercises to a strengthening exercise program. The exercises could be performed in 90-minute supervised sessions, twice a week, for 10 to 16 weeks. For CINP, motor control exercises and nonspecific muscle strengthening had a similar effect. Exercises could be performed in 30- to 60-minute supervised sessions, 2 to 3 times a week, for 7 to 12 weeks. **Conclusions:** The choice of parameters regarding exercises should emphasize global exercises in nociplastic pain conditions (such as fibromyalgia and CWAD) and specific exercises in non-nociplastic pain conditions (such as CINP) and be based on patient's preference and therapist's skills.

Prospero registration number: CRD42019123271

Keywords: Fibromyalgia; Chronic whiplash-associated disorders; Chronic idiopathic neck pain; Exercise therapy; Central sensitization.

BACKGROUND

Chronic pain ranks as the fifth leading cause of years lived with disability (Vos et al., 2012). There is a large variety of chronic pain conditions, ranging from arthritis to primary chronic pain syndromes (Ossipov and Porreca, 2006). Several chronic pain conditions can be situated along a continuum in which the predominant pain mechanism is widely responsible for the chronic pain. Distinct mechanisms have different clinical presentations and require a tailored approach. The main types of pain mechanisms described are: neuropathic, nociceptive, and nociplastic pain (Chimenti et al., 2018; International Association for the Study of Pain (IASP), 2017 [update from 2012]). Nociplastic pain involves altered nociception despite no clear evidence of actual or threatened tissue damage leading to the activation of peripheral nociceptors or evidence of disease or lesion in the somatosensory system (Chimenti et al., 2018; International Association for the Study of Pain (IASP), 2017 [update from 2012]). Nociplastic pain can be observed in clinical conditions characterized by evidence of altered nociceptive processing, spread of hypersensitivity, and altered descending pain inhibition (Kosek et al., 2016). Such presentation includes manifestations of central sensitization, which may help to explain the phenomena that maintain and, possibly, increase pain intensity in several clinical conditions.

Quantitative sensory tests are commonly used to assess pain phenomena associated with central sensitization (Meeus et al., 2015). However, from a clinical point of view, sensitization may be inferred indirectly from phenomena such as hyperalgesia or allodynia (International Association for the Study of Pain (IASP), 2017 [update from 2012]). Central sensitization may be involved in the development of pain in patients when an obvious source of nociception is absent, may contribute to the transition from acute to chronic pain (Nijs et al., 2014; Sterling et al., 2003), and also may mediate treatment responses (Coombes et al., 2012; Jull et al., 2007; Nijs et al., 2014). Patients with central sensitization report severe pain, long pain duration, several number of painful areas, more widespread pain, poor general health-related quality of life, and high levels of pain-related disability, depression, and anxiety (Nogueira et al., 2016; Smart et al., 2012).

Some examples of painful conditions with different predominance of nociplastic pain include fibromyalgia, chronic whiplash-associated disorders (CWAD), and chronic idiopathic neck pain (CINP). In fibromyalgia, due to the absence of tissue pathology, structural abnormality, or a clear source of chronic stimulation of pain afferents (Simms et al., 1994), central sensitization represents the most prominent hypothesis of the pathophysiological mechanism to explain widespread pain (Häuser et al., 2015). Meanwhile, CWAD is a painful condition that may involve both peripheral and central sensitization. A systematic review (van Oosterwijck et al., 2013) presents evidence that the central nervous system (CNS) is hypersensitized in patients with CWAD, and that central sensitization plays a crucial role in the persistence of pain. Finally, some chronic pain conditions rarely show signs of central sensitization such as CINP (Coppieters et al., 2017; Malfliet et al., 2015). Patients with CINP present recurrent pain, but CINP is more episodic in nature (Guzman et al., 2008) and leads to interruptions in the nociceptive input. These characteristics may prevent the development of the pathophysiological processes in the CNS involved in central sensitization (Malfliet et al., 2015).

Despite the differences in clinical manifestation and pain mechanism, physical exercise is recommended as a treatment for all of these three chronic conditions (Busch et al., 2013; Bussières et al., 2016; Fitzcharles et al., 2013; Häuser et al., 2017; Macfarlane et al., 2016; TRACsa: Trauma and Injury Recovery, 2008). Even with the existing evidence regarding the improvement of clinical outcomes, the literature is scarce on the parameters for the prescription of therapeutic exercises and on whether these parameters should be different depending on the predominance of nociplastic pain. The current evidence from reviews and guidelines regarding weekly frequency and intensity of exercise prescription (Booth et al., 2017; Bussières et al., 2016; Geneen et al., 2017; Häuser et al., 2010) encompasses chronic pain in general, without taking into account specific characteristics or pain mechanism of each painful condition. Thus, the recommendation to prescribe exercise programs is varied and generic for patients with chronic pain. Additionally, exercise prescription is often dependent on the clinician's individual preferences and abilities. Together, these facts may contribute to the underestimation or overestimation of exercise prescription parameters in specific chronic pain conditions (Booth et al., 2017). Considering that patients with nociplastic pain usually have dysfunctional endogenous analgesic control, which contributes to exercise-induced hyperalgesia (Lima et al., 2017; Meeus et al., 2016), and that exercise prescription can directly influence the outcomes of an intervention, it is important to synthetize the evidence about exercise parameters in the prescription for patients with painful conditions in the continuum of nociplastic pain. Thus, the aim of this study was to systematically review the effects of different exercise prescriptions and synthetize the exercise parameters for pain management in patients with chronic pain along the continuum of nociplastic pain: fibromyalgia (situated at the end of the continuum), CWAD (different degrees of predominance of nociplastic pain), and CINP (nociplastic pain is not a dominant feature).

METHODS

Protocol registration

The present systematic review was reported following the Preferred Reported Items for Systematic Reviews and Meta-analyses (PRISMA) statement (Moher et al., 2009). The systematic review protocol was prospectively registered in the Prospero website (CRD42019123271).

Eligibility criteria

The inclusion criteria for this systematic review were: 1) randomized controlled trials (RCTs); 2) studies with patients over 18 years of age with fibromyalgia who were diagnosed by the American College of Rheumatology criteria of 1990, 2010, 2011, or 2016 (Wolfe et al., 2016; Wolfe et al., 2011; Wolfe et al., 2010; Wolfe et al., 1990); or patients over 18 years of age who suffered from a chronic whiplash injury (more than 12 weeks) classified as CWAD grade 1 and 2 (Grade 1 - neck complaints, such as pain, tenderness, and stiffness, but no physical signs; Grade 2 - neck complaints with musculoskeletal signs, such as decreased range of motion or muscle weakness (Spitzer, 1995)), because these patients normally receive conservative interventions (Bussières et al., 2016; TRACsa: Trauma and Injury Recovery, 2008; Verhagen et al., 2007); or studies with patients over 18 years of age with CINP (more than 12 weeks); 3) at least two physical exercise interventions to control pain should be prescribed. Exercise was defined as a planned, structured, and repetitive physical activity (Caspersen et al., 1985)); and 4) studies with a minimum duration of 3 weeks of exercise.

The exclusion criteria were: 1) studies in which exercise was a component of a multimodal treatment; 2) studies that only included a single bout of exercise, but not an exercise program; 3) studies in which patients with fibromyalgia, CWAD, and CINP had recently undergone surgery or suffered a new acute neck injury; 4) studies in which patients with CINP had other comorbidities (such as shoulder pain, temporomandibular disorders, radiculopathies, among others); and 5) studies that did not describe any parameters of the prescribed exercises.

Search strategy

Systematic electronic searches were carried out in the following databases: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (PubMed), EMBASE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Physiotherapy Evidence Database (PEDro) from inception until November 19th, 2018. An additional hand search was performed in the references of pre-selected articles for inclusion in this review and in systematic reviews and clinical guidelines published on each condition (Bidonde et al., 2017; Busch et al., 2013; Bussières et al., 2016; Gross et al., 2015; Häuser et al., 2010; Macfarlane et al., 2016; O'Riordan et al., 2014; Sosa-Reina et al., 2017; Verhagen et al., 2007). Searches were not restricted by language or publication date.

The terms used in the searches were based on the strategies proposed by the Updated Search Strategies of the Cochrane Group (van Tulder et al., 2003) and systematic reviews on the topic (Bidonde et al., 2017; Busch et al., 2013; Gross et al., 2015; Verhagen et al., 2007). To systematize the searches, six thematic blocks were constructed with synonyms and variants related to chronic pain, fibromyalgia, neck pain, whiplash, exercise, and outcomes. In addition, filters were used to include only randomized controlled trial and humans (Appendix 1). The words within a block were combined by the Boolean operator "OR" and between blocks by the Boolean operator "AND".

Data extraction

Two assessors (KFMF and DL) conducted, independently, the selection of the studies, data extraction of the included studies, and analysis of the methodological quality. In cases of disagreement, a third assessor (MM) made the final decision.

Risk of bias assessment

The risk of bias of the eligible studies was analyzed using the criteria from the Cochrane Risk of Bias tool with seven items (Higgins and Green, 2011). Each item was scored as 'yes', 'no', or 'unclear'. Studies that met at least three or more of the seven criteria were considered as having a low risk of bias. In studies with an exercise intervention, blinding of participants and care providers is not possible (Busch et al., 2013). Thus, a low risk was assumed when participants were kept unaware of other treatment arms, a high risk was assumed when authors clearly stated in the text that participants were not blinded to intervention, and an unclear risk was assumed when no information on blinding of participants was reported.

Quality of the evidence

Two assessors (KFMF and YRSF) rated the quality of the evidence using the GRADE approach (Schünemann et al., 2011) via the GRADE PRO website. The large heterogeneity prevented the pooling of similar studies. Therefore, the quality of the evidence was only performed for pain and for studies included in the meta-analyses and was described along with these results. The GRADE approach proposes domains to assess the quality of the body of evidence for each outcome. The criteria used were: 1) risk of bias (downgraded if more than 25% of the participants were from studies with a high risk of bias); 2) inconsistency of results (downgraded if significant heterogeneity was presented considering $I^2 > 50\%$); 3) indirectness (downgraded if more than 50% of the participants or interventions were outside of interest); 4) imprecision (downgraded if less than 400 participants were included in the comparison); and 5) other (for example, publication bias) (Balshem et al., 2011; Higgins and Green, 2011; Schünemann et al., 2011). For each domain that did not meet the criterion, quality was downgraded by one level, from high to moderate, low or very low quality. Based on these criteria, the GRADE approach assigns grades of evidence per cluster ranging from high to very low level of evidence (Balshem et al., 2011).

Data extraction and analysis

The primary outcome was the effect of any exercise parameter prescription (type of exercise, duration, frequency, number of sets, number of repetitions, rest time between sets and between sessions, initial load, intensity, progression of load, clinical criteria used for progression, and criteria for the change of exercise in case of non-progression, among others) on pain intensity. Secondary outcomes were the effect of any exercise parameter on disability, impact of fibromyalgia, quality of life, satisfaction with treatment, and adverse effects of physical exercise in patients with fibromyalgia, CWAD, and CINP.

Data extraction forms encompassed the following information from the studies: 1) authors and year of publication; 2) aim of the study; 3) characteristics of the sample (sample size, age, sex, weight, height, body mass index, and duration of symptoms); 3) physical exercise parameters from the experimental group; 4) physical exercise parameters from the comparison group; 5) outcome measures; 6) instruments used to assess outcomes; 7) follow-up (short-term: between 3 and 23 weeks; medium-term: between 24 and 51 weeks; and long-term: more than 52 weeks (Furlan et al., 2015)); and 8) study results, i.e. mean and standard deviation (SD) values (or median and interquartile range) of each group, mean difference (MD), confidence intervals at 95% (95% CI), effect size for the comparisons between groups, and whether the intervention effect was minimally important for pain (between 10% and 20% or 10 mm in the visual analogue scale - VAS) (Dworkin et al., 2008). When the between-group results were not presented, we used the means and standard deviations (or medians and interquartile ranges) of each group to calculate the MD and 95% CI between the groups using the RevMan calculator (RevMan 5.3). The analysis of the studies was clustered based on the categories of physical exercise.

Data analysis

A meta-analysis was only performed for the primary outcome (pain intensity) at short-term follow-up (Furlan et al., 2015; Geneen et al., 2017) and was conducted using the Review Manager Analysis software (RevMan 5.3) from the Cochrane Collaboration. We used MDs with 95% CIs for continuous data (Higgins and Green, 2011). MDs were calculated from the means and SDs of each intervention, except for the comparison "high-intensity aerobic vs low-intensity aerobic exercise" for fibromyalgia, because the included studies only provided within-group difference values. The combined results were assessed using a random-effects model, which is more conservative than a fixed-effects model, and incorporates both within- and between-study variance. Overall effects were assessed using the Z statistic; $p < 0.05$ allowed the conclusion that a systematic effect had been demonstrated (Sosa-Reina et al., 2017). Heterogeneity was assessed using the I^2 statistic, interpreted as follows: $I^2 < 40\%$, might not represent important heterogeneity; $I^2 = 30–60\%$, may represent moderate heterogeneity; $I^2 = 50–90\%$, may represent substantial heterogeneity; and $I^2 = 75–100\%$, considerable heterogeneity (Higgins and Green, 2011).

When data were not extractable, the primary authors were contacted. Continuous outcomes reported as medians, interquartile range, and range were transformed into mean and standard deviation using RevMan 5.3 (Higgins and Green, 2011; Hozo et al., 2005).

RESULTS

Study selection

The search strategy returned 1,413 articles. After exclusion of duplicates, screening of title and abstracts, and reading the full texts, 50 RCTs were included in the descriptive synthesis. Only 24 studies were included in the quantitative analyses due to differences between interventions. Three studies were excluded because they were published in a language that could not be translated (Turkish (Yuruk and Gultekin, 2008), Persian (Arami et al., 2012), and Finnish (Ylinen et al., 2004)). Details on the search and screening process can be found in Figure 1.

Insert Figure 1 here

Included studies

A total of 3,562 participants were included. Of these, 26 studies (1,649 participants) examined exercises for patients with fibromyalgia (Assis et al., 2006; Assumpção et al., 2018; Bircan et al., 2008; Bjersing et al., 2012; Calandre et al., 2009; Demir-Göçmen et al., 2013; Duruturk et al., 2015; Evcik et al., 2008; Fernandes et al., 2016; Gavi et al., 2014; Genc et al., 2015; Jentoft et al., 2001; Jones et al., 2002; Kayo et al., 2012; Mannerkorpi et al., 2010; McCain et al., 1988; Nørregaard et al., 1997; Ramsay et al., 2000; Richards and Scott, 2002; Rooks et al., 2007; Sañudo et al., 2010; Schachter et al., 2003; Sevimli et al., 2015; Valim et al., 2003; van Santen et al., 2002; Wang et al., 2018), two studies (326 participants) examined exercises for patients with CWAD (Seferiadis et al., 2016; Vikne et al., 2007), and 22 studies (1,587 participants) examined exercises for patients with CINP (Andersen et al., 2008; Bobos et al., 2016; Borisut et al., 2013; Cramer et al., 2013; Falla et al., 2006; Häkkinen et al., 2008; Izquierdo et al., 2016; Javanshir et al., 2015; Karlsson et al., 2014; Khan et al., 2014; Kietrys et al., 2007; Kim and Kwag, 2016; Lansinger et al., 2013; Lansinger et al., 2007; Lauche et al., 2016;

O'Leary et al., 2012; Rendant et al., 2011; Salo et al., 2012; Salo et al., 2010; Senthil et al., 2016; von Trott et al., 2009; Ylinen et al., 2003). The results are presented by clinical condition.

General characteristics of the studies

Patients with fibromyalgia had a mean age of 45.8 years, and only 36 patients (2.2%) were male. Aerobic exercise was tested in 28 treatment groups (Assis et al., 2006; Bircan et al., 2008; Bjersing et al., 2012; Duruturk et al., 2015; Fernandes et al., 2016; Genc et al., 2015; Jentoft et al., 2001; Kayo et al., 2012; Mannerkorpi et al., 2010; McCain et al., 1988; Nørregaard et al., 1997; Ramsay et al., 2000; Richards and Scott, 2002; Sañudo et al., 2010; Schachter et al., 2003; Sevimli et al., 2015; Valim et al., 2003; van Santen et al., 2002; Wang et al., 2018), including walking, exercise on a cycle ergometer/bicycle, exercise on a treadmill, land-based or water-based exercise, or exercise with high and low intensity. Muscle strengthening was tested in five treatment groups (Assumpção et al., 2018; Bircan et al., 2008; Gavi et al., 2014; Jones et al., 2002; Kayo et al., 2012), stretching in eight (Assumpção et al., 2018; Calandre et al., 2009; Demir-Göçmen et al., 2013; Gavi et al., 2014; Genc et al., 2015; Jones et al., 2002; McCain et al., 1988; Valim et al., 2003), a combination of different types of exercise in nine (Demir-Göçmen et al., 2013; Evcik et al., 2008; Nørregaard et al., 1997; Richards and Scott, 2002; Rooks et al., 2007; Sañudo et al., 2010; Sevimli et al., 2015), Tai Chi in two (Calandre et al., 2009; Wang et al., 2018), and balance exercises in one treatment group (Duruturk et al., 2015).

Patients with CWAD had a mean age of 48.0 years, and only one study reported demographic data (Seferiadis et al., 2016). In this study, 32 (28.3%) of the 113 participants were male (Seferiadis et al., 2016). One study compared different types of exercise (strengthening, aerobic, and coordination) with body awareness exercises (Seferiadis et al., 2016), and the other study compared the combination of muscle strengthening and endurance with the addition of sling exercises to the same combination (Vikne et al., 2007).

Patients with CINP had a mean age of 42.8 years, and approximately 139 participants (8.7%) were male. Muscle strengthening (strength exercise, endurance, or both) was tested in 12 treatment groups (Bobos et al., 2016; Borisut et al., 2013; Javanshir et al., 2015; Karlsson et al., 2014; Khan et al., 2014; Kietrys et al., 2007; Kim and Kwag, 2016; O'Leary et al., 2012; Salo et al., 2010; Ylinen et al., 2003). Motor control exercises were examined in nine treatment groups (Andersen et al., 2008; Bobos et al., 2016; Borisut et al., 2013; Falla et al., 2006; Izquierdo et al., 2016; Javanshir et al., 2015; Kim and Kwag, 2016; O'Leary et al., 2012; Senthil et al., 2016), stretching in four (Häkkinen et al., 2008; Karlsson et al., 2014; Kietrys et al., 2007; Salo et al., 2012), a combination of different types of exercises in nine (Cramer et al., 2013; Häkkinen et al., 2008; Lansinger et al., 2013; Lansinger et al., 2007; Lauche et al., 2016; Rendant et al., 2011; Salo et al., 2012; Senthil et al., 2016; von Trott et al., 2009), specific techniques (Qigong, Tai Chi and Yoga) in six (Cramer et al., 2013; Lansinger et al., 2013; Lansinger et al., 2007; Lauche et al., 2016; Rendant et al., 2011; von Trott et al., 2009), and aerobic exercise (Andersen et al., 2008), active range of motion exercises (Khan et al., 2014) and proprioceptive exercises (Izquierdo et al., 2016) in one treatment group each.

Risk of bias

Results on the risk of bias assessment are provided in Figures 2 and 3. In general, the studies presented a low risk of bias. High risk of bias and uncertainty were identified in the categories allocation and blinding of participants (Figures 2a, 2b and 2c).

Insert Figure 2 here

Twelve studies presented high risk of bias considering incomplete outcome data (eight in fibromyalgia (Assis et al., 2006; Calandre et al., 2009; Gavi et al., 2014; Jentoft et al., 2001; Nørregaard et al., 1997; Schachter et al., 2003; Valim et al., 2003; van Santen et al., 2002) and four in CINP (Andersen et al., 2008; Häkkinen et al., 2008; Lansinger et al., 2013; Salo et al., 2012)), because these studies had different dropout rates between groups, did not use intention-to-treat analysis, or used non-recommended imputation methods (Figure 3). The assessment of selective reporting bias was difficult because only one research protocol was available (Wang et al., 2015). Nine studies, six in fibromyalgia (Kayo et al., 2012; Mannerkorpi et al., 2010; Richards and Scott, 2002; Rooks et al., 2007; Sañudo et al., 2010; Sevimli et al., 2015) and three in CINP (Kietrys et al., 2007; Salo et al., 2010; Ylinen et al., 2003), were rated as having a high risk of selective reporting (Figure 3). These studies did not analyze the between-group difference after treatment or follow-ups, which is usually the main analysis of RCTs. There was no other potential risk of bias in the included studies and therefore the risk due to other sources was rated as low.

Insert Figure 3 here

Effects of intervention

Meta-analyses for pain intensity at short-term follow-up were performed for fibromyalgia and CINP, and the results will be presented below. Other data can be found in Supplementary File 1 (characteristics of the included studies are presented in Supplementary Table 1, details on exercise prescription in each treatment group in Supplementary Table 2, and the quality of evidence in Supplementary Table 3) and Supplementary File 2 (descriptive data for fibromyalgia and CINP studies). Descriptive results related to CWAD will be presented in the text because it was not possible to perform any meta-analyses.

Exercise prescription parameters for fibromyalgia

Type of therapeutic exercise

Aerobic exercise versus Muscle strengthening

For this comparison, a meta-analysis with two studies (Bircan et al., 2008; Kayo et al., 2012) showed low-quality evidence of no difference between aerobic exercises and muscle strengthening for pain reduction [MD: 2.0 mm; 95% CI: -4.6 to 8.6; assessed using Visual analogue scale (VAS), 0 to 100 mm] (Figure 4a).

Aerobic exercise versus Muscle stretching

A meta-analysis with three studies (Genc et al., 2015; McCain et al., 1988; Valim et al., 2003) showed low-quality evidence of a small effect of aerobic exercise on pain reduction [MD: -8.1 mm; 95% CI: -15.2 to -0.9; assessed using VAS, 0 to 100 mm] (Figure 4b).

Land-based aerobic exercise versus Water-based aerobic exercise

A meta-analysis with four studies (Assis et al., 2006; Fernandes et al., 2016; Jentoft et al., 2001; Sevimli et al., 2015) showed very low-quality evidence of no difference between exercises performed on land or in water for pain reduction [MD: -3.0 mm; 95% CI: -11.3 to 5.2; assessed using VAS, 0 to 100 mm] (Figure 4c).

Muscle strengthening versus Muscle stretching

A meta-analysis with three studies (Assumpção et al., 2018; Gavi et al., 2014; Jones et al., 2002) showed low-quality evidence of a small effect of muscle strengthening on pain reduction compared to muscle stretching [MD: -7.0 mm; 95% CI: -8.1 to -5.8; assessed using VAS, 0 to 100 mm] (Figure 4d).

Supervised exercises

A meta-analysis with five studies and six comparisons (Demir-Göçmen et al., 2013; Evcik et al., 2008; Genc et al., 2015; Ramsay et al., 2000; Sevimli et al., 2015) showed very low-quality evidence of a superior and clinically relevant effect of supervised exercises on pain reduction compared to unsupervised exercises [MD: -10.0 mm; 95% CI: -19.6 to -0.3; assessed using VAS, 0 to 100 mm]. The heterogeneity of this meta-analysis was very high ($I^2 = 90\%$) because different types of exercise were included (Figure 4e).

Intensity of the exercise

A meta-analysis with three studies (Bjersing et al., 2012; Mannerkorpi et al., 2010; van Santen et al., 2002) showed low-quality evidence of no difference between high and low intensity aerobic exercises for pain reduction [MD: -1.1 mm; 95% CI: -8.0 to 5.9; assessed using VAS, 0 to 100 mm] (Figure 4f).

Insert Figure 4 here

Adverse effects of exercise

The following adverse effects were reported during aerobic exercise: transient knee pain (McCain et al., 1988), minor musculoskeletal events (Wang et al., 2018), and increase in pain intensity during high-intensity aerobic exercise (van Santen et al., 2002).

Furthermore, muscle pain during land-based aerobic exercise was more frequently reported than during water-based aerobic exercise (Assis et al., 2006). An adverse effect during muscle strengthening exercise was worsening of pain (Assumpção et al., 2018; Jones et al., 2002). During stretching exercise, adverse effects reported were worsening of pain (Jones et al., 2002) and Achilles tendinitis (McCain et al., 1988). During Tai Chi, worsening of pain (Calandre et al., 2009) and minor musculoskeletal events (Wang et al., 2018) were reported. All these adverse effects were reported in a small number of patients (details in Supplementary File 1, Supplementary Table 1).

Exercise prescription parameters for chronic whiplash-associated disorders

Type of therapeutic exercise

Body awareness exercise versus Combined exercise

One study (Seferiadis et al., 2016) showed no difference between body awareness exercise and combined exercise (aerobic plus strengthening plus coordination exercises) for pain and disability in the short-term. However, body awareness exercises were superior for quality of life in the short-term.

Combined exercise versus other Combined exercise

One study (Vikne et al., 2007) showed no difference between sling exercise plus strengthening plus endurance exercises and a program of strengthening plus endurance exercises for pain and disability in the short- and long-term.

Supervised exercises

All included studies (Seferiadis et al., 2016; Vikne et al., 2007) used supervised exercise. One study added unsupervised exercise for the period of 32 weeks after the supervised intervention (Vikne et al., 2007) and showed that exercising at home had no additional effect on pain and disability management.

Duration of the session

Only one study (Seferiadis et al., 2016) reported the duration of the exercise session, which was 90 minutes of body awareness exercises or aerobic plus strengthening plus coordination exercises per session.

Weekly treatment frequency

One study (Seferiadis et al., 2016) reported that the weekly frequency of exercise sessions was twice a week.

Duration of treatment

One study (Seferiadis et al., 2016) conducted the treatment for 10 weeks, while the other (Vikne et al., 2007) conducted supervised therapy for 16 weeks, and the two groups also conducted 32 weeks of the same therapy at home.

Intensity of the exercise

Neither of the included studies (Seferiadis et al., 2016; Vikne et al., 2007) reported the intensity of the exercises.

Adverse effects of exercise

Worsening of pain was reported in both body awareness and combined exercises (Seferiadis et al., 2016) in a small number of patients (details in Supplementary File 1, Supplementary Table 1).

Exercise prescription parameters for chronic idiopathic neck pain

Type of therapeutic exercise

Muscle strengthening versus Motor control

Six studies compared motor control exercises to muscle strengthening. Two studies (Borisut et al., 2013; Falla et al., 2006) compared motor control exercises to a combination of muscle strength and muscle endurance exercises, and four studies (Bobos et al., 2016; Javanshir et al., 2015; Kim and Kwag, 2016; O'Leary et al., 2012) compared motor control exercises to nonspecific strengthening of the neck muscle; however, one of these studies (Bobos et al., 2016) did not provide enough information to be included in the meta-analysis. Therefore, a meta-analysis of the three remaining studies (Javanshir et al., 2015; Kim and Kwag, 2016; O'Leary et al., 2012) was carried out and showed very low-quality evidence of no difference between motor control exercises and nonspecific strengthening of the neck muscles for pain reduction [MD: -3.2 mm; 95% CI: -13.8 to 7.5; assessed using VAS, 0 to 100 mm] (Figure 5a).

Mind-body exercises (Qigong and Tai Chi) versus Combined exercise

A meta-analysis of three studies (Lansinger et al., 2007; Lauche et al., 2016; von Trott et al., 2009) showed low-quality evidence of a small effect of several combined exercise modalities (aerobic, strengthening, stretching, active range of motion, and proprioceptive exercises) on pain reduction [MD: 6.5 mm; 95% CI: 0.8 to 12.2; assessed using VAS, 0 to 100 mm] (Figure 5b).

Insert Figure 5 here

Adverse effects of exercise

During Yoga, minor adverse events, pain worsening, and muscle soreness were reported (Cramer et al., 2013). During Tai Chi, migraine and Achilles tendon pain were reported (Lauche et al., 2016). During Qigong, muscle soreness, myogelosis (painful change in muscle structure correlated with the myofascial trigger points (Windisch et al., 1999)), other pain, neck twinge, headache, and vertigo/nausea were reported (Rendant et al., 2011; von Trott et al., 2009). During combined exercises, knee pain and vertigo were reported (Lauche et al., 2016), as well as worsening of neck pain and tinnitus, muscle soreness, myogelosis, headache, and vertigo/nausea (Rendant et al., 2011; von Trott et al., 2009). All these adverse effects were reported in a small number of patients (details in Supplementary File 1, Supplementary Table 1).

A summary of the exercise prescriptions recommended for each condition is presented in Table 1.

Insert Table 1 here

DISCUSSION

Summary of the main results

The aim of this systematic review was to compare the effects of different exercise prescriptions for pain management in patients with chronic pain along the continuum of nociplastic pain (represented by patients with fibromyalgia, CWAD, and CINP). Effect sizes found were generally below the minimal clinically important difference threshold of 20% or 10 mm. There was very low- to low-quality of evidence, using the GRADE approach, creating a high degree of uncertainty in these results. The main findings of this systematic review were:

Fibromyalgia

Aerobic exercise and muscle strengthening showed similar small effects, but both exercises were better than stretching exercises alone. Apparently, there was no difference between performing land or pool-based aerobic exercise or aerobic exercise at low or high intensity. Supervised exercises were a little better than unsupervised exercises. The majority of exercise sessions for patients with fibromyalgia were performed for 50 to 60 minutes, 2 to 3 times a week, for a period of 13 to 24 weeks of treatment. Intensity of the aerobic exercises were set at 40% to 80% of the maximal heart rate or at a perceived exertion between 9 to 15 on the Rated Perceived Exertion scale. The intensity of muscle strengthening was 45 to 50% of 1 repetition maximum and stretching was performed until the patient experienced moderate discomfort.

Chronic whiplash associated disorder

Body awareness exercises had similar effects to the combination of aerobic + strengthening + coordination exercises. There was no difference in adding sling exercises to the combination of muscle strengthening + muscle endurance exercises. Regarding exercise prescription, the exercises were supervised in 90-minute sessions, twice a week, for a period of 10 to 16 weeks.

Chronic idiopathic neck pain

Motor control exercises were similar to nonspecific muscle strengthening, but combined exercise was better than meditative therapies (Tai Chi and Qigong). The majority of the exercises were performed in a supervised manner, in sessions of 30 to 60 minutes duration, 2 to 3 times a week, for a period of 7 to 12 weeks of treatment. Regarding exercise intensity, aerobic exercises were performed at 50% to 75% of the VO2max, muscle strengthening at 20 to 80% of the maximum voluntary contraction/maximal isometric contraction or between 15 to 8 maximal repetitions, and motor control exercises with isometric contractions of 10 seconds and an inflated pressure biofeedback device at 20 to 33 mmHg.

Similarities and discrepancies with other studies or reviews

The literature shows that interventions based on physical exercise have a beneficial effect on the treatment of chronic pain (Booth et al., 2017; Geneen et al., 2017). Thus, knowledge about the best type of exercise and prescription for patients with chronic pain is extremely important. Currently, the major challenge for clinicians is to correctly tailor exercise to maximize clinical effect without exacerbating symptoms. Regarding exercise prescription for patients with chronic pain in general, a previous clinical update (Booth et al., 2017) recommended that aerobic exercises be performed for 20 to 60 minutes, twice a week, for a minimum of 6 weeks, with mild to moderate intensity (40 to 70% of maximum heart rate [HRmax]). For strengthening exercises, the same study recommended one to two sets of 15 to 20 repetitions, 2 to 3 times a week, for at least 6 weeks, with mild to moderate intensity (40 to 60% 1 Repetition maximum [RM]). Some of these findings were similar to ours. However, our results showed that, for patients with fibromyalgia and CINP, exercise intensity can be higher than previously recommended, taking care to increase intensity gradually (40% to 80% HRmax for fibromyalgia, and 50% to 75% of VO_2max for CINP).

One study (Polaski et al., 2019) assessed factors related to exercise prescription that could influence the improvement of pain in chronic health conditions and showed that, when exercise frequency per week was increased, a substantial increase in analgesic effect was found. However, when the duration of exercise (expressed in minutes per week) or duration of the study was increased, the model predicted a decrease in analgesic effect. In the present study, a meta-analysis for weekly frequency and duration of treatment could not be performed. Nevertheless, we observed an ideal frequency of 2 to 3 times a week in most of the included studies. In addition, we observed that treatment for painful conditions with predominance of central sensitization should last longer (at least 10 to 13 weeks for patients with CWAD and fibromyalgia) than treatment for painful conditions without nociplastic pain (at least 7 weeks for CINP).

None of the previous studies considered the central sensitization for exercise prescription. Currently, there are few methods to assess patients who present central sensitization characteristics in clinical practice. Current evidence suggests that the qualitative tests and the Central Sensitization Inventory (Mayer et al., 2012; Neblett et al., 2013) are the main clinical criteria for the classification of central sensitization pain (Nijs et al., 2014). In addition, some aspects related to central sensitization, such as dysfunctional endogenous analgesic control, can be quantitatively assessed using the conditioned pain modulation and temporal summation tests, and hyperalgesia can be assessed using an algometer (pressure pain threshold) (Meeus et al., 2015). With this information, the therapist can assess whether the patient's pain has a nociceptive or nociplastic predominance, and thus, prescribe an adequate exercise program. In fact, the investigation of central sensitization should be considered in clinical practice before exercise prescription (Chimenti et al., 2018; Nijs et al., 2012) given that patients with painful conditions with predominance of central sensitization probably have dysfunctional endogenous analgesia, which might predispose them to exercise-induced hyperalgesia (Nijs et al., 2012). In these cases, a narrative review (Nijs et al., 2012) suggests the following strategies to prevent exercise-induced hyperalgesia: 1) Prescription of aerobic exercise and motor control training, as well as caution with eccentric exercise; 2) Inclusion of exercise for non-painful areas; 3) Allowing a small increase in pain during exercise, but avoiding a continuous increase in pain intensity over time and changing the exercise if pain intensity increases; 4) Use of a time-contingent approach with appropriate baseline assessment; 5) Opting for a conservative baseline; and 6) Use of multiple and long recovery breaks between exercises.

Some of these strategies were observed in the results of the present review, such as the prescription of aerobic and more general exercises and a progression of exercise based on time-contingent approach, being careful with any increase in pain intensity for the majority of the studies with patients with fibromyalgia. These observed strategies show that general exercises may be performed without pain exacerbation (Chimenti et al., 2018; Lannersten and Kosek, 2010; Nijs et al., 2012). In contrast, studies on CINP, the health condition without predominance of nociplastic pain, prescribed exercises focusing only on the neck area and with high intensity. By adding more specific exercises to the treatment, the therapist can improve the central effect generated by the exercise, while also generating local effects on muscles and joints (Andersen et al., 2008; Meeus et al., 2016). In the studies that assessed CWAD, the prescription depended on the predominance of nociplastic pain presented by the patient. These results show that these characteristics can now be used as a basis for a more individualized prescription.

Strengths and weaknesses

The recommendations made by this systematic review are based on very low- to low-quality evidence, mainly because of the low number of studies comparing different aspects of exercise prescription, the heterogeneity of the intervention protocols, and the low number of patients assessed. These factors resulted in great heterogeneity and small sample sizes for the comparisons and indicate that further studies are necessary. Moreover, the included studies presented poor description of the exercise parameters, which hindered data extraction. Many RCTs did not perform between-group comparisons and did not provide data for each group at each treatment time, hampering the performance of proper meta-analyses.

As a strength, this systematic review included only RCTs in which the comparison groups were composed of physical exercise in order to assess whether the prescribed exercise parameters would influence patient-centered clinical outcomes. Meta-analyses of all possible comparisons were performed, which provides more accurate and specific quantitative results. Another strength of our study is that we described the results highlighting the clinical relevance of the effect sizes found in the meta-analyses, which provides the clinical significance of the results for the clinician and, most importantly, for the patient. In addition, this systematic review provides relevant information to clinical practice because we extensively summarized the available evidence on each aspect of exercise prescription per conditions of chronic pain along the continuum of nociplastic pain, which is a current and highly relevant topic.

Implications for practice

For pain conditions with predominance of nociplastic pain (i.e. fibromyalgia), clinicians should consider prescribing aerobic, muscle strengthening, and mind-body exercises (i.e. Qigong or Tai Chi). Supervised sessions with 50- to 60-minute duration, 2 to 3 times a week, for 13 weeks or more are recommended. For pain conditions with varying degrees of predominance of nociplastic pain (as CWAD), clinicians may mix general and specific neck exercises. Supervised sessions performed twice a week for up to 90 minutes, for 10 to 16 weeks can be prescribed. Finally, for pain conditions without predominance of nociplastic pain (as CINP), motor control and muscle strengthening exercises may be considered by clinicians. Supervised sessions with 30- to 60-minute duration, 2 to 3 times a week, for a period of 7 to 12 weeks of treatment are recommended. The results of this review may aid in the exercise prescription for other pain conditions as well, considering the situation within the continuum of nociplastic pain.

Implications for research

To increase the quality of the evidence, more studies comparing different parameters of exercise prescription with larger samples are recommended. Additionally, adequate recording and description of the types and exact dosage of the exercise programs are also important to facilitate translation into clinical practice, as well as for the pooling of data to improve the directness of the outcomes. Therefore, we recommend the use of the guidelines by the Template for Intervention Description and Replication (TIDieR), which guides the best way to report interventions (Yamato et al., 2016). It is of the utmost importance that authors follow the CONSORT guidelines (Schulz et al., 2010) and do not fail to perform between-group comparison analyses.

CONCLUSION

This systematic review found that there is no difference between the majority of exercises for pain reduction, considering the health conditions included in this review. Regarding fibromyalgia, aerobic and muscle strengthening exercises are slightly superior to isolated stretching exercises, which can be performed in supervised sessions with 50- to 60-minute duration, 2 to 3 times a week, for a treatment period of 13 weeks or more. For CWAD, body awareness exercises and combined exercises (aerobic plus strengthening plus coordination exercises) can be prescribed, and the addition of sling exercises to a combination of strength plus endurance exercises does not provide additional effects. The exercises can be performed in supervised sessions, twice a week for up to 90 minutes, for a treatment period of 10 to 16 weeks or more. Finally, for CINP, motor control, nonspecific muscle strengthening, and a combination of strengthening plus endurance exercises can be prescribed, with combined exercises (aerobic, strengthening, stretching, active range of motion, proprioceptive exercises) being slightly superior to mind-body exercises. The exercises can be performed in supervised sessions with 30- to 60-minute duration, 2 to 3 times a week, for a period of 7 to 12 weeks.

AUTHOR CONTRIBUTIONS

Katherinne Franco, Mira Meeus, Cristina Cabral, and Felipe Reis developed the study. Katherinne Franco, Dorine Lenoir, and Yuri Franco collected the data. Katherinne Franco and Yuri Franco performed the meta-analysis. All authors contributed to the improvement of the paper, approved the manuscript, and agreed with its submission to the European Journal of Pain.

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APPENDIX 1 - Search strategy

MEDLINE (Pubmed) search strategy

(((((chronic pain OR "Chronic Pain"[Mesh] OR long-lasting pain OR persisting pain OR long-term pain) AND (((idiopathic OR aspecific OR non-specific OR non-traumatic) AND (neck pain OR neckache OR cervical pain OR Cervical disorder* OR "Neck Pain"[Mesh])) OR fibromyalgia OR fibrositis OR "myofascial pain syndromes"[Mesh] OR "Fibromyalgia"[Mesh] OR whiplash OR whiplash injuries OR "Whiplash Injuries"[Mesh] OR whiplash associated disorders) AND (exercise OR exercise therap* OR "Exercise Movement Techniques"[Mesh] OR "Exercise Therapy"[Mesh] OR "Exercise"[Mesh] OR Rehabilitation[Mesh] OR Rehabilitation OR Hydrotherapy[Mesh] OR Water therap* OR Physical Fitness OR Physical Endurance OR Pliability OR "Tai Ji"[Mesh] OR Movement OR rehab OR Run OR Ran OR Running OR Jog OR Jogging OR Swim* OR swimming OR Walk* OR walking OR cycle* OR cycling OR bicycl* OR Motor Activit* OR Training* OR Stretch* OR Strengthening OR strength* OR Motion therap* OR gymnast* OR isometric* OR isotonic* OR isokinetic* OR aerobic* OR physiotherap* OR kinesiotherap* OR Stabili* OR segment* OR "motor control" OR ((McKenzie OR Alexander OR William OR Feldenkrais) adj (technique OR method OR methods)) OR Yoga OR Pilates OR Aerobic exercise* OR Endurance OR Therapeutic exercise*) AND (pain OR "Neck Pain"[Mesh] OR pain perception OR "Pain Perception"[Mesh] OR pain intensity OR disability OR functionality OR "Disability Evaluation"[Mesh]OR treatment outcome[Mesh] OR therapy effect)))))

Limits:

Clinical Study; Clinical Trial; Clinical Trial, Phase I; Clinical Trial, Phase II; Clinical Trial, Phase III; Clinical Trial, Phase IV; Comparative Study; Controlled Clinical Trial; Randomized Controlled Trial; Humans

EMBASE search strategy

('chronic pain' OR 'chronic pain'/exp OR 'long-lasting pain' OR 'persisting pain' OR 'long-term pain') AND ((idiopathic OR aspecific OR 'non specific' OR 'non traumatic') AND ('neck pain' OR neckache OR 'cervical pain' OR 'cervical disorder*' OR 'neck pain'/exp) OR fibromyalgia OR fibrositis OR 'myofascial pain syndromes'/exp OR 'fibromyalgia'/exp OR whiplash OR 'whiplash injuries' OR 'whiplash injuries'/exp OR 'whiplash associated disorders') AND (exercise OR 'exercise therap*' OR 'exercise movement techniques'/exp OR 'exercise therapy'/exp OR 'exercise'/exp OR 'rehabilitation'/exp OR rehabilitation OR 'hydrotherapy'/exp OR 'water therap*' OR 'physical fitness' OR 'physical endurance' OR pliability OR 'tai ji'/exp OR movement OR rehab OR run OR ran OR running OR jog OR jogging OR swim* OR swimming OR walk* OR walking OR cycle* OR cycling OR bicycl* OR 'motor activit*' OR training* OR stretch* OR strengthening OR strength* OR 'motion therap*' OR gymnast* OR isometric* OR isotonic* OR isokinetic* OR aerobic* OR physiotherap* OR kinesiotherap* OR stabili* OR segment* OR 'motor control' OR ((mckenzie OR alexander OR william OR feldenkrais) AND adj AND (technique OR method OR methods)) OR yoga OR pilates OR 'aerobic exercise*' OR endurance OR 'therapeutic exercise*') AND (pain OR 'neck pain'/exp OR 'pain perception' OR 'pain perception'/exp OR 'pain intensity' OR disability OR functionality OR 'disability evaluation'/exp OR 'treatment outcome'/exp OR 'therapy effect') AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim) AND ([article]/lim OR [article in press]/lim) AND [humans]/lim AND [embase]/lim

Cochrane Central Register of Controlled Trials (CENTRAL) search strategy

((("chronic pain" OR [mh "Chronic Pain"] OR "long-lasting pain" OR "persisting pain" OR "long-term pain") AND (((idiopathic OR aspecific OR non-specific OR non-traumatic) AND ("neck pain" OR neckache OR "cervical pain" OR "Cervical disorder*" OR [mh "Neck Pain"])) OR fibromyalgia OR fibrositis OR [mh "myofascial pain syndromes"] OR [mh Fibromyalgia] OR whiplash OR "whiplash injuries" OR [mh "Whiplash Injuries"] OR "whiplash associated disorders") AND (exercise OR "exercise therap*" OR [mh "Exercise Movement Techniques"] OR [mh "Exercise Therapy"] OR [mh Exercise] OR [mh Rehabilitation] OR Rehabilitation OR [mh Hydrotherapy] OR "Water therap*" OR "Physical Fitness" OR "Physical Endurance" OR Pliability OR [mh "Tai Ji"] OR Movement OR rehab OR Run OR Ran OR Running OR Jog OR Jogging OR Swim* OR swimming OR Walk* OR walking OR cycle* OR cycling OR bicycl* OR "Motor Activit*" OR Training* OR Stretch* OR Strengthening OR strength* OR "Motion therap*" OR gymnast* OR isometric* OR isotonic* OR isokinetic* OR aerobic* OR physiotherap* OR kinesiotherap* OR Stabili* OR segment* OR "motor control" OR ((McKenzie OR Alexander OR William OR Feldenkrais) adj (technique OR method OR methods)) OR Yoga OR Pilates OR "Aerobic exercise*" OR Endurance OR "Therapeutic exercise*") AND (pain OR [mh "Neck Pain"] OR "pain perception" OR [mh "Pain

Perception"] OR "pain intensity" OR disability OR functionality OR [mh "Disability Evaluation"] OR [mh "treatment outcome"] OR "therapy effect")))

Limits:

Trials; Search word variations

Cumulative Index to Nursing and Allied Health Literature (CINAHL) search strategy

((("chronic pain" OR (MH "Chronic Pain+") OR "long-lasting pain" OR "persisting pain" OR "long-term pain") AND (((idiopathic OR aspecific OR non-specific OR non-traumatic) AND ("neck pain" OR neckache OR "cervical pain" OR "Cervical disorder*" OR (MH "Neck Pain+"))) OR fibromyalgia OR fibrositis OR (MH "myofascial pain syndromes+") OR (MH "Fibromyalgia+") OR whiplash OR "whiplash injuries" OR (MH "Whiplash Injuries+") OR "whiplash associated disorders") AND (exercise OR "exercise therap*" OR (MH "Exercise Movement Techniques+") OR (MH "Exercise Therapy+") OR (MH "Exercise+") OR (MH "Rehabilitation+") OR Rehabilitation OR (MH "Hydrotherapy+") OR "Water therap*" OR "Physical Fitness" OR "Physical Endurance" OR Pliability OR (MH "Tai Ji+") OR Movement OR rehab OR Run OR Ran OR Running OR Jog OR Jogging OR Swim* OR swimming OR Walk* OR walking OR cycle* OR cycling OR bicycl* OR "Motor Activit*" OR Training* OR Stretch* OR Strengthening OR strength* OR "Motion therap*" OR gymnast* OR isometric* OR isotonic* OR isokinetic* OR aerobic* OR physiotherap* OR kinesiotherap* OR Stabili* OR segment* OR "motor control" OR ((McKenzie OR Alexander OR William OR Feldenkrais) adj (technique OR method OR methods)) OR Yoga OR Pilates OR "Aerobic exercise*" OR Endurance OR "Therapeutic exercise*") AND (pain OR (MH "Neck Pain+") OR "pain perception" OR (MH "Pain Perception+") OR "pain intensity" OR disability OR functionality OR (MH "Disability Evaluation+") OR (MH "treatment outcome+") OR "therapy effect")))

Limits:

Exclude MEDLINE records; Human; Randomized Controlled Trials

Search modes - SmartText Searching

Physiotherapy Evidence Database (PEDro) search strategy

exercise AND fibromyalgia

exercise AND neck pain

exercise AND whiplash

Limits: Method: clinical trial

FIGURE LEGENDS

Figure 1. Flow diagram of procedures for selection of studies.

Figure 2. Risk of bias graph. (a) Fibromyalgia; (b) Chronic Whiplash-Associated Disorders; (c) Chronic Idiopathic Neck Pain.

Figure 3. Risk of bias summary of included studies. (a) Fibromyalgia; (b) Chronic Whiplash-Associated Disorders; (c) Chronic Idiopathic Neck Pain.

Figure 4. Meta-analyses on exercise prescription for the treatment of pain in patients with fibromyalgia.

Figure 5. Meta-analyses on exercise prescription for the treatment of pain in patients with chronic idiopathic neck pain. Abbreviation: nonspecific str – Nonspecific strengthening; mind-body ther – Mind-body therapy; combined exer – Combined exercise.

Table 1

Table 1. Summary of the exercise prescriptions recommended by this review

FIBROMYALGIA	
Type of exercise	Global exercises were more researched and presented better results, such as: Aerobic exercises; Muscle strengthening; Combined exercises (balance + motor control exercises OR relaxation + stretching exercises OR aerobic + strengthening + stretching exercises); Tai Chi. No difference between land and pool-based aerobic exercise.
Supervision	Supervised
Duration of the session	50 to 60 minutes
Weekly frequency	2 to 3 times a week
Duration of treatment	13 to 24 weeks
Intensity	
Aerobic exercises	40% to 80% HRmax; or Perceived exertion between 9 to 15 on RPE
Muscle strengthening	45 to 50% of 1RM
Muscle stretching	Until moderate discomfort
CHRONIC WHIPLASH-ASSOCIATED DISORDER (CWAD)	
Type of exercise	The most recommended exercises were: Body awareness exercises; Combined exercises (aerobic + strengthening + coordination exercises OR muscle strength + muscle endurance exercises with or without sling exercises). The addition of sling exercises to the combination of muscle strength + muscle endurance exercises did not make any difference. This recommendation is based on only two studies.
Supervision	Supervised
Duration of the session	90 minutes
Weekly frequency	Twice a week
Duration of treatment	10 to 16 weeks
Intensity	No information
CHRONIC IDIOPATHIC NECK PAIN (CINP)	
Type of exercise	Specific exercises were more researched and presented better results, such as: Motor control; Muscle strengthening (muscle strength + muscle endurance); Combined exercises (aerobic + active range of motion of the cervical OR shoulder/thoracic + muscle endurance + muscle strength + stretching exercises OR proprioceptive + isometric + dynamic mobilization + stretching + strengthening of the neck + core exercises); Active range of motion exercises; Yoga; Proprioceptive exercises. No difference between performing muscle strengthening exercise with focus on muscle strength or muscle endurance.
Supervision	Supervised
Duration of the session	30 to 60 minutes
Weekly frequency	2 to 3 times a week
Duration of treatment	7 to 12 weeks
Intensity	

Aerobic exercises	50% to 75% of VO_2max
Muscle strengthening	20 to 80% of MVC maximum voluntary contraction/or MIC; or 15 to 8 RMs
Motor control	Isometric contractions of 10 sec using an inflated pressure biofeedback device of 20 to 33 mmHg

Abbreviations - HRmax: Maximal heart rate; RPE: Rated perceived exertion scale; RM: Repetition maximum; MVC: Maximum voluntary contraction; MIC: Maximal isometric contraction; VO2max: Maximal oxygen uptake; sec: Seconds.

Figure 1

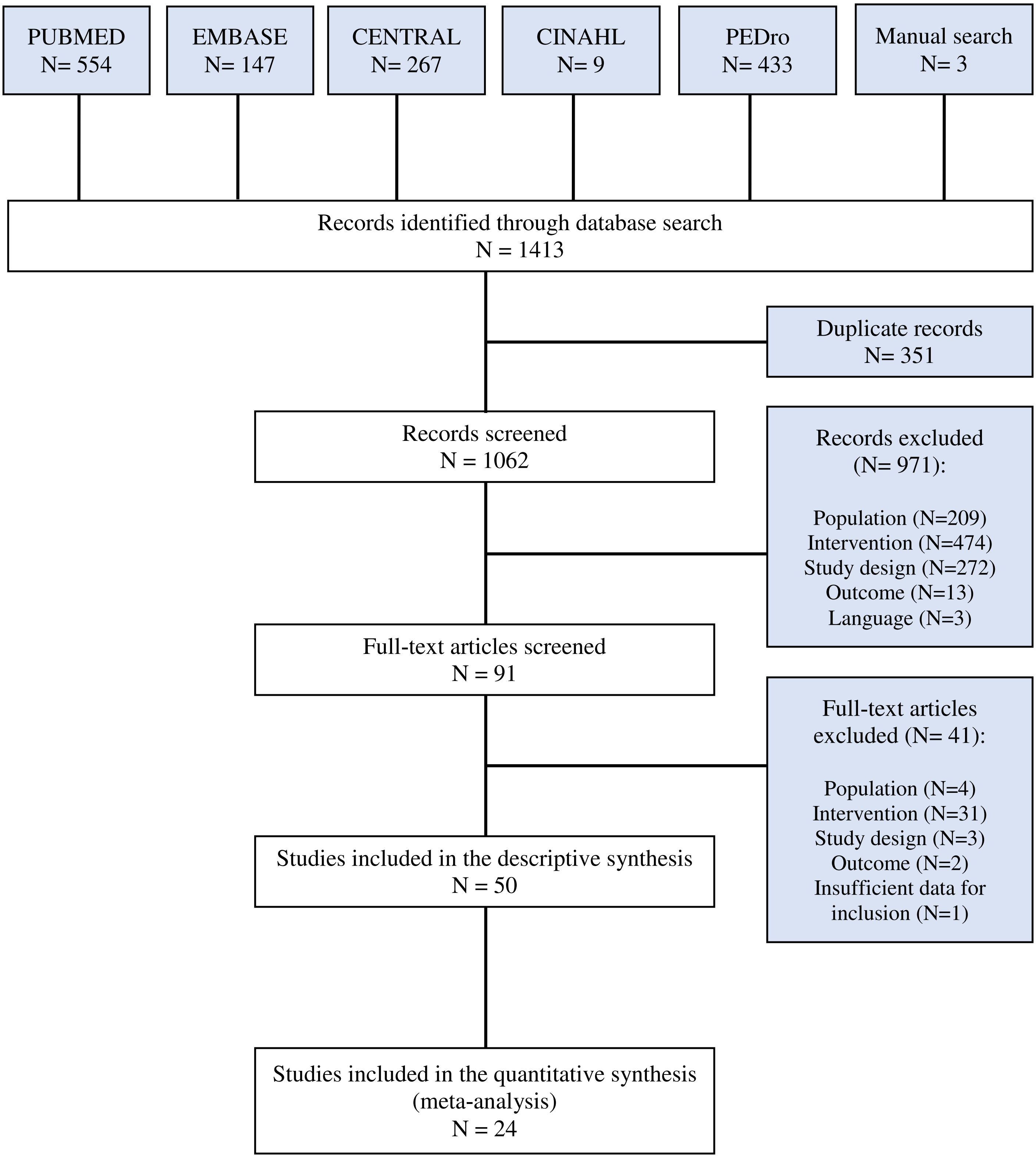
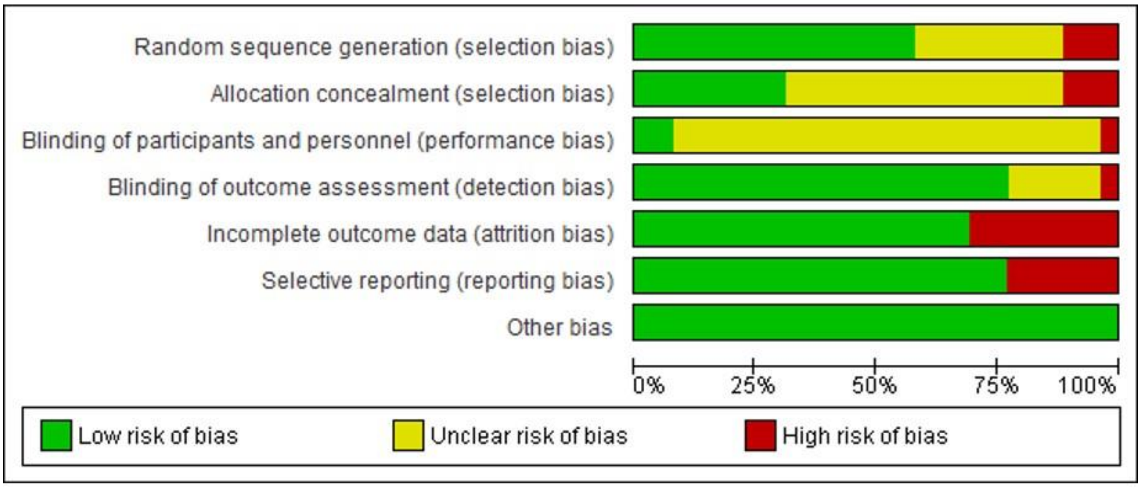
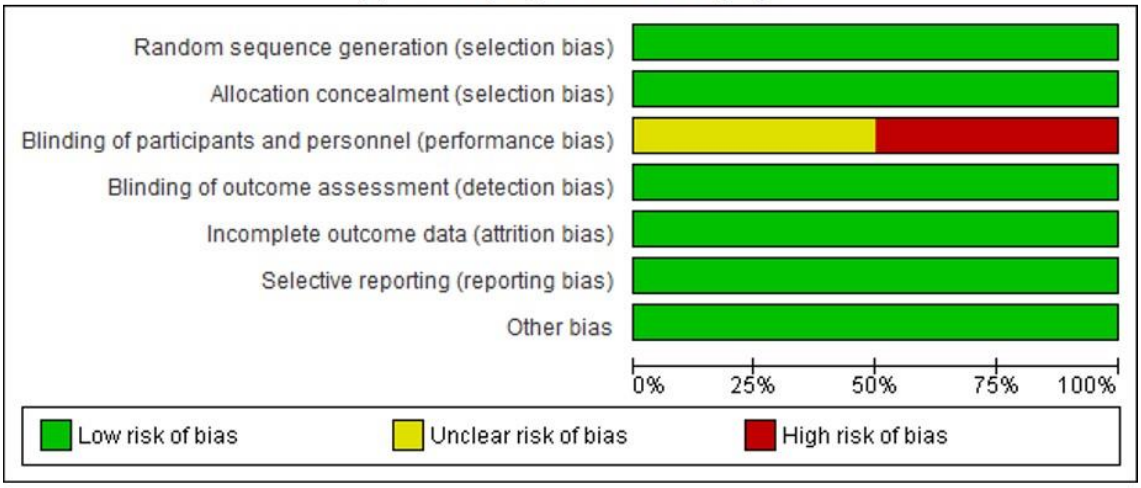

PUBMED
N= 554
EMBASE
N= 147
CENTRAL
N= 267
CINAHL
N= 9
PEDro
N= 433
Manual search
N= 3
Records identified through database search
N = 1413
Duplicate records
N= 351
Records screened
N = 1062
Records excluded
(N= 971):
Population (N=209)
Intervention (N=474)
Study design (N=272)
Outcome (N=13)
Language (N=3)
Full-text articles screened
N = 91
Full-text articles
excluded (N= 41):
Population (N=4)
Intervention (N=31)
Study design (N=3)
Outcome (N=2)
Insufficient data for
inclusion (N=1)
Studies included in the descriptive synthesis
N = 50
Studies included in the quantitative synthesis
(meta-analysis)
N = 24

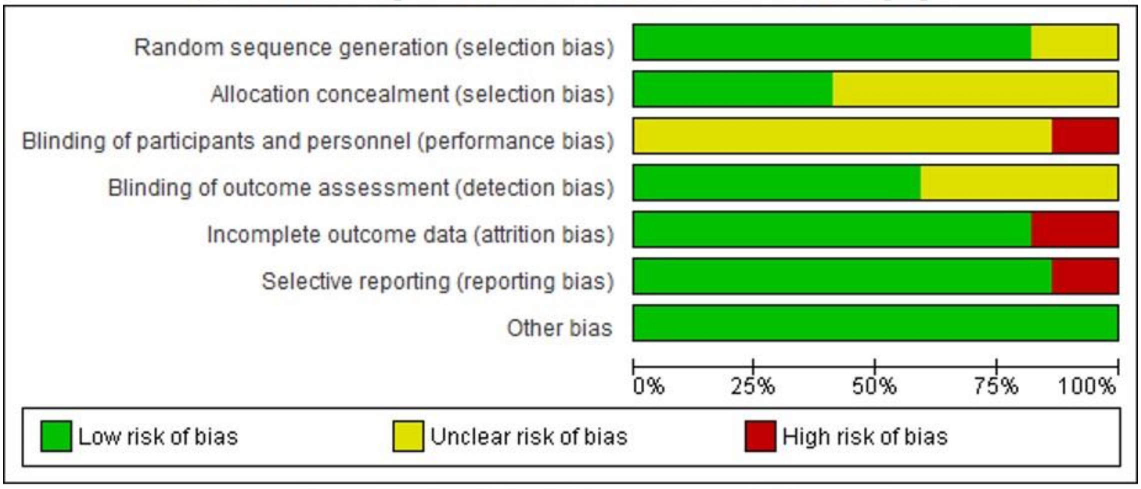
Figure 2



(a) Fibromyalgia risk of bias graph



(b) Chronic Whiplash Associated Disorders risk of bias graph



(c) Chronic Idiopathic Neck Pain risk of bias graph

Figure 3

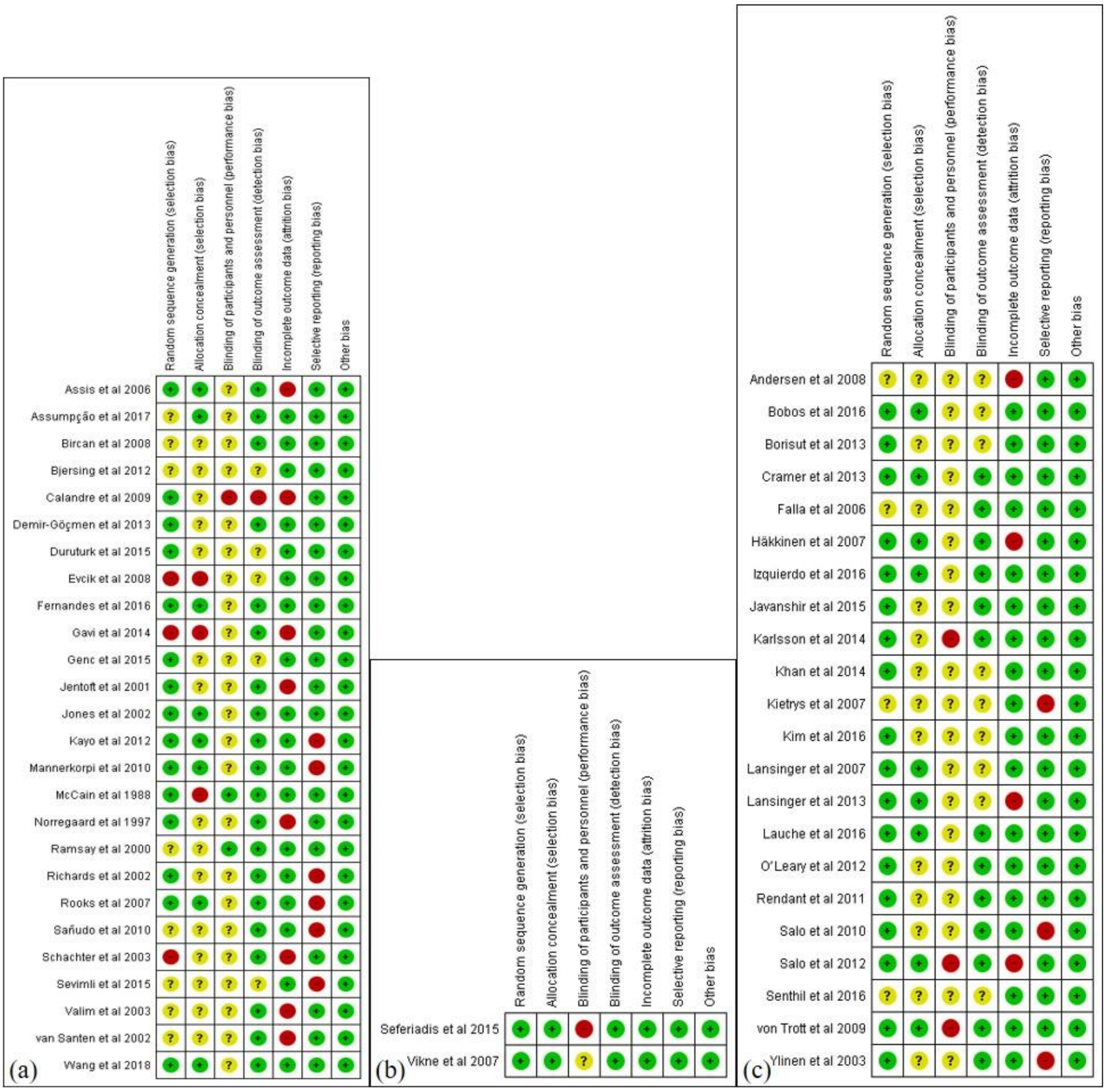
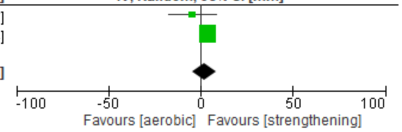

Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
Assis et al 2006
Assumpção et al 2017
Bircan et al 2008
Bjersing et al 2012
Calandre et al 2009
Demir-Göçmen et al 2013
Duruturk et al 2015
Evcik et al 2008
Fernandes et al 2016
Gavi et al 2014
Genc et al 2015
Jentoft et al 2001
Jones et al 2002
Kayo et al 2012
Mannerkorpi et al 2010
McCain et al 1988
Norregaard et al 1997
Ramsay et al 2000
Richards et al 2002
Rooks et al 2007
Sañudo et al 2010
Schachter et al 2003
Sevimli et al 2015
Valim et al 2003
van Santen et al 2002
Wang et al 2018
(a)
Seferiadis et al 2015
Vikne et al 2007
(b)
Andersen et al 2008
Bobos et al 2016
Borisut et al 2013
Cramer et al 2013
Falla et al 2006
Häkkinen et al 2007
Izquierdo et al 2016
Javanshir et al 2015
Karlsson et al 2014
Khan et al 2014
Kietrys et al 2007
Kim et al 2016
Lansinger et al 2007
Lansinger et al 2013
Lauche et al 2016
O'Leary et al 2012
Rendant et al 2011
Salo et al 2010
Salo et al 2012
Senthil et al 2016
von Trott et al 2009
Ylinen et al 2003
(c)

Figure 4

Study or Subgroup	Aerobic Mean [mm]	Aerobic SD [mm]	Aerobic Total	Strengthening Mean [mm]	Strengthening SD [mm]	Strengthening Total	Weight	Mean Difference IV, Random, 95% CI [mm]
Bircan et al 2008	21.9	18.8	13	26.5	14.1	13	20.8%	-4.60 [-17.37, 8.17]
Kayo et al 2012	51	6.1	30	47.3	5.5	30	79.2%	3.70 [0.76, 6.64]
Total (95% CI)			**43**			**43**	**100.0%**	**1.97 [-4.63, 8.58]**

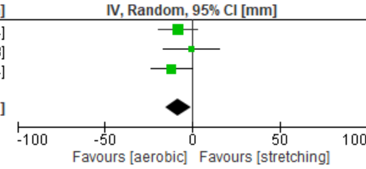
Heterogeneity: Tau² = 12.08; Chi² = 1.54, df = 1 (P = 0.21); I² = 35%
Test for overall effect: Z = 0.59 (P = 0.56)



(a) Forest plot - Aerobic exercise versus Muscle strengthening for pain in short-term

Study or Subgroup	Aerobic Mean [mm]	Aerobic SD [mm]	Aerobic Total	Stretching Mean [mm]	Stretching SD [mm]	Stretching Total	Weight	Mean Difference IV, Random, 95% CI [mm]
Genc et al 2015	55.5	20.1	25	63.9	19	25	43.5%	-8.40 [-19.24, 2.44]
McCain et al 1988	46.9	30.6	18	47.4	17	20	20.0%	-0.50 [-16.48, 15.48]
Valim et al 2003	34.2	25	32	46	21.8	28	36.5%	-11.80 [-23.64, 0.04]
Total (95% CI)			**75**			**73**	**100.0%**	**-8.06 [-15.21, -0.91]**

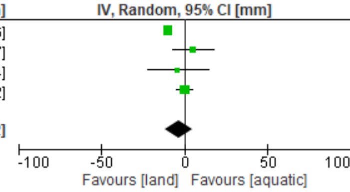
Heterogeneity: Tau² = 0.00; Chi² = 1.25, df = 2 (P = 0.54); I² = 0%
Test for overall effect: Z = 2.21 (P = 0.03)



(b) Forest plot - Aerobic exercise versus Muscle stretching for pain in short-term

Study or Subgroup	Land Mean [mm]	Land SD [mm]	Land Total	Aquatic Mean [mm]	Aquatic SD [mm]	Aquatic Total	Weight	Mean Difference IV, Random, 95% CI [mm]
Assis et al 2006	46	0.8	30	56	2.5	30	35.8%	-10.00 [-10.94, -9.06]
Fernandes et al 2016	36	28	36	31	27	39	19.7%	5.00 [-7.47, 17.47]
Jentoft et al 2001	52	31	16	56	23	18	12.8%	-4.00 [-22.54, 14.54]
Sevimli et al 2015	48.2	8.8	25	48	9.3	25	31.7%	0.20 [-4.82, 5.22]
Total (95% CI)			**107**			**112**	**100.0%**	**-3.04 [-11.29, 5.22]**

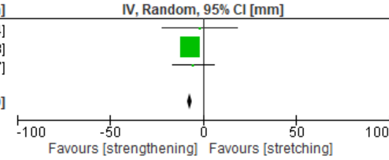
Heterogeneity: Tau² = 49.37; Chi² = 20.95, df = 3 (P = 0.0001); I² = 86%
Test for overall effect: Z = 0.72 (P = 0.47)



(c) Forest plot - Land-based aerobic exercise versus Pool-based aerobic exercise for pain in short-term

Study or Subgroup	Strengthening Mean [mm]	Strengthening SD [mm]	Strengthening Total	Stretching Mean [mm]	Stretching SD [mm]	Stretching Total	Weight	Mean Difference IV, Random, 95% CI [mm]
Assumpção et al 2017	44	30	16	46	26	14	0.3%	-2.00 [-22.04, 18.04]
Gavi et al 2014	49.6	2.2	35	56.6	2.6	31	98.6%	-7.00 [-8.17, -5.83]
Jones et al 2002	46.1	21	28	51.4	22	28	1.1%	-5.30 [-16.57, 5.97]
Total (95% CI)			**79**			**73**	**100.0%**	**-6.97 [-8.13, -5.80]**

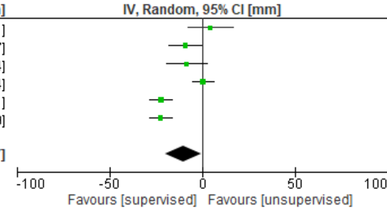
Heterogeneity: Tau² = 0.00; Chi² = 0.32, df = 2 (P = 0.85); I² = 0%
Test for overall effect: Z = 11.75 (P < 0.00001)



(d) Forest plot - Muscle strengthening versus Muscle stretching for pain in short-term

Study or Subgroup	Supervised Mean [mm]	Supervised SD [mm]	Supervised Total	Unsupervised Mean [mm]	Unsupervised SD [mm]	Unsupervised Total	Weight	Mean Difference IV, Random, 95% CI [mm]
Demir-Göçmen et al 2013	55	25	25	50.4	19	25	14.6%	4.60 [-7.71, 16.91]
Evcik et al 2008	42	16	31	51	19	30	16.5%	-9.00 [-17.83, -0.17]
Genc et al 2015	55.5	20.1	25	63.9	19	25	15.4%	-8.40 [-19.24, 2.44]
Ramsay et al 2000	60.5	13.27	37	60	11.42	37	17.9%	0.50 [-5.14, 6.14]
Sevimli et al 2015	48.2	8.8	25	70.4	12.5	25	17.8%	-22.20 [-28.19, -16.21]
Sevimli et al 2015	48	9.3	25	70.4	12.5	25	17.8%	-22.40 [-28.51, -16.29]
Total (95% CI)			**168**			**167**	**100.0%**	**-9.95 [-19.62, -0.27]**

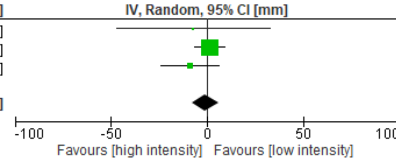
Heterogeneity: Tau² = 127.51; Chi² = 48.98, df = 5 (P < 0.00001); I² = 90%
Test for overall effect: Z = 2.02 (P = 0.04)



(e) Forest plot - Supervised versus Unsupervised exercise for pain in short-term

Study or Subgroup	High Intensity Mean [mm]	High Intensity SD [mm]	High Intensity Total	Low Intensity Mean [mm]	Low Intensity SD [mm]	Low Intensity Total	Weight	Mean Difference IV, Random, 95% CI [mm]
Bjersing et al 2012	-13.9	70.42	26	-6.5	71.77	23	3.0%	-7.40 [-47.31, 32.51]
Mannerkorpi et al 2010	-4	14.5	29	-5.3	16.3	29	76.3%	1.30 [-6.64, 9.24]
van Santen et al 2002	-11	19.8	17	-2	22.1	13	20.7%	-9.00 [-24.26, 6.26]
Total (95% CI)			**72**			**65**	**100.0%**	**-1.09 [-8.03, 5.85]**

Heterogeneity: Tau² = 0.00; Chi² = 1.48, df = 2 (P = 0.48); I² = 0%
Test for overall effect: Z = 0.31 (P = 0.76)

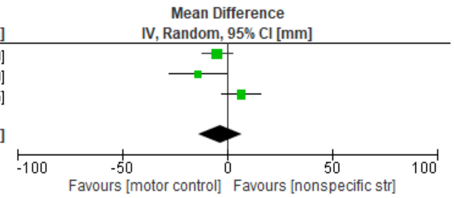


(f) Forest plot - High intensity aerobic exercise versus Low intensity aerobic exercise for pain in short-term

Figure 5

Study or Subgroup	Motor control Mean [mm]	Motor control SD [mm]	Motor control Total	Nonspecific strengthening Mean [mm]	Nonspecific strengthening SD [mm]	Nonspecific strengthening Total	Weight	Mean Difference IV, Random, 95% CI [mm]
Javanshir et al 2015	22.7	15.1	30	27.5	14.1	30	38.6%	-4.80 [-12.19, 2.59]
Kim et al 2016	17	18	14	31	19	14	26.5%	-14.00 [-27.71, -0.29]
O'Leary et al 2012	20.9	18	19	14	10.2	20	34.9%	6.90 [-2.35, 16.15]
Total (95% CI)			**63**			**64**	**100.0%**	**-3.16 [-13.78, 7.47]**

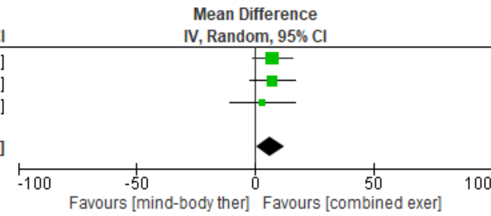
Heterogeneity: Tau² = 62.01; Chi² = 7.04, df = 2 (P = 0.03); I² = 72%
Test for overall effect: Z = 0.58 (P = 0.56)



(a) Forest plot - Motor control versus Nonspecific strengthening exercise for pain in short-term

Study or Subgroup	Mind-body therapies Mean	Mind-body therapies SD	Mind-body therapies Total	Combined exercises Mean	Combined exercises SD	Combined exercises Total	Weight	Mean Difference IV, Random, 95% CI
Lansinger et al 2007	41.2	22.8	60	34	24.2	62	46.9%	7.20 [-1.14, 15.54]
Lauche et al 2016	32.4	23.5	38	25.2	18.3	37	36.0%	7.20 [-2.32, 16.72]
von Trott et al 2009	47.4	30.8	31	44.5	25.7	35	17.2%	2.90 [-10.89, 16.69]
Total (95% CI)			**129**			**134**	**100.0%**	**6.46 [0.75, 12.17]**

Heterogeneity: Tau² = 0.00; Chi² = 0.31, df = 2 (P = 0.86); I² = 0%
Test for overall effect: Z = 2.22 (P = 0.03)



(b) Forest plot - Mind-body therapies versus Combined exercise for pain in short-term

Supplementary file 1 – Supplmentary Tables 1, 2 and 3

Supplementary Table 1. Characteristics of the included studies

First author/ Year	Participants	Outcomes	Follow-ups	Adverse effects	Results
FIBROMYALGIA					
Assis et al 2006[4]	**Land-based exercises - LBE** (n = 30): Age: 42.2 ± 10.0 Gender: 30 (100%) BMI: 26.9 ± 4.6 Duration of symptoms: 6.9 ± 4.6 **Deep water running - DWR** (n = 30): Age: 43.4 ± 10.7 Gender: 30 (100%) BMI: 27.3 ± 5.4 Duration of symptoms: 5.2 ± 4.0	1. Pain (VAS) 2. Impact of fibromyalgia (FIQ) 3. Health related quality of life (SF-36)	8 and 15 weeks	**LBE** (n=16): Muscle pain (n=12) Impingement syndrome (n=1) Bilateral ankle arthritis (n=1) Baker cyst (n=1) **DWR** (n=10): Muscle pain (n=4) Tinea pedis (n=1)	**8 weeks:** LBE x DWR: P > 0.05 **15 weeks:** 1. Pain: LBE x DWR: P > 0.05 2. Impact of fibromyalgia: LBE x DWR✱: F = 3.8, P < 0.02 3. Health related quality of life: LBE x DWR: P > 0.05
Assumpção et al 2017[5]	**Stretching exercise - SE** (n = 14): Age: 47.9 ± 5.3 Gender: 100% BMI: 28.9 ± 4.2 **Resistance exercise - RE** (n = 16): Age: 45.7 ± 7.7 Gender: 100% BMI: 28.1 ± 4.7	1. Pain (VAS) 2. Pain threshold over tender points (Dolorimeter) 3. Impact of fibromyalgia (FIQ) 4. Health related quality of life (SF-36)	12 weeks	**RE** (n=1): Worsening pain	1. Pain: SE x RE: P = 0.11 2. Pain threshold: SE x RE: P = 0.14 3. Impact of fibromyalgia: SE x RE✱: P=0.02 and P=0.03 (depression and physical functioning). 4. Health related quality of life: SE✱ x RE: P=0.01 and P=0.01 (physical functioning and bodily pain).
Bircan et al 2008[9]	**Aerobic exercise - AE** (n = 13): Age: 48.3 ± 5.3 Gender: 100% Duration of symptoms: 3.8 ± 3.3 **Strengthening exercise - SE** (n = 13): Age: 46 ± 8.5 Gender: 100% Duration of symptoms: 4.6 ± 5.2	1. Pain (VAS) 2. Health related quality of life (SF-36)	8 weeks	**SE** (n=1): Pneumonia	1. Pain: AE x SE: P = 0.18 2. Health related quality of life: AE x SE: P > 0.05
Bjersing et al 2012[10]	**Moderate-to-high intensity Nordic walking - MHNW** (n = 26) **Low-intensity walking - LIW** (n = 23)	1. Pain (FIQ - subscale Pain)	15 and 30 weeks	Not reported	**15 weeks:** MHNW x LIW: P > 0.05

	Age (total)ʃ: 52 (48-56) Gender (total): 100% Duration of symptoms (total)ʃ: 11 (7-15)	2. Pain threshold over tender points (Algometer)			**30 weeks:** MHNW x LIW: $P > 0.05$
Calandre et al 2009[16]	**Tai Chi - TC** (n = 42): Age: 49.0 ± 8.4 Gender: 39 (92.8%) Duration of symptoms: 15.6 ± 8.7 **Stretching exercise - SE** (n = 39): Age: 51.0 ± 8.0 Gender: 34 (87.2%) Duration of symptoms: 14.1 ± 8.4	1. Impact of fibromyalgia (FIQ) 2. Health related quality of life (Physical and Mental components of the SF-12)	4, 6 and 12 weeks	**TC** (n=3): Chlorine hypersensitivity (n=1) Pain exacerbation (n=2)	**4 weeks:** TC x SE: $P > 0.05$ **6 weeks:** TC x SE: $P > 0.05$ **12 weeks:** TC x SE: $P > 0.05$
Demir-Göçmen et al 2013[21]	**Supervised stretching and balance–coordination exercises - SSBE** (n = 25): Age: 44.6 ± 5.3 Gender: 25 (100%) **Home stretching exercises - HSE** (n = 25): Age: 44.4 ± 5.2 Gender: 25 (100%)	1. Pain (VAS) 2. Pain threshold over tender points (Algometer) 3. Impact of fibromyalgia (FIQ)	12 and 24 weeks	Not reported	**12 weeks:** SSBE x HSE: $P > 0.05$ **24 weeks:** SSBE x HSE: $P > 0.05$
Duruturk et al 2015[22]	**Aerobic exercises - AE** (n = 14): Age: 48.1 ± 7.4 Gender: 14 (100%) BMI: 19.1 ± 4.1 Duration of symptoms: 5.8 ± 4.5 **Balance exercises - BE** (n = 12): Age: 54.0 ± 6.6 Gender: 12 (100%) BMI: 20.6 ± 3.7 Duration of symptoms: 5.5 ± 9.0	1. Pain (VAS) 2. Pain threshold over tender points - TMS (Digital palpation) 3. Impact of fibromyalgia (FIQ)	6 weeks	No adverse effects	1. Pain: AE x BE: $P = 0.08$ 2. Pain threshold - TMS: AE✱ x BE: $P = 0.02$ 3. Impact of fibromyalgia: AE x BE: $P = 0.95$
Evcik et al 2008[23]	**Aquatic exercise - AE** (n = 31): Age: 43.8 ± 7.7 Gender: 31 (100%) BMI: 25.6 ± 3.8 Duration of symptoms: 3.0 ± 2.3 **Home-based exercise - HE** (n = 30): Age: 42.8 ± 7.6	1. Pain (VAS) 2. Impact of fibromyalgia (FIQ)	4, 12 and 24 weeks	No adverse effects	**4 weeks:** 1.Pain: AE✱ x HE: $P = 0.05$ 2. Impact of fibromyalgia: AE x HE: $P > 0.05$

	Gender: 29 (96,77%) BMI: 27.9 ± 5.1 Duration of symptoms: 3.0 ± 1.9				**12 weeks:** 1.Pain: AE✳ x HE: P = 0.04 2. Impact of fibromyalgia: AE x HE: P > 0.05 **24 weeks:** 1.Pain: AE✳ x HE: P = 0.01 2. Impact of fibromyalgia: AE x HE: P > 0.05
Fernandes et al 2016[25]	**Swimming exercise - SE** (n = 39): Age: 48.3 ± 8.9 Gender: 100% BMI: 25.4 ± 4.9 Duration of symptoms: 11.1 ± 7.4 **Walking exercise - WE** (n = 36): Age: 49.3 ± 9.2 Gender: 100% BMI: 26.5 ± 6.3 Duration of symptoms: 12.1 ± 8.7	1. Pain (VAS) 2. Impact of fibromyalgia (FIQ) 3. Health related quality of life (SF-36)	6 and 12 weeks	Not reported	**6 weeks:** 1. Pain: SE x WE: ES = 0.2 (95% CI: 0.6 to 0.9); P = 0.66 2. Impact of fibromyalgia: SE x WE: P > 0.05 3. Health related quality of life: SE x WE: P > 0.05 **12 weeks:** SE x WE: P > 0.05
Gavi et al 2014[28]	**Strengthening exercise - SgthE** (n = 35): Age: 44.3 ± 7.9 Gender: 35 (100%) BMI: 26.1 ± 4.1 **Stretching exercises - SingE** (n = 31): Age: 48. ± 7.6 Gender: 31 (100%) BMI: 27.8 ± 4.8	1. Pain (VAS) 2. Impact of fibromyalgia (FIQ) 3. Health related quality of life (SF-36)	Every 4 weeks (pain), 8 and 16 weeks	No adverse effects	**4 weeks:** 1. Pain: SgthE✳ x SingE: P ≤ 0.05 **8 weeks:** SgthE x SingE: P > 0.05 **12 weeks:** SgthE x SingE: P > 0.05 **16 weeks:** 1. Pain: SgthE✳ x SingE: P ≤ 0.05 2. Impact of fibromyalgia: SgthE x SingE: P= 0.95

					3. Health related quality of life SgthE x SingE: P > 0.05
Genc et al 2015[29]	**Home stretching exercises - HSE** (n = 25): Age: 36.9 Gender: 25 (100%) Duration of symptoms: 5.2 **Aerobic exercises - AE** (n = 25): Age: 35.1 Gender: 25 (100%) Duration of symptoms: 5.6	1. Pain (VAS) 2. Impact of fibromyalgia (FIQ) 3. Health related quality of life (SF-36)	6 weeks	Not reported	1.Pain: HSE x AE✱: P = 0.01 2. Impact of fibromyalgia: HSE x AE: P > 0.05 3. Health related quality of life HSE x AE: P > 0.05
Jentoft et al 2001[42]	**Pool-based aerobic exercise - PAE** (n = 18): Age: 42.9 ± 8.6 Gender: 18 (100%) Duration of symptoms: 11.1 ± 5.7 **Land-based aerobic exercise -LAE** (n = 16): Age: 39.4 ± 8.8 Gender: 16 (100%) Duration of symptoms: 11.1 ± 8.4	1. Exercise-induced pain (VAS) 2. Impact of fibromyalgia (FIQ)	20 and 46 weeks	Not reported	**20 weeks:** PAE x LAE: P > 0.05 **46 weeks:** PAE x LAE: P > 0.05
Jones et al 2002[43]	**Strengthening exercise - SgthE** (n = 28): Age: 49.2 ± 6.3 Gender: 28 (100%) Duration of symptoms: 6.9 ± 6.6 **Stretching exercises - SingE** (n = 28): Age: 46.4 ± 8.5 Gender: 28 (100%) Duration of symptoms: 7.7 ± 5.5	1. Pain (FIQ - subscale Pain) 2. Pain threshold over tender points - TMS (Digital palpation) 3. Impact of fibromyalgia (FIQ) 4. Health related quality of life (QLF)	14 weeks	**SgthE** (n = 3): Worsening pain (n=3) **SingE** (n = 3): Worsening pain (n=3)	SgthE x SingE: P > 0.05
Kayo et al 2012[46]	**Aerobic exercise - AE** (n = 30): Age: 47.7 ± 5.3 Gender: 30 (100%) BMI: 26.3 ± 4.5 Duration of symptoms: 4.0 ± 3.1 **Strengthening exercises - SE** (n = 30):	1. Pain (VAS) 2. Impact of fibromyalgia (FIQ) 3. Health related quality of life (SF-36)	8, 16 and 28 weeks	No adverse effects	**8 weeks:** AE x SE: P > 0.05 **16 weeks:** AE x SE: P > 0.05

	Age: 46.7 ± 6.3 Gender: 30 (100%) BMI: 26.2 ± 4.8 Duration of symptoms: 4.7 ± 5.7				**28 weeks:** AE x SE: P > 0.05 Health related quality of life‡.
Mannerkorpi et al 2010[56]	**Moderate-to-high intensity Nordic walking - MHNW** (n = 29): Age: 48 ± 7.8 Gender: 100% BMI: 28 ± 4.0 Duration of symptoms: 11 ± 5.4 **Low-intensity walking - LIW** (n = 29): Age: 50 ± 7.6 Gender: 100% BMI: 28 ± 4.5 Duration of symptoms: 12 ± 5.3	1. Pain (FIQ - subscale Pain) 2. Disability (FIQ - subscale Physical) 3. Impact of fibromyalgia (FIQ - Total score)	16 and 24 weeks	Not reported	**16 weeks:** 1. Pain: MHNW x LIW: P = 0.63 2. Disability: MHNW✱ x LIW: ES = 0.64; P = 0.03 3. Impact of fibromyalgia: MHNW x LIW: P = 0.06 **24 weeks‡**
McCain et al 1988[57]	**Aerobic exercise - AE** (n = 18): Age: 38.5 ± 11.1 Gender: not reported. **Stretching exercise - SE (**n = 20): Age: 45.9 ± 8.2 Gender: 100%	1. Pain (VAS) 2. Pain threshold over tender points - TMS (Dolorimeter)	20 weeks	**AE** (n=4): Transient knee pain (n=2) Previously undergone artificial hip replacement surgery (n=1) Benign premature atrial contractions (n=1) **SE** (n=1): Achilles tendinitis (n=1)	1. Pain: AE x SE: P < 0.09 2. Pain threshold - TMS: AE✱ x SE: P < 0.02
Norregaard et al 1997[61]	**Aerobic exercise - AE** (n = 5): Age: 44.0 ± 8.0 Gender: 11 (100%) **Steady exercise - SE** (n = 11): Age: 51.0 ± 14.0 Gender: 11 (100%)	1. Pain (10-point ordinal scale) 2. Impact of fibromyalgia (FIQ)	12 weeks	Not reported	AE x SE: P > 0.05
Ramsay et al 2000[66]	**Home aerobic exercise - HE** (n = 37) **Supervised aerobic exercise - SE** (n = 37)	1. Pain (VAS)	12, 24 and 48 weeks	Not reported	**12 weeks:** HE x SE: P > 0.05

	No demographic data were reported.	2. Pain threshold over tender points - TMS (Dolorimeter)			**24 weeks:** HE x SE: P > 0.05 **48 weeks:** HE x SE: P > 0.05
Richards et al 2002[68]	**Aerobic exercise - AE** (n = 69): Ageʃ: 48 (38-56) Gender: 62 (89.8%) Duration of symptomsʃ: 6.5 (3-10) **Relaxation and stretching exercises - RSE** (n = 67): Ageʃ: 45 (38-52) Gender: 64 (95.5%) Duration of symptomsʃ: 4 (3-9)	1. Pain (Short form McGill pain questionnaire) 2. Impact of fibromyalgia (FIQ) 3. Health related quality of life (SF-36)	12, 24 and 52 weeks	No adverse effects	**12 weeks:** 1. Pain AE x RSE: P > 0.05 2. Impact of fibromyalgia: AE x RSE: MD = 1.9 (95% CI: -2.5 to 6.3); P = 0.5 3. Health related quality of life AE x RSE: P > 0.05 **24 weeks:** 1. Pain‡ 2. Impact of fibromyalgia: AE x RSE: MD = 4.4 (95% CI: -0.3 to 9.0); P = 0.05 3. Health related quality of life‡ **52 weeks:** 1. Pain‡ 2. Impact of fibromyalgia: AE x RSE: MD = 2.5 (95% CI: -2.7 to 7.8); P = 0.07 3. Health related quality of life‡
Rooks et al 2007[69]	**Aerobic and stretching exercises - ASE** (n = 35): Age: 48.0 ± 11.0 Gender: 35 (100%) BMI: 29.0 ± 6.0 Duration of symptoms: 5.0 ± 4.0 **Strengthening, aerobic, and stretching exercise - SASE** (n = 35): Age: 50.0 ± 11.0	1. Pain (FIQ - subscale Pain) 2. Disability (SF-36 -physical function subscale) 3. Impact of fibromyalgia (FIQ - Total score)	16 and 24 weeks	No adverse effects	**16 weeks‡:** 1. Pain: ASE x SASE: MD = -0.4 (95% CI: -1.5 to 0.7) 2. Impact of fibromyalgia: ASE x SASE: MD = -1.9 (95% CI: -8.5 to 4.7) 3. Health related quality of life:

	Gender: 35 (100%) BMI: 30.0 ± 6.0 Duration of symptoms: 6.0 ± 4.0	4. Health related quality of life (SF-36)			ASE x SASE: MD = -2.1 [95% CI: -11.4 to 7.2] (Physical function); MD = 8.8 [95% CI: -4.1 to 21.7] (Social function); MD = 5.7 [95% CI: -4.1 to 15.5] (Mental health); MD = 5.7 [95% CI: -4.1 to 15.5] (Bodily pain); MD = -0.2 [95% CI: -11.8 to 11.4] (Vitality); MD = -1.0 [95% CI: -17.2 to 19.2] (Role physical); MD = -6.6 [95% CI: -13.3 to 26.5] (Role emotional); MD = -1.4 [95% CI: -11.0 to 8.2] (General health). **24 weeks‡**
Sañudo et al 2010[72]	**Aerobic exercise - AE** (n = 18): Age: 55.9 ± 6.8 Gender: 18 (100%) BMI: 29.6 ± 4.7 **Combined program of aerobic, muscle strengthening, and stretching exercises - ASSE** (n = 17): Age: 55.9 ± 7.0 Gender: 17 (100%) BMI: 27.6 ± 4.5	1. Impact of fibromyalgia (FIQ) 2. Health related quality of life (SF-36)	24 weeks	Not reported	**24 weeks‡:** 1. Impact of fibromyalgia: AE x ASSE: MD = 0.0 (95% CI: -8.6 to 8.6) 2. Health related quality of life: AE x ASSE: MD = -0.5 (95% CI: -7.5 to 6.5).
Schachter et al 2003[73]	**Long bout of aerobic exercise - LBE** (n = 51): Age: 41.3 ± 8.7 Gender: 51 (100%) Duration of symptoms: 8.8 ± 6.2 **Short bout of aerobic exercise - SBE** (n = 56): Age: 41.9 ± 8.6 Gender: 56 (100%) Duration of symptoms: 8.6 ± 6.0	1. Pain (VAS) 2. Pain threshold over tender points - TMS (Dolorimeter) 3. Impact of fibromyalgia (FIQ) 4. Physical function (AIMS2)	8 and 16 weeks	Not reported	**8 weeks:** LBE x SBE: P > 0.05 **16 weeks:** LBE x SBE: P > 0.05

Sevimli et al 2015[78]	**Home-based isometric strengthening and stretching exercise - HISS** (n = 25) **Gym-based aerobic exercise - GAE** (n = 25) **Pool-based aquatic aerobic exercise - PAAE** (n = 25) Age (total): 35.0 ± 8.8 Gender (total): 75 (100%)	1. Pain (VAS) 2. Impact of fibromyalgia (FIQ) 3. Health related quality of life (Physical and Mental components of the SF-36)	12 weeks	Not reported	**12 weeks‡:** 1. Pain: HISS x GAE✳: MD = -22.2 (95% CI: -28.2 to -16.2) HISS x PAAE✳: MD = -22.4 (95% CI: -28.5 to -16.3) GAE x PAAE: MD = -0.2 (95% CI: -5.2 to 4.8) 2. Impact of fibromyalgia: HISS x GAE✳: MD = -26.3 (95% CI: -35.1 to -17.5) HISS x PAAE✳: MD = -28.0 (95% CI: -37.2 to -18.8) GAE x PAAE: MD = -1.7 (95% CI: -10.8 to 7.4) 3. Health related quality of life: Physical component HISS x GAE✳: MD = 16.8 (95% CI: 12.9 to 20.7) HISS x PAAE✳: MD = 13.5 (95% CI: 9.1 to 17.9) GAE x PAAE: MD = -3.3 (95% CI: -6.9 to 0.3) Mental component HISS x GAE✳: MD = 13.2 (95% CI: 8.6 to 17.8) HISS x PAAE✳: MD = 17.4 (95% CI: 12.5 to 22.3) GAE x PAAE: MD = 4.2 (95% CI: -0.1 to 8.5)
Valim et al 2003[85]	**Aerobic exercise - AE** (n = 32): Age: 47.0 ± 10.0 Gender: 32 (100%) BMI: 26.0 ± 3.0 **Stretching exercise - SE** (n = 28): Age: 44.0 ± 11.0	1. Pain (VAS) 2. Impact of fibromyalgia (FIQ) 3. Health related quality of life (Physical and	10 and 20 weeks	Not reported	**10 weeks:** 1. Pain: AE✳ x SE: F test = 5.7; P = 0.02 2. Impact of fibromyalgia: AE✳ x SE: F test: 14.9; P = 0.01 3. Health related quality of life:

	Gender: 28 (100%) BMI: 28.0 ± 6.0	Mental components of the SF-36)			Mental Component Summary AE✳ x SE: F test: 8.6; P = 0.005 Physical Component Summary AE x SE: F test: 0.8 (P=0.38) **20 weeks:** AE x SE: P > 0.05
van Santen et al 2002[87]	**High intensity physical fitness - HIF** (n = 17): Age†: 39.0 (20–54) Gender: 17 (100%) Duration of symptoms†: 9.0 (2–27) **Low intensity physical fitness - LIF** (n = 13): Age†: 45.0 (25–58) Gender: 13 (100%) Duration of symptoms†: 12.0 (1–36)	1. Pain (VAS) 2. Pain threshold over tender points - TMS (Dolorimeter)	20 weeks.	**HIF:** Pain increased 11 mm post-treatment in this group **LIF:** Pain increased 2 mm post-treatment in this group	**20 weeks:** HIF x LIF: P > 0.05
Wang et al 2018[93]	**Aerobic exercise - AE** (n = 75): Age: 50.9 ± 12.5 Gender: 72 (96.0%) BMI: 30.0 ± 6.8 Duration of symptoms: 11.3 ± 8.7 **Tai Chi once a week, 12 weeks - TC1,12** (n = 39): Age: 53.0 ± 12.6 Gender: 33 (84.6%) BMI: 30.6 ± 6.4 Duration of symptoms: 11.1 ± 8.8 **Tai Chi twice a week, 12 weeks - TC2,12** (n = 37): Age: 52.1 ± 10.3 Gender: 30 (81.1) BMI: 30.4 ± 6.8 Duration of symptoms: 12.6 ± 12.1 **Tai Chi once a week, 24 weeks - TC1,24** (n = 39): Age: 50.8 ± 11.8 Gender: 38 (97.4%)	1. Impact of fibromyalgia (FIQ) 2. Health related quality of life (Physical and Mental components of the SF-36)	12, 24 and 52 weeks	**TC** (n=117): Related to the intervention (n=8) Serious adverse events (n=7) **AE** (n= 37): Related to the intervention (n=4) Serious adverse events (n=3)	**12 weeks:** 1. Impact of fibromyalgia: AE x Combined TC✳: MD = 5.4 (95% CI: 0.6 to 10.1); P = 0.03 AE x TC2,24✳: MD = 10.9 (95% CI: 3.4 to 18.5); P = 0.01 TC12 x TC24: P > 0.05 TC1 x TC2: P > 0.05 2. Health related quality of life Physical component: P > 0.05 Mental component: P > 0.05 **24 weeks:** 1. Impact of fibromyalgia: AE x Combined TC✳: MD = 5.5 (95% CI: 0.6 to 10.4); P = 0.03 AE x TC2,24✳: MD = 16.2 (95% CI: 8.7 to 23.6); P < 0.01 TC12 x TC24✳: MD = 9.6 (95% CI: 2.6 to 16.6); P = 0.01

	BMI: 29.9 ± 6.4 Duration of symptoms: 12.0 ± 8.3 **Tai Chi twice a week, 24 weeks - TC2,24** (n = 36): Age: 52.1 ± 13.3 Gender: 36 (100.0%) BMI: 29.3 ± 7.4 Duration of symptoms: 13.8 ± 10.4 **Combination of groups for analysis:** All Tai Chi groups combined - Combined TC Tai Chi once a week groups combined - TC1 Tai Chi twice a week groups combined - TC2 Tai Chi 12 weeks groups combined - TC12 Tai Chi 24 weeks groups combined - TC24				TC1 x TC2: P > 0.05 2. Health related quality of life Physical component: P > 0.05 Mental component: AE x Combined TC: P > 0.05 AE x TC2,24*: MD = 6.2 (95% CI: 1.9 to 10.6); P = 0.01 TC12 x TC24: MD = 4.4 (95% CI: 0.8 to 8.1); P = 0.02 TC1 x TC2: P > 0.05 **52 weeks:** 1. Impact of fibromyalgia: AE x Combined TC: MD = 2.7 (95% CI: -2.3 to 7.7); P = 0.29 AE x TC2,24*: MD = 11.1 (95% CI: 2.7 to 19.6); P = 0.01 TC12 x TC24: MD = 5.8 (95% CI: −1.4 to 13.0); P = 0.11 TC1 x TC2: P > 0.05 2. Health related quality of life Physical component: P > 0.05 Mental component: P > 0.05
CHRONIC WHIPLASH-ASSOCIATED DISORDERS (CWAD)					
First author/ Year	**Participants**	**Outcomes**	**Follow-ups**	**Adverse effects**	**Results**
Seferiadis et al 2015[76]	**Exercise therapy - ET** (n = 57): Age: 48.7 ± 11.3 Gender: 44 (77%) Duration of symptoms: 9.3 ± 7.7 **Body awareness therapy - BAT** (n = 56): Age: 47.3 ± 13.3 Gender: 37 (66%) Duration of symptoms: 10.0 ± 9.5	1. Disability (NDI) 2. Health related quality of life (SF-36)	10 and 22 weeks	**ET** (n=4): Discontinued treatment due to harms (n=4) Increased pain (n=18) **BAT** (n=1): Discontinued treatment due to harms (n=1)	**10 weeks:** 1. Disability: ET x BAT: P > 0.05 2. Health related quality of life: ET x BAT*: ES = -0.54; P = 0.03 (physical function) ET x BAT: P > 0.05 (other components) **22 weeks:** 1. Disability:

First author/ Year	Participants	Outcomes	Follow-ups	Adverse effects	Results
				Increased pain (n=10)	ET x BAT: P > 0.05 2. Health related quality of life: ET x BAT✻: ES = -0.4, P = 0.04 (Bodily pain) ET x BAT: P > 0.05 (other components)
Vikne et al 2007[90]	**New sling exercise therapy - NSET** (n = 51) **New sling exercise therapy + home exercise - NSET+** (n = 54) **Traditional physiotherapy - TP** (n = 53) **Traditional physiotherapy + home exercise - TP+** (n = 55) No demographic data were reported.	1. Pain and complaints (VAS and a scale from 1 to 9) 2. Disability (Modified RM)	16 and 52 weeks	Not reported	**16 weeks:** NSET x NSET+ x TP x TP+: P > 0.05 **52 weeks:** NSET x NSET+ x TP x TP+: P > 0.05
CHRONIC IDIOPATHIC NECK PAIN (CINP)					
First author/ Year	**Participants**	**Outcomes**	**Follow-ups**	**Adverse effects**	**Results**
Andersen et al 2008[1]	**Specific strengthening training - SST** (n = 18): Age: 44.0 ± 9.0 BMI: 27.0 ± 5.0 **Aerobic exercise - AE** (n = 16): Age: 45.0 ± 9.0 BMI: 27.0 ± 7.0	1. Pain in the trapezius muscle (VAS)	10 weeks	Not reported	**10 weeks:** SST✻ x AE: P = 0.01
Bobos et al 2016[11]	**Deep neck flexors' training - DNFT** (n = 23): Age: 38.4 ± 12.7 Gender: 18 (78.2%) **Superficial muscle training - SMT** (n = 22): Age: 40.4 ± 13.5 Gender: 18 (81.8%)	1. Pain (NPRS) 2. Disability (NDI) 3. Pain pressure thresholds (Mechanical algometer) 4. Health status (SF-12) 5. Satisfaction (CSQ-8)	7 weeks	Not reported	**7 weeks:** DNFT x SMT: P > 0.05
Borisut et al 2013[13]	**Strengthening-endurance exercise - SEE** (n = 25): Age: 32.7 ± 3.1	1. Pain (VAS) 2. Disability (NDI)	12 weeks	Not reported	**12 weeks:** 1. Pain:

	Gender: 25 (100%) BMI: 20.3 ± 2.4 **Cranio-cervical flexion exercise - CCFE** (n = 25): Age: 30.1 ± 3.5 Gender: 25 (100%) BMI: 22.5 ± 5.5 **Combined exercise - CE** (n = 25): Age: 30.2 ± 2.9 Gender: 25 (100%) BMI: 20.2 ± 2.7				SEE x CE*: P < 0.05 CCFE x CE*: P < 0.05 SEE x CCFE: P > 0.05 2. Disability: SEE x CE: P > 0.05 CCFE x CE: P > 0.05 SEE x CCFE: P > 0.05
Cramer et al 2013[20]	**Yoga - Y** (n = 25): Age: 46.2 ± 11.2 Gender: 84% BMI: 24.2 ± 3.8 Duration of symptoms: 7.7 ± 6.6 **Home exercise - HE** (n = 26): Age: 49.5 ± 9.5 Gender: 80.8% BMI: 25.1 ± 5.1 Duration of symptoms: 8.4 ± 6.1	1. Present pain and Pain at motion (VAS) 2. Pressure pain threshold (Digital algometer) 3. Disability (NDI) 4. Health related quality of life (SF-36)	9 weeks	**Y** (n=12): Worsening of neck pain or muscle soreness (n=9) Other minor adverse effects (n=3) **HE** (n=10): Worsening of neck pain or muscle soreness (n=8) Other minor adverse effects (n=2)	**9 weeks:** 1. Present pain Y* x HE: MD = 13.9 (95% CI: 26.4 to 1.4); ES = -0.8 (95% CI: -1.4 to -0.1); P = 0.03 1. Pain at motion: Y x HE: MD = -2.6 (95% CI: -13.2 to 8.0); ES = -0.1 (95% CI: -0.7 to 0.4); P = 0.63 2. Pressure pain threshold: Y* x HE: MD = 99.5 (95% CI: 60.3 to 138.7); ES = 1.0 (95% CI: 0.6 to 1.5); P < 0.01 3. Disability: Y* x HE: MD = -7.8 (95% CI: -13.4 to -2.2]; ES = -0.8 [95% CI: -1.4 to -0.2]; P = 0.01 4. Health related quality of life Y* x HE: MD = 7.8 (95% CI: 3.1 to 12.5); ES = 1.3 (95% CI: 0.5 to 2.1); P = 0.01 (bodily pain) MD = 6.0 (95% CI: 0.7 to 11.2); ES = 0.7 (95% CI: 0.1 to 1.3); P = 0.03 (social functioning)

					MD = 7.9 (95% CI: 2.4 to 13.4); ES= 0.9 (95% CI: 0.3 to 1.5); P = 0.01 (emotional role functioning) MD = 4.9 (95% CI: 0.6 to 9.3); ES = 0.7 (95% CI: 0.1 to 1.2); P = 0.03 (mental health) MD = 6.1 (95% CI: 1.1 to 11.1); ES = 0.8 (95% CI: 0.1 to 1.4); P = 0.02 (mental component)
Falla et al 2006[24]	**Strengthening - endurance exercise - SEE** (n = 29): Age: 38.1 ± 10.7 Gender: 29 (100%) Duration of symptoms: 8.3 ± 7 **Cranio-cervical flexion exercise - CCFE** (n = 29): Age: 37.7 ± 9.9 Gender: 29 (100%) Duration of symptoms: 7.5 ± 5.9	1. Pain (NPRS) 2. Disability (NDI)	6 weeks	No adverse effects	**6 weeks:** SEE x CCFE: P > 0.05
Häkkinen et al 2007[33]	**Strengthening and stretching exercises - SSE** (n= 49): Age: 41.0 ± 9.0 Gender: 47 (90%) BMI: 25.1 ± 3.4 Duration of symptoms: 5.8 ± 5.7 **Stretching exercises - SE** (n = 52): Age: 40.0 ± 10.0 Gender: 44 (90%) BMI: 24.3 ± 4.2 Duration of symptoms: 5.5 ± 5.2	1. Pain (VAS) 2. Disability (Modified NSPDI and NDI)	8 and 52 weeks	Not reported	**8 weeks:** SSE x SE: P > 0.05 **52 weeks:** 1. Pain: SSE x SE: MD = -5.0 (95% CI: -15.0 to 5.0); P = 0.53 2. Disability: SSE x SE: MD = 0.0 (95% CI: - 6.0 to 7.0); P = 0.76 (Modified NSPDI) MD = 0.0 (95% CI: - 4.0 to 5.0); P = 0.79 (NDI)
Izquierdo et al 2016[40]	**Cranio-cervical flexion training - CCFT** (n = 14): Age: 28.4 ± 6.1 BMI: 23.7 ± 3.9 **Proprioceptive training - PT** (n = 14): Age: 29.9 ± 7.3 BMI: 22.0 ± 0.7	1. Pain (VAS) 2. Pressure pain threshold (Analogue algometer) 3. Disability (NDI)	4 and 8 weeks	Not reported	**4 weeks:** CCFT x PT: P > 0.05 **8 weeks:** CCFT x PT: P > 0.05

	Gender (total): 64.3%				
Javanshir et al 2015[41]	**Cranio-cervical flexion training - CCFT** (n = 30): Age: 36.8 ± 3.5 Duration of symptoms: 3.3 ± 3.22 **Cervical flexion training- CFT** (n = 30): Age: 35.7 ± 5.0 Duration of symptoms: 3.3 ± 3.22 Gender (total): 66.7%	1. Pain (NPRS) 2. Disability (NDI)	10 weeks	Not reported	**10 weeks:** 1. Pain: CCFT x CFT: F = 1.5, P = 0.31; ES = 0.35 2. Disability: CCFT x CFT: F = 2.0, P = 0.2; ES = 0.35
Karlsson et al 2014[45]	**Strengthening exercise - SgthE** (n = 34): Age□: 46.0 (40, 50) Gender: 34 (100%) Duration of symptoms□: 10.0 (6, 15) **Stretching exercise - SingE** (n = 23): Age□: 42.0 (33, 47) Gender: 23 (100%) Duration of symptoms□: 6.0 (4, 13)	1. Pain (NPRS) 2. Disability (NDI)	16 to 24 and 52 weeks	Not reported	**16 to 24 weeks:** SgthE x SingE: P > 0.05 **52 weeks:** SgthE x SingE: P > 0.05
Khan et al 2014[47]	**Isometric exercise - IE** (n = 34) **General exercise - GE** (n = 34) Age (total): 34.4 ± 2.7 Gender (total): 41 (60%)	1. Pain (VAS) 2. Disability (NPNPQ)	12 weeks	Not reported	**12 weeks‡:** 1. Pain: IE x GE: MD = -0.3 (95% CI: -1.2 to 0.5) 2. Disability: IE⁕ x GE: MD = -6.2 (95% CI: -7.1 to -5.2)
Kietrys et al 2007[48]	**Resistance exercise - RE** **Stretching exercise -SE** Participants (total): 72 Age (total): 41.2 ± 9.7 Gender (total): 56	1. Pain (VAS) 2. Disability (NDI) 3. Satisfaction (5-ISS) 4. Pain impact (VAS, pain drawing and NDI)	4 weeks	Not reported	**4 weeks:** 1. Pain‡ 2. Disability‡ 3. Satisfaction‡ 4. Pain impact: RE x SE: F = 0.6; P = 0.71
Kim et al 2016[49]	**Deep cervical flexor exercise - DCFE** (n = 15): Age: 46.7 ± 4.2 Gender: 8 (53.3%)	1. Pain (NPRS) 2. Disability (NDI)	4 and 8 weeks	Not reported	**4 weeks:** DCFE x GSE: P > 0.05 **8 weeks:** 1. Pain:

	General strengthening exercise - GSE (n = 15): Age: 45.4 ± 5.1 Gender: 7 (46.6%)				DCFE✳ x GSE: P < 0.05 2. Disability: DCFE✳ x GSE: P < 0.05
Lansinger et al 2007[52]	**Qigong therapy - QT** (n = 60): Age: 44.9 ± 12.3 Gender: 44 (73%) Duration of symptoms: 9 (15%) 3 months – 1 year; 23 (38%) > 1 year; 13 (22%) > 5 years; 15 (25%) > 10 years. **Exercise therapy - ET** (n = 62): Age: 42.8 ± 1.4 years; Gender: 42 (67%); Duration of symptoms: 12 (19.5%) 3 months – 1 year; 23 (37%) > 1 year; 15 (24%) > 5 years; 12 (19.5%) > 10 years.	1. Pain intensity (VAS) 2. Disability and activity level (NDI)	12, 24 and 52 weeks	Not reported	**12 weeks:** QT x ET: P > 0.05 **24 weeks:** QT x ET: P > 0.05 **52 weeks:** QT x ET: P > 0.05
Lansinger et al 2013[51]	**Qigong therapy - QT** (n = 60): Age: 44.9 ± 12.3 Gender: 44 (73%) Duration of symptoms: 9 (15%) 3 months – 1 year; 23 (38%) > 1 year; 13 (22%)> 5 years; 15 (25%) > 10 years. **Exercise therapy - ET** (n = 62): Age: 42.8 ± 1.4 Gender: 42 (67%) Duration of symptoms: 12 (19.5%) 3 months – 1 year; 23 (37%) > 1 year; 15 (24%) > 5 years; 12 (19.5%) > 10 years.	1. Health related quality of life (SF-36)	12 and 52 weeks	Not reported	**12 weeks:** QT x ET: P > 0.05 **52 weeks:** QT x ET: P > 0.05

Lauche et al 2016[53]	**Tai Chi - TC** (n = 38): Age: 52.0 ± 10.9 Gender: 28 (73.7%) BMI: 27.2 ± 4.0 kg/m². **Neck exercises - NE** (n = 37): Age: 47.0 ± 12.3 Gender: 31 (83.7%) BMI: 25.8 ± 6.0	1. Current pain and pain on movement (VAS) 2. Disability (NDI) 3. Health related quality of life (SF-36) 4. Satisfaction (VAS)	12 and 24 weeks.	**TC** (n=10): Respiratory infections (n=4) Migraine (n=1) Achilles tendon pain (n=2) Bruises - not during practice (n=1) Meniscal tear (n=1) Mononucleosis infection (n=1) **NE** (n=10): Respiratory infections (n=4) Knee pain (n=1) Vertigo (n=1) Mononucleosis infection (n=1) Idiopathic hearing loss (n=1) Appendicitis (n=1) Dental root infection (n=1)	**12 weeks:** 1. Pain: TC x NE: MD = 3.4 (95% CI: -9.5 to 12.3); P = 0.45 1. Pain on movement: TC x NE: MD = 3.7 (95% CI: - 3.2 to 10.6) 2. Disability: TC x NE: MD = -1.7 (95% CI: -5.9 to 2.4) 3. Health related quality of life: TC x NE: P > 0.05 4. Satisfaction: TC: 76.1 ± 28.9; NE: 80.0 ± 27.7 **24 weeks:** 1. Pain: TC x NE: MD = -0.5 (95% CI: -11.8 to 10.7) 1. Pain on movement: TC x NE: MD = -5.6 (95% CI: -13.0 to 1.8) 2. Disability: TC x NE: MD = -1.4 (95% CI: -6.7 to 4.0) 3. Health related quality of life: TC x NE: P > 0.05
O'Leary et al 2012[62]	**Mobility training - MTr** (n = 20): Age: 37.7 ± 12.7 Gender: 55% Duration of symptoms: 6.2 ± 5.0 **Coordination training - CTr** (n = 20): Age: 37.8 ± 12.6 Gender: 60% Duration of symptoms: 7.1 ± 4.6 **Endurance training - Etr** (n = 20): Age: 38.2 ± 12.8 Gender: 60%	1. Pain (VAS) 2. Disability (NDI)	10 and 26 weeks	Not reported	**10 weeks:** 1. Pain: ETr x CTr: MD = 6.9 (95% CI: -3.6 to 17.5) ETr x MTr: MD = 0.1 (95% CI: -10.4 to 10.6) CTr x MTr: MD = -6.8 (95% CI: -17.5 to 3.9) 2. Disability: ETr x CTr: MD = 0.8 (95% CI: -1.9 to 3.4)

	Duration of symptoms: 7.2 ± 8.2				ETr x MTr: MD = -1.6 (95% CI: -4.2 to 1.2) CTr x MTr: MD = -2.4 (95% CI: -5.0 to 0.3) **26 weeks:** 1. Pain: ETr x CTr: MD = -0.8 (95% CI: -11.5 to 9.9) ETr x MTr: MD = 4.7 (95% CI: -6.1 to 15.5) CTr x MTr: MD = 5.5 (95% CI: -5.3 to 16.3) 2. Disability: ETr x CTr: MD = 0.3 (95% CI: -2.4 to 2.9) ETr x MTr: MD = 0.1 (95% CI: -2.6 to 2.7) CTr x MTr: MD = -0.2 (95% CI: -2.9 to 2.6)
Rendant et al 2011[67]	**Qigong therapy -** QT (n = 42): Age: 44.7 ± 10.8 Gender: 85.7% BMI: 23.8 ± 4.4 Duration of symptoms: 3.4 ± 1.5 **Exercise therapy - ET** (n = 39): Age: 44.4 ± 10.9 Gender: 89.7% BMI: 24.4 ± 4.3 Duration of symptoms: 3.2 ± 1.6	1. Pain (VAS) 2. Disability (NPDS) 3. Health related quality of life (SF-36)	12 and 24 weeks	**QT** (n=19): Muscle soreness (n = 15) Myogelosis (n = 12) Vertigo (n = 10) Other pain (n = 4) Headache (n = 3) Thirst (n = 1) Engorged hands (n = 1) Twinge in the neck (n = 1) Urinary urgency (n = 1) Bursitis of left shoulder (n = 1) **ET** (n=16):	**12 weeks:** 1. Pain: QT x ET: MD = 1.3 (95% CI: –8.1 to 10.8); P = 0.78 2. Disability: QT x ET: MD = 1.5 (95% CI: –4.9 to 8.0); P = 0.64 3. Health related quality of life: QT✱ x ET: MD = 8.2 (95% CI: 1.3 to 15.1); P = 0.02 (vitality) MD = 13.8 (95% CI: 0.0 to 27.6); P = 0.05 (role emotional) **24 weeks:** 1. Pain: QT x ET: MD = –0.7 (95% CI: –9.1 to 7.7); P = 0.87 2. Disability:

				Muscle soreness (n = 14) Myogelosis (n = 11) Headaches (n = 5) Vertigo (n = 2) Change in mood (n = 1) Worsening of neck pain (n = 1) Worsening of tinnitus (n = 1) Hospitalization (n=2)	QT x ET: MD = –1.5 (95% CI: –7.4 to 4.3); P = 0.61 3. Health related quality of life: QT x ET: P > 0.05
Salo et al 2010[71]	**Strengthening training - ST** (n = 60): Age: 45.0 ± 6.0 Gender: 60 (100%) BMI: 25.0 ± 3.0 Duration of symptoms: 8.0 ± 6.0 **Endurance training - ET** (n = 60): Age: 46.0 ± 6.0 Gender: 60 (100%) BMI: 25.0 ± 3.0 Duration of symptoms: 9.0 ± 6.0	1. Health related quality of life (15D - HRQoL)	52 weeks	Not reported	**52 weeks‡:** ST x ET: MD = 0.0 (95% CI: -0.1 to 0.1)
Salo et al 2012[70]	**Combined strengthening training and stretching exercise - CSS** (n = 49): Age: 41.0 ± 9.0 Gender: 47 (96%) BMI: 25.0 ± 3.0 Duration of symptoms: 5.5 ± 5.2 **Stretching exercise - SE** (n = 52): Age: 40.0 ± 10.0 Gender: 44 (85%) BMI: 24.0 ± 4.0 Duration of symptoms: 5.8 ± 5.7	1. Health related quality of life (RAND36)	52 weeks	Not reported	**52 weeks:** CSS x SE: P > 0.05
Senthil et al 2016[77]	**Deep cervical flexor exercise - DCFE** (n = 15)	1. Disability (PSFS)	6 weeks	Not reported	**6 weeks:** DCFE❋ x GE: P < 0.05

	General exercise - GE (n = 15) No demographic data were reported.				
von Trott et al 2009[91]	**Qigong therapy - QT** (n = 38): Age: 75.9 ± 7.6 Gender: 95% BMI: 28.0 ± 5.3 Duration of symptoms: 20.1 ± 14.2 **Exercise therapy - ET** (n = 39): Age: 76.0 ± 7.2 Gender: 95% BMI: 27.0 ± 4.3 Duration of symptoms: 17.1 ± 13.5	1. Pain (VAS) 2. Disability (NPDS) 3. Health related quality of life (SF-36)	12 and 24 weeks	**QT** (n=6): Died of cancer in hospital (n=1) Nausea (n=2) Muscle aches (n=2) Muscle tension (n=1) **ET** (n=5): Died of cancer in hospital (n=1) Nausea (n=1) Muscle aches (n=1) Muscle tension (n=2)	**12 weeks:** 1. Pain: QT x ET: MD = -2.5 (95% CI: -15.4 to 10.3); P = 0.70 2. Disability: QT x ET: MD = 2.3 (95% CI: -6.2 to 10.8); P = 0.60 3. Health related quality of life: QT x ET: MD = -0.5 (95% CI: -3.6 to 2.5); P = 0.74 (physical component) MD = 2.3 (95% CI: -2.8 to 7.4); P = 0.37 (mental component) **24 weeks:** 1. Pain: QT x ET: MD = 0.1 (95% CI: -13.4 to 13.7); P = 0.99 2. Disability: QT x ET: MD = 7.4 (95% CI: -1.4 to 16.1); P = 0.10 3. Health related quality of life: QT x ET: MD = 0.4 (95% CI: -2.8 to 3.6); P = 0.79 (physical component) MD = 1.1 (95% CI: -4.0 to 6.2); P = 0.66 (mental component)
Ylinen et al 2003[95]	**Strength training - ST** (n = 60): Age: 45.0 ± 6.0 Gender: 60 (100%) BMI: 25.0 ± 3.0 Duration of symptoms: 8.0 ± 6.0 **Endurance training - ET** (n = 60): Age: 46.0 ± 6.0 Gender: 60 (100%) BMI: 25.0 ± 3.0 Duration of symptoms: 9.0 ± 6.0	1. Pain (VAS) 2. Disability (Modified NSPDI and VNDI)	52 weeks	Not reported	**52 weeks:** ST x ET: P > 0.05

Throughout the result, when there was a difference between groups, it was individually expressed for which outcome. When there was no difference in any outcome, only p > 0.05 was described, without specifying outcomes.
Participants: age (in years), gender (N, % of women), BMI (kg/m²), duration of symptoms (years).

∗ Statistically significant difference in favor of this group; ʃ Median (interquartile range); † Mean (range); □ Median (25, 75 percentile); ǂ The between-group difference was not reported; ‡ Calculated by the authors, because the study did not provide difference between groups.
Abbreviations - BMI: Body mass index; VAS: Visual Analog Scale; FIQ: Fibromyalgia Impact Questionnaire; SF-36: Short Form 36 Health Survey; SF-12: Short Form 12 Health Survey; QLF: Quality of Life Scale; TMS: Total Myalgic Score; AIMS2: Arthritis Impact Measurement Scale 2; NDI: Neck Disability Index; Modified RM: Modified version of the Roland & Morris; NPRS: Numeric Pain Rating Scale; CSQ-8: Client Satisfaction Questionnaire 8; Modified NSPDI: Modified Neck and Shoulder Pain and Disability Index; NPNPQ: Northwick Park Neck Pain Questionnaire; 5-ISS: 5-item satisfaction survey; NPDS: Neck Pain and Disability Scale; 15D - HRQoL:15 Dimensional HRQoL instrument; RAND36: RAND36- Item Health Survey 1.0; PSFS: Patient Specific Functional Scale; VNDI: Vernon Neck Disability Index; ES: Effect size; MD: Mean difference; CI: Confidence interval.

Table 2. Exercise prescription details.

FIBROMYALGIA					
First author/ Year	**Interventions**	**Treatment period**	**Session frequency/ length**	**Intensity of the exercise**	**Supervision/group vs individual**
Assis et al 2006[4]	**Land-based exercises - LBE:** Walking or jogging exercise.	15 weeks.	3 x/week: 60 min.	Anaerobic threshold.	Supervised
	Deep water running - DWR: Heated pool - Simulated running with floating belt.	15 weeks.	3 x/week: 60 min.	Anaerobic threshold. DWR group: 9 beats/min lower than LBE group.	Supervised
Assumpção et al 2017[5]	**Stretching exercise - SE:** triceps surae, gluteus, hamstrings, paravertebral, latissimus dorsi, hip adductor and pectoralis.	12 weeks.	2 x/ week: 40 min.	Stretch intensity: gradual increase to the point of moderate discomfort.	Supervised.
	Resistance exercise – RE: triceps surae, quadriceps, hip adductors and abductors, hip flexors, elbow flexors and extensors, pectoralis major, and rhomboids (sets of 8 rep).	12 weeks.	2 x/ week: 40 min.	No load (first sessions). Progression: 0.5 kg per week if slightly intense on the Borg scale.	Supervised.
Bircan et al 2008[9]	**Aerobic exercise - AE:** Walking on treadmill. Start & end: 5 min stretching.	8 weeks.	3 x/ week: 30 to 40 min.	Heart rate: 60 to 70% HRmax.	Supervised.
	Strengthening exercise - SE: Upper, lower limbs and trunk muscles. Start & end: 5 min stretching.	8 weeks.	3 x/ week: 40 min.	Start: 4 to 5 rep, Resistance level: easy. Progression: 12 rep, Resistance: gradual increase.	Supervised/Group
Bjersing et al 2012[10]	**Moderate-to-high intensity Nordic walking - MHNW:** Performed moderate to high-intensity Nordic Walking.	15 weeks.	2 x/ week: 40 to 45 min.	Not reported.	Supervised.
	Low-intensity walking - LIW: Performed low-intensity walking.	15 weeks.	2 x/ week: 40 to 45 min.	Not reported.	Supervised.
Calandre et al 2009[16]	**Tai Chi - TC:** Heated pool - 16 movements. Deep breathing + slow, broad movements of the arms, legs, and torso. Start & end: 10 min relaxation.	6 weeks.	3 x/ week: 60 min.	Not reported.	Supervised/Group (13 to 15 patients).
	Stretching exercise - SE: Heated pool - stretching of cervical area, upper and lower extremities, and trunk. Start & end: 10 min relaxation.	6 weeks.	3 x/ week: 60 min.	Not reported.	Supervised/Groups (13 to 15 patients).
Demir-Göçmen et al 2013[21]	**Supervised stretching and balance–coordination exercises - SSBE:** Stretching exercises for neck, shoulder, dorsal,	12 weeks.	3 x/ week: 60 min.	Not reported.	Supervised.

	lumbar, gluteal, thigh, and cruris (1 set, 10 rep). Balance-coordination exercises - balancing on one foot and on both feet, tandem exercises, standing with a partner, bending, squatting, lateral and backward movements, skipping, scissoring, rolling, and twisting.				
	Home stretching exercises - HSE: Neck, shoulder, dorsal, lumbar, gluteal, thigh, and cruris muscle groups stretches (1 set, 10 rep).	12 weeks.	3 x/ week.	Not reported.	Unsupervised/ Individual.
Duruturk et al 2015[22]	**Aerobic exercises - AE:** With a treadmill. Warm-up & Cool-down: 5 min.	6 weeks.	3 x/ week: 20 to 45 min.	Heart rate: 60 to 75% HRmax. Progression: increased if Borg < 4 and decreased if Borg > 7.	Supervised.
	Balance exercises - BE: A computer-based system allowed 4 different postural biofeedback exercises (catch, speedball, sky ball and gotcha).	6 weeks.	3 x/ week: 20 to 30 min.	Not reported.	Supervised.
Evcik et al 2008[23]	**Aquatic exercise - AE:** Warm-up (active ROM, and relaxation), followed by walking backwards and forwards in the pool; aerobic exercises (jumping and jogging); active ROM; stretching of neck and the extremities; and relaxation such as lying supine and low impact swimming.	5 weeks.	3 x/ week: 60 min.	Not reported.	Supervised/Groups.
	Home-based exercise - HE: ROM, relaxation, aerobic, stretching exercises.	5 weeks.	3 x/ week: 60 min.	Not reported.	Unsupervised/ Individual.
Fernandes et al 2016[25]	**Swimming exercise - SE:** Freestyle swimming without flotation devices.	12 weeks.	3 x/ week: 50 min.	Heart rate: 11 beats below the anaerobic threshold.	Supervised/Groups (4 to 8 patients).
	Walking exercise - WE: Open-air walking.	12 weeks.	3 x/ week: 50 min.	Heart rate: 11 beats below the anaerobic threshold.	Supervised/Groups (4 to 8 patients).
Gavi et al 2014[28]	**Strengthening exercise - SgthE:** Progressive training using weight machines (leg press, leg extension, hip flexion, pectoral fly, triceps extension, shoulder flexion, leg curl, calf, pull down, shoulder abduction, biceps flexion and shoulder extension), 3 sets of 12 rep, each exercise.	16 weeks.	2 x/ week: 45 min.	Moderate, 45% of 1 RM.	Supervised.
	Stretching exercises - SingE: Stretching of major muscles.	16 weeks.	2 x/ week: 45 min.	Not reported.	Supervised.

Genc et al 2015[29]	**Home stretching exercises - HSE:** A card with 12 flexibility (trunk, hips, ankle, shoulders, and wrist) and 12 stretching (neck, lateral side, chest, shoulder, arm, triceps, quadriceps, ankle, calf, hamstring stretch) movement illustrations was given to patients.	6 weeks.	Twice a day, every day.	Not reported.	Unsupervised/Individual.
	Aerobic exercises - AE: Same home exercise program + aerobic exercise (walking on a treadmill).	6 weeks.	3 x/ week: 40 to 45 min.	Heart rate: 60 to 75% HRmax.	Aerobic exercise was supervised.
Jentoft et al 2001[42]	**Land-based aerobic exercise -LAE:** Standardized exercise program based on the Norwegian Aerobic Fitness Model (body awareness, ergonomics, aerobic dance, muscle stretching, muscle strengthening and relaxation training).	20 weeks.	2 x/ week: 60 min.	60 to 80% HRmax (at least 40 to 50% of the 60 min exercise)	Supervised/Groups.
	Pool-based aerobic exercise - PAE: Heated pool - A modified version of the Norwegian Aerobic Fitness Model, adapted to the water.	20 weeks.	2 x/ week: 60 min.	60 to 80% HRmax (at least 40 to 50% of the 60 min exercise)	Supervised/Groups.
Jones et al 2002[43]	**Strengthening exercise - SgthE:** Progressive muscle strengthening without machine weights (gastrocnemius, tibialis anterior, quadriceps, hamstrings, gluteus, abdominals, erector spinae, pectorals, latissimus dorsi and rhomboids, deltoids, biceps and triceps). The exercises minimized eccentric contractions. End with stretching.	12 weeks.	2 x/ week: 60 min.	Start: 1 set, 4 to 5 rep. Progression: 12 rep and increased resistance.	Supervised/Individual.
	Stretching exercises - SingE: Same muscle groups of SghtE group. Stretches - (1) static rather than ballistic, (2) minimized in FM tender point locations, and (3) individualized.	12 weeks.	2 x/ week: 60 min.	Not reported.	Supervised/Individual.
Kayo et al 2012[46]	**Aerobic exercise - AE:** Walking outdoors or indoors (gymnasium).	16 weeks.	3 x/ week: 60 min.	40 to 70% HRR.	Supervised.
	Strengthening exercises - SE: 11 free active exercises, using free weights and body weight performed in the standing, sitting, and lying positions to improve the muscle strength of the upper and lower limbs and trunk muscles.	16 weeks.	3 x/ week: 60 min.	Start: without load (2 weeks). Progression: intensity increased according to Borg Scale (every 2 weeks) and load was included after week 5.	Supervised.

Mannerkorpi et al 2010[56]	**Moderate-to-high intensity Nordic walking - MHNW:** NW is walking using poles, which implies that muscles in the upper body are also activated and that the length of steps can be increased.	15 weeks.	2 x/ week: 40 to 50 min.	Start: light exercise (9 to 11 RPE), after 2 min intervals of moderate-to-high intensity exercise (13 to 15 RPE), alternated with 2 min of low-intensity exercise (10 to 11 RPE).	Supervised/Groups (7 to 15 patients).
	Low-intensity walking - LIW: Walked at a low intensity level.	15 weeks.	1 x/ week: 40 to 50 min.	Low intensity (9 to 11 RPE).	Supervised/Groups (7 to 5 patients).
McCain et al 1988[57]	**Aerobic exercise - AE:** Sustained heart rate elevation training in a bicycle ergometer.	20 weeks.	3 x/ week: 60 min.	Heart rate: 150 beats/min.	Supervised/Groups.
	Stretching exercise - SE: Only flexibility maneuvers.	20 weeks.	3 x/ week.	Heart rate greater than 115 beats/min was not attained.	Supervised/Groups.
Norregaard et al 1997[61]	**Aerobic exercise - AE:** Dance program. Free-standing exercise involving all body regions.	12 weeks.	3 x/ week: 50 min.	40 to 50% of VO_2max.	Supervised/Groups (6 to 8 patients).
	Steady exercise - SE: Body awareness, balance and motor control and stretching exercises. Free-standing gymnastic exercises performed at a steady speed.	12 weeks.	2 x/ week: 50 min.	No specific target increases in heart rate.	Supervised/Groups (6 to 8 patients).
Ramsay et al 2000[66]	**Home aerobic exercise - HE:** Aerobic exercises, stretching and relaxation techniques were given by a physiotherapist in 1 session. Aerobic exercises consisted of a program of graded circuit exercises (step-ups, sitting to standing, skipping, jogging on the spot, alternate side bends, circling arms with increasing weights).	12 weeks.	Not reported.	Not reported.	1 supervised session. Others unsupervised/ Individual.
	Supervised aerobic exercise - SE: The same program of the HE group but supervised.	12 weeks.	60 min.	Not reported.	Supervised.
Richards et al 2002[68]	**Aerobic exercise - AE:** Walking on treadmills and cycling on exercise bicycles.	12 weeks.	2 x/ week: 60 min.	An intensity that made patients sweat slightly while being able to talk comfortably.	Supervised/Groups of up to 18 patients.
	Relaxation and stretching exercises - RSE: Upper and lower limb stretches and relaxation techniques (contract and relax).	12 weeks.	2 x/ week: 60 min.	Not reported.	Supervised/Groups of up to 18 patients.
Rooks et al 2007[69]	**Aerobic and stretching exercises - ASE:** Aerobic exercise on the treadmill. End with flexibility exercises.	16 weeks.	2 x/ week 60 min.	Moderate effort of aerobic exercise.	Supervised.

	Strengthening, aerobic, and stretching exercise - SASE: Aerobic exercise on the treadmill, strengthening training exercises on machines (chest press, seated row, and leg press), hand weights (standing biceps curl and triceps kickback), and calisthenics (modified abdominal crunches). End with flexibility exercises.	16 weeks.	2 x/ week: 60 min.	Strengthening training - 50% 1 RM (leg press). 1 set of 6 rep at a resistance level the participant could perform easily with proper technique initially. Resistance exercises progressed to 2 sets of 10 to 12 rep.	Supervised.
Sañudo et al 2010[72]	**Aerobic exercise - AE:** Steady-state - continuous walking with arm movements and jogging; interval training (aerobic dance and jogging; and relaxation training).	24 weeks.	2 x/ week: 45 to 60 min.	60% to 65% of HRmax; Interval training at 75% to 80% HRmax	Supervised.
	Combined program of aerobic, muscle strengthening, and stretching exercises - ASSE: Aerobic exercise + muscle strengthening + flexibility exercises. Strengthening and flexibility (deltoids, biceps, trapezius, gluteus, quadriceps, latissimus dorsi, pectoralis major, abdominals).	24 weeks.	2 x/ week: 45 to 60 min.	AE: 65% to 70% HRmax. Resistance exercise: load of 1–3kg.	Supervised.
Schachter et al 2003[73]	**Long bout of aerobic exercise - LBE:** Low-impact aerobic exercise performed with music and once daily. Rhythmic movements designed to use all major muscle groups of the lower extremities.	16 weeks.	3 to 5 x/ week: 10 to 30 min.	Start: 40% to 50% HRR (week 1). Progression: 65% to 75% HRR (week 12). Training duration: 10 min/ session to 30 min/ session.	Supervised (Groups) and unsupervised (Individual).
	Short bouts of aerobic exercise - SBE: Low-impact aerobic exercise performed with music for 2 sessions/day separated by at least 4 hours. Rhythmic movements designed to use all major muscle groups of the lower extremities.	16 weeks.	3 to 5 x/ week: 2 sessions - 5 to 15 min.	Start: 40% to 50% HRR (week 1). Progression: 65% to 75% HRR (week 12). Training segment duration: 5 to 15 min/ session.	Supervised (Groups) and unsupervised (Individual).
Sevimli et al 2015[78]	**Home-based isometric strengthening and stretching exercise - HISS:** Flexibility, muscle strengthening and aerobic endurance based on graduated activity.	12 weeks.	Every day: 15 min/ day.	Low to moderate intensity (first month). High intensity (second month) - 30 sec rest period between 4 sets were performed.	Unsupervised/ Individual.

	Gym-based aerobic exercise - GAE: Flexibility, muscle strengthening, and aerobic endurance based on graduated activity.	12 weeks.	2 x/ week: 40 to 50 min.	60 to 80% HRmax.	Supervised/Groups.
	Pool-based aquatic aerobic exercise - PAAE: Flexibility, muscle strengthening, and aerobic endurance based on graduated activity.	12 weeks.	2 x/ week: 40 to 50 min.	60 to 80% HRmax.	Supervised/Groups.
Valim et al 2003[85]	**Aerobic exercise - AE:** Walking program.	20 weeks.	3 x/ week: 45 min.	Heart rate: Load beat immediately preceding the anaerobic threshold.	Supervised.
	Stretching exercise - SE: 17 exercises, including face, cervical, trunk, and extremities. Each maximum position was sustained for 30 sec.	20 weeks.	3 x/ week: 45 min.	Not reported.	Supervised.
van Santen et al 2002[87]	**High intensity physical fitness - HIF:** Ball games and stretching exercises of lower extremities, bicycling on an ergometer.	20 weeks.	3 x/ week: 60 min.	Heart rate: 70% HRmax. Heart rate above 150 beats/ min (20 to 30 min).	Supervised/Groups.
	Low intensity physical fitness - LIF: Postural muscle stretching, intensive aerobic exercises alternating with general flexibility and balance exercises, isometric muscle strengthening, stretching and relaxation exercises.	20 weeks.	2 x/ week: 60 min.	Defined by the patient.	Supervised/Groups.
Wang et al 2018[93]	**Aerobic exercise - AE:** Low intensity movements and dynamic stretching, choreographed aerobic training, and low intensity movements, dynamic and static stretching.	24 weeks.	2 x/ week: 60 min.	Low to moderate intensity (50 to 70% HRmax).	Supervised/Groups.
	Tai Chi once week, 12 weeks - TC1,12: TC once a week for 12 weeks. (1) warm-up and a review of TC principles and techniques; (2) TC movement; (3) breathing techniques; (4) relaxation methods.	12 weeks.	1 x/ week: 60 min.	Not reported.	Supervised.
	Tai Chi twice week, 12 weeks - TC2,12: Performed TC session twice a week for 12 weeks.	12 weeks.	2 x/ week: 60 min.	Not reported.	Supervised.
	Tai Chi once a week, 24 weeks - TC1,24: Performed TC session once a week for 24 weeks.	24 weeks.	1 x/ week: 60 min.	Not reported.	Supervised.
	Tai Chi twice a week, 24 weeks - TC2,24: Performed TC session twice a week for 24 weeks.	24 weeks.	2 x/ week: 60 min.	Not reported.	Supervised.
CHRONIC WHIPLASH-ASSOCIATED DISORDERS (CWAD)					
First author/ Year	**Interventions**	**Treatment period**	**Session frequency/ length**	**Intensity of the exercise**	**Supervision/group vs individual**

Seferiadis et al 2015[76]	**Exercise therapy - ET:** Muscle strengthening (whole body, neck and shoulders, and specifically targeting deep neck flexor muscles), aerobic exercise and coordination exercises; stretching exercise; progressive muscle relaxation.	10 weeks.	2 x/ week: 90 min.	Not reported.	Supervised/Groups (maximum 12 patients).
	Body awareness therapy - BAT: Exercises based on activities of daily living (sitting, walking, lying down and standing), meditation and exercises inspired in Tai Chi.	10 weeks.	2 x/ week: 90 min.	Not reported.	Supervised/Groups (maximum 12 patients).
Vikne et al 2007[90]	**Traditional physiotherapy - TP:** Strengthening and endurance training of the neck, back and abdominal muscles. Home training program based on these exercises started after 3 weeks.	16 weeks + 32 weeks at home.	24 sessions.	Not reported.	Supervised (16 weeks) and unsupervised (32 weeks)/ Individual.
	Traditional physiotherapy + home exercise - TP+: Same treatment as the TP group. In the follow-up period patients continued their home training program.	16 weeks + 32 weeks at home - monthly supervised.	24 sessions.	Not reported.	Supervised (16 weeks) and unsupervised (32 weeks)/ Individual.
	New sling exercise therapy - NSET: TP + specific exercises in a ceiling-mounted sling (i.e.: using 3 wide slings, the patient's body was suspended hanging in a supine position. The head rests on an air-filled balance cushion. Pressing the occipital region into the cushion and extending the head on the cervical spine, the patient moved their body gently using their neck and head muscles).	16 weeks + 32 weeks at home.	24 sessions.	Not reported.	Supervised (16 weeks) and unsupervised (32 weeks)/ Individual.
	New sling exercise therapy + home exercise - NSET+: Same treatment as the NSET group. In the follow-up period patients continued their home training program (with exercises in a ceiling-mounted sling at home).	16 weeks + 32 weeks at home - monthly supervised.	24 sessions.	Not reported.	Supervised (16 weeks) and unsupervised (32 weeks)/ Individual.
		CHRONIC IDIOPATHIC NECK PAIN (CINP)			
First author/ Year	**Interventions**	**Treatment period**	**Session frequency/ length**	**Intensity of the exercise**	**Supervision/group vs individual**
Andersen et al 2008[1]	**Specific strengthening training - SST:** For neck and shoulder muscles (1- arm row, shoulder	10 weeks.	3 x/ week: 20 min.	12 RM (70% of maximal intensity) to 8 RM (80% of maximal intensity).	Supervised.

	abduction, shoulder elevation, reverse flies, and upright row).				
	Aerobic exercise - AE: On a bicycle ergometer. Patients should relax the shoulders during training.	10 weeks.	3 x/ week: 20 min.	50–70% of VO_2max.	Supervised.
Bobos et al 2016[11]	**Deep neck flexors' training - DNFT:** Cranio-cervical flexion test (CCFT) with air pressure biofeedback, nodding from supine, pronation and sitting position.	7 weeks.	2 x/ week: 30 to 40 min.	Gradual increase (intensity and rep).	Supervised.
	Superficial muscle training - SMT: Posterior head movement from sitting and supine position, movement in all directions from pronation, and "cat-camel motion exercise".	7 weeks.	2 x/ week: 30 to 40 min.	Gradual increase (intensity and rep).	Supervised.
Borisut et al 2013[13]	**Strength-endurance exercise - SEE:** Progressive resistance exercise (sternocleidomastoid, anterior scalenes and cervical erector spinae). Neck flexion and extension in the supine and prone positions.	12 weeks.	Every day.	Phase 1: 12 to15 rep (12 RM load). Phase 2: 3 sets of 15 rep (initial 12 RM load).	Unsupervised/ Individual.
	Cranio-cervical flexion exercise - CCFE: Low load exercise for the cranio-cervical flexor muscles. Cranio-cervical flexion inner range, guided by biofeedback pressure device.	12 weeks.	Every day.	15 rep of 10 sec each contraction on biofeedback inflated from 22 to 30 mmHg.	Unsupervised/ Individual.
	Combined exercise - CE: First, performed the CCFE and 5 min after performed the SEE.	12 weeks.	Every day.	The same intensity of SEE and CCFE.	Unsupervised/ Individual.
Cramer et al 2013[20]	**Yoga - Y:** 8 to 11 yoga postures. The focus was on lengthening and strengthening muscles of the neck and shoulder region and to improve stability and posture.	9 weeks.	1 x/ week: 90 min.	Not reported.	Supervised/Groups.
	Home exercise - HE: Self-care manual with exercise program for the neck and shoulder region. Stretching exercises for the neck and shoulders, strengthening and isometric exercises for the neck-shoulder region, and combined stretching and strengthening exercises for the neck-shoulder region with a towel.	9 weeks.	Every day: 10 min.	Not reported.	Unsupervised/ Individual.
Falla et al 2006[24]	**Strength-endurance exercise - SEE:** Progressive resistance exercise program for the neck flexors.	6 weeks.	Twice a day, every day: 10 to 20 min/day.	1st stage: 12 to 15 rep (12 RM load). 2nd stage: 3 sets of 15 rep (initial 12 RM load).	Supervised (once a week) and unsupervised at home/ Individual.

	Cranio-cervical flexion exercise - CCFE: Cranio-cervical flexion while maintaining the superficial flexor muscles relaxed. Progressively increasing ranges of cranio-cervical flexion using biofeedback pressure device.	6 weeks.	Twice a day, every day: 10 to 20 min/day.	Not reported.	Supervised (once a week) and unsupervised at home/ Individual.
Häkkinen et al 2007[33]	**Strengthening and stretching exercises - SSE:** Neck flexor muscles: 1 set directly forwards and 1 set obliquely towards the right and towards the left each. Neck extensor muscles: 1 set backwards. For shoulders and upper extremities: dumbbell shrugs, presses, curls, bent-over rows, flyers, and pullovers. 1 set of a dynamic abdominal exercise against body weight, a back exercise, squats and stretching of the neck, shoulders and upper extremities muscles.	52 weeks.	3 x/ week at home. Supervision of 1 x/ week (beginning); 1x/ every two months (after 6 weeks).	80% of maximum isometric strengthening. Shoulder/upper extremities strengthening: highest load possible.	Supervised and unsupervised/Groups (6 to 8 patients).
	Stretching exercises - SE: Stretch the muscles in the region of the neck, shoulders and upper extremities.	52 weeks.	3 x/ week at home.	Not reported.	1x supervised and unsupervised/ Individual.
Izquierdo et al 2016[40]	**Cranio-cervical flexion training - CCFT:** Deep flexor muscles (longus capitis and longus colli). Progressively increasing ranges of cranio-cervical flexion using biofeedback pressure device.	8 weeks.	6 x in 8 weeks: 45 min.	10 rep of 10 sec each contraction with biofeedback inflated from 20 to 30 mmHg.	Supervised/Individual.
	Proprioceptive training - PT: Exercises of head relocation, eye-follow, gaze stability and eye-head coordination. Active movements (flexion, extension, rotation, lateral flexion) were performed.	8 weeks.	6 x in 8 weeks: 45 min.	Increasing the speed and range of motion.	Supervised/Individual.
Javanshir et al 2015[41]	**Cranio-cervical flexion training - CCFT:** Cranio-cervical flexion while maintaining the superficial flexor muscles relaxed. Progressively increasing ranges of cranio-cervical flexion using biofeedback pressure device.	10 weeks.	3 x/ week: 30 min.	10 rep of 10 sec each contraction with biofeedback inflated from 20 to 30 mmHg.	Supervised/Individual.
	Cervical flexion training- CFT: In supine, to lift slowly the head through full range of motion as much as possible without reproducing the symptoms.	10 weeks.	3 x/ week: 30 min.	From 12 RM to 15 RM	Supervised/Individual.
Karlsson et al 2014[45]	**Strengthening exercise - SgthE:** Specific strengthening training of the neck and shoulder muscles (arm abduction, upright throw, biceps curls, fly's, reverse fly's, and pullovers). Lifting the	52 weeks.	3 x/ week.	1st 8 weeks: 2-kg dumbbells; After 8 weeks: heaviest weight to perform 10 rep.	Not reported.

	head up (without resistance) from a supine position. Dynamic exercises for the trunk and legs (sit-ups, back extensions, and squats) and stretching exercises for the neck, shoulders, and upper limb muscles ended the exercise session.				
	Stretching exercise - **SingE:** Retraction of the neck and stretching (upper and middle portion of trapezius, sternocleidomastoideus, rhomboids, pectoralis major, and flexors and extensors of the wrist).	52 weeks.	3 x/ week.	Not reported.	Not reported.
Khan et al 2014[47]	**Isometric exercise - IE:** Neck flexors, extensors, and bilateral flexors and rotators muscles (20 rep).	12 weeks.	3 x/ week (supervised), and 2 x/ day, at least 5 days (home).	Not reported.	Supervised and unsupervised.
	General exercise - GE: General range of movement exercises for flexors, extensors, and bilateral flexors and rotators neck muscles (20 rep).	12 weeks.	3 x/ week (supervised), and 2 x/ day, at least 5 days (home).	Not reported.	Supervised and unsupervised.
Kietrys et al 2007[48]	**Resistance exercise - RE:** Isometric cervical spine rotation with manual resistance (5 sec hold, 5 rep in each direction), shoulder shrugs and scapular retraction with elastic band resistance (12 rep).	4 weeks.	Twice a day, every day.	Not reported.	Unsupervised/ Individual.
	Stretching exercise -SE: Lateral cervical, a posterior neck and an anterior arm/forearm stretching (5 sec hold, 5 rep).	4 weeks.	Twice a day, every day.	Not reported.	Unsupervised/ Individual.
Kim et al 2016[49]	**Deep cervical flexor exercise - DCFE:** Longus capitis and longus colli muscles. Cranio-cervical flexion while maintaining the superficial flexor muscles relaxed. Progressively increasing ranges of cranio-cervical flexion using biofeedback pressure device.	4 weeks.	3 x/ week.	10 rep of 10 to 15 sec each contraction with biofeedback inflated from 20 to 30 mmHg.	Not reported.
	General strengthening exercise - GSE: Conventional isocratic and gradual exercise. Isometric exercise (1st 2 weeks). Gradual exercise (next 4 weeks), maintained toward the front, both sides, and backward for 10 sec, and neck stretching, neck bending over, neck bending to both sides, and neck rotation.	4 weeks.	3 x/ week.	Not reported.	Not reported.

Lansinger et al 2007[52]	**Qigong therapy - QT:** Medical qigong. Started with information about the philosophy, 14 qigong exercises. Soft movements for the whole body, specific slow movement sequences + breathing techniques, meditation, relaxation, soft stretching, and self-performed body massage.	12 weeks.	1 to 2 x/ week: 60 min.	Not reported.	Supervised/Groups (10 to 15 patients).
	Exercise therapy - ET: Cervical and shoulder/thoracic region. Stationary bicycle, active movements of the cervical and shoulder/thoracic regions, different muscle exercises (endurance and strength), and stretching exercises.	12 weeks.	1 to 2 x/ week: 60 min.	30% to 70% of maximum muscle capacity.	Supervised/Individual.
Lansinger et al 2013[51]	**Qigong therapy - QT:** Medical qigong. Started with information about the philosophy, 14 qigong exercises. Soft movements for the whole body, specific slow movement sequences + breathing techniques, meditation, relaxation, soft stretching, and self-performed body massage.	12 weeks.	1 to 2 x/ week: 60 min.	Not reported.	Supervised/Groups (10 to 15 patients).
	Exercise therapy - ET: Cervical and shoulder/thoracic region. Stationary bicycle, active movements of the cervical and shoulder/thoracic regions, different muscle exercises (endurance and strength), and stretching exercises.	12 weeks.	1 to 2 x/ week: 60 min.	30% to 70% of maximum muscle capacity.	Supervised/Individual.
Lauche et al 2016[53]	**Tai Chi - TC:** Based on Yang style.	12 weeks.	1 x/ week: 75 to 90 min.	Not reported.	Supervised/Groups (10 to 15 patients).
	Neck exercises - NE: Basic training of ergonomic principles, proprioceptive exercises, isometric and dynamic mobilization, stretching, and strengthening neck and core exercises.	12 weeks.	1 x/ week: 60 to 75 min.	Not reported.	Supervised/Groups (10 to 15 patients).
O'Leary et al 2012[62]	**Mobility training - MTr:** Active movement exercises in an upright posture in the direction of cervical flexion, extension, and axial rotation (3 to 10 rep and 1 to 4 sets).	10 weeks.	Twice a day, every day + 8 sessions.	Not reported.	Supervised (8 sessions) and unsupervised at home/Individual.
	Coordination training - CTr: Flexor muscles training (cranio-cervical flexion) in the supine position with pressure biofeedback device and active movement exercise in the directions of cervical extension and axial rotation (like MTr group).	10 weeks.	Twice a day, every day + 8 sessions.	10 sec of contraction with biofeedback inflated from 22 to 30 mmHg.	Supervised (8 sessions) and unsupervised at home/Individual.

	Endurance training - Etr: Isometric exercise for flexor muscles in an upright posture with a purpose-built device setup within their home at the initial consultation (10 rep, with 10 sec), and active movement exercise in the directions of cervical extension and axial rotation (like MTr group).	10 weeks.	Twice a day, every day + 8 sessions.	20% to 50% of MCV.	Supervised (8 sessions) and unsupervised at home/Individual.
Rendant et al 2011[67]	**Qigong therapy - QT:** Neiyanggong, a special silent and slow form of qigong. 12 neck exercises, 9 exercises for the shoulder and breathing and moving exercises.	26 weeks.	1 x/ week (first 3 months), and biweekly: 90 min.	Not reported.	Supervised.
	Exercise therapy - ET: Based on a standard program for chronic neck pain. Repeated active cervical rotations, strengthening and flexibility exercises.	26 weeks.	1 x/ week (first 3 months), and biweekly.	Not reported.	Supervised.
Salo et al 2010[71]	**Strength training - ST:** The neck muscles were trained with elastic band directly forwards, obliquely toward right and left and directly backwards (1 set of 15 rep), exercises of the upper extremity (dumbbell shrugs, presses, curls, bent-over rows, fly's, and pullovers), squats, sit-ups, and back extension exercises and stretching of the muscles trained.	52 weeks.	3 x/ week: 45 min.	80% of maximum isometric strengthening. Upper limb exercises: highest load possible.	Supervised (12 days) and unsupervised (52 weeks)/Groups (10 patients).
	Endurance training - ET: The neck muscles were trained by lifting the head up from supine position (3 sets of 20 rep), upper extremity exercise (dumbbell shrugs, presses, curls, bent-over rows, fly's, and pullovers), squats, sit-ups, back extension exercises and stretching of the muscles trained.	52 weeks.	3 x/ week: 45 min.	Not reported.	Supervised (12 days) and unsupervised (52 weeks)/Groups (10 patients).
Salo et al 2012[70]	**Combined strengthening training and stretching exercise - CSS:** Isometric neck strengthening exercises directly forward, obliquely toward the right and left and directly backwards (1 set of 15 rep), shoulders and upper extremities exercises (shrugs, presses, curls, bent over rows, flyers and pullovers using dumbbells), squats, sit-ups, back extension and stretching of the neck, shoulder and upper limb muscles.	52 weeks.	1 x/ week (beginning), and 1x/ every 2 months. 3 x/ week (home).	80% of maximum isometric strength. Upper limb exercises: highest load possible.	Supervised (10 sessions) and unsupervised (52 weeks)/Groups (6 to 8 patients).

	Stretching exercise - SE: Neck, shoulder, and upper limb muscles.	52 weeks.	3 x/ week (home).	Not reported.	Supervised (1 session) and unsupervised (52 weeks)/Individual.
Senthil et al 2016[77]	**Deep cervical flexor exercise - DCFE:** Passive stretching of tight muscles (upper trapezius, levator scapulae, sternocleidomastoid, sub-occipitalis muscles), isolated activation of deep cervical flexor muscles in supine, wall-support and in sitting, and shoulder elevation and functional movements.	6 weeks.	3 x/ week.	Not reported.	Not reported.
	General exercises - GE: Active exercises of neck flexion, extension, side-flexion, scapular elevation-depression and protraction-retraction movement, and isometric neck exercise (3 sets of 10 rep).	6 weeks.	3 x/ week.	Not reported.	Not reported.
von Trott et al 2009[91]	**Qigong therapy - QT:** 10 to 12 small qigong-specific exercises for hip, legs, shoulders, arms, and the head; 4 Dantian exercises; striking the meridians, circles over the lower Dantian and rubbing the kidney region.	12 weeks.	2 x/week: 45 min.	Not reported.	Supervised/Groups (6 to 12 patients).
	Exercise therapy - ET: Repeated active cervical rotations as well as strength and flexibility exercises.	12 weeks	2 x/week: 45 min.	Not reported.	Supervised/Groups (6 to 12 patients).
Ylinen et al 2003[95]	**Strength training - ST:** The neck muscles were trained with elastic band directly forwards, obliquely toward right and left and directly backwards (1 set of 15 rep), exercises of the upper extremity (dumbbell shrugs, presses, curls, bent-over rows, fly's, and pullovers), squats, sit-ups, and back extension exercises and stretching of the muscles trained.	52 weeks.	Supervised (5x/ week), and unsupervised (3 x/ week): 45 min.	80% of maximum isometric strength. Upper limb exercises: highest load possible.	Supervised (12 days) and unsupervised (52 weeks)/Groups (10 patients).
	Endurance training - ET: The neck muscles were trained by lifting the head up from supine position (3 sets of 20 rep), upper extremity exercise (dumbbell shrugs, presses, curls, bent-over rows, fly's, and pullovers), squats, sit-ups, back extension exercises and stretching of the muscles trained.	52 weeks.	Supervised (5x/ week), and unsupervised (3 x/ week): 45 min.	Not reported.	Supervised (12 days) and unsupervised (52 weeks)/Groups (10 patients).

Abbreviation - Min: Minutes; Sec: Seconds; Rep: Repetitions; RM: Maximal repetitions; MVC: Maximum voluntary contraction; RPE: Rated Perceived Exertion scale; HRmax: Maximal heart rate; HRR: Heart rate reserve; VO_2max: Maximal oxygen uptake; ROM: Range of motion.

Table 3. Quality of the evidence (GRADE)

Population: Patients with fibromyalgia				
Comparison: **Aerobic exercises versus Stretching exercises**				
Outcomes	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality of evidence (GRADE)**	**Comments**
Pain: scale 0 to 100 milimeters Follow-up: short term (less than six months)	Mean difference -8.06 (-15.21 to -0.91)	148 patients (3 studies)	●●○○ Low quality[1]	The difference is only statistically significant with small effect
Comparison: **Aerobic exercises versus Strengthening exercises**				
Outcomes	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality of evidence (GRADE)**	**Comments**
Pain: scale 0 to 10 millimeters Follow-up: short term (less than six months)	Mean difference 1.97 (-4.63 to 8.58)	86 patients (2 studies)	●●○○ Low quality[1]	The difference is not statistically or clinically significant
Comparison: **High intensity aerobic exercises versus Low intensity aerobic exercises**				
Outcomes	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality of evidence (GRADE)**	**Comments**
Pain: scale 0 to 10 millimeters Follow-up: short term (less than six months)	Mean difference -1.09 (-8.03 to 5.85)	137 patients (3 studies)	●●○○ Low quality[1]	The difference is not statistically or clinically significant
Comparison: **Land aerobic exercise versus Aquatic aerobic exercise**				
Outcomes	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality of evidence (GRADE)**	**Comments**
Pain: scale 0 to 10 millimeters Follow-up: short term (less than six months)	Mean difference -3.94 (-11.29 to 5.22)	219 patients (4 studies)	●○○○ Very low quality[1,2]	The difference is not statistically or clinically significant

Comparison: **Strengthening exercise versus Stretching exercise**				
Outcomes	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality of evidence (GRADE)**	**Comments**
Pain: scale 0 to 10 millimeters Follow-up: short term (less than six months)	Mean difference -6.18 (-8.13 to -5.8)	152 patients (4 studies)	●●○○ Low quality[1]	The difference is only statistically significant with small effect
Comparison: **Supervised exercise versus Unsupervised exercise**				
Outcomes	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality of evidence (GRADE)**	**Comments**
Pain: scale 0 to 10 millimeters Follow-up: short term (less than six months)	Mean difference -9.95 (-19.62 to 0.27)	335 patients (4 studies)	●○○○ Very low quality[1,2]	The difference is not statistically or clinically significant
Population: Patients with chronic idiopathic neck pain				
Comparison: **Mind-body exercises versus Combined exercises**				
Outcomes	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality of evidence (GRADE)**	**Comments**
Pain: scale 0 to 10 millimeters Follow-up: short term (less than six months)	Mean difference 6.46 (0.75 to 12.17)	335 patients (4 studies)	●●○○ Low quality[1]	The difference is only statistically significant with small effect.
Comparison: **Motor control exercise versus Specific strengthening**				
Outcomes	**Relative effect (95% CI)**	**Number of participants (studies)**	**Quality of evidence (GRADE)**	**Comments**
Pain: scale 0 to 10 millimeters Follow-up: short term (less than six months)	Mean difference -3.16 (-13.78 to 7.47)	127 patients (3 studies)	●●○○ Low quality[1]	The difference is not statistically or clinically significant

[1] Downgraded due to imprecision (less than 400 participants were included in the comparison).
[2] Downgraded due to inconsistency (heterogeneity was presented, $I^2 > 50\%$).

Supplementary file 2 - Descriptive analysis of the studies

EXERCISE PRESCRIPTION PARAMETERS FOR FIBROMYALGIA	
Type of therapeutic exercise	*Aerobic exercise versus Muscle strengthening* - No differences between these exercises for the short-term impact of fibromyalgia (Bircan et al., 2008; Kayo et al., 2012), and for the medium-term pain (Kayo et al., 2012). *Aerobic exercise versus Muscle stretching* - Aerobic exercise was superior to muscle stretching for pressure pain threshold (McCain et al., 1988), impact of fibromyalgia and mental component of quality of life (Valim et al., 2003) in the short-term. *Aerobic exercise versus Balance exercise* - There was no difference between these exercises to improve pain and impact of fibromyalgia, but aerobic exercise had a superior effect on pressure pain threshold improvement in the short-term (Duruturk et al., 2015). *Aerobic exercise versus Tai Chi* - Tai Chi had a superior and clinically relevant effect to improve impact of fibromyalgia in the short-,

medium- and long-term, and to improve the mental component of quality of life in the medium-term (Wang et al., 2018).

Aerobic exercise versus Combined exercise

- Aerobic exercises performed in land or water had a superior and clinically relevant effect compared to isometric exercise plus stretching to improve pain, impact of fibromyalgia and quality of life in the short-term (Sevimli et al., 2015).
- There was no difference between aerobic exercises and balance plus motor control exercises (Nørregaard et al., 1997), stretching exercises plus relaxation (Richards and Scott, 2002) and the combination of aerobic plus strengthening plus stretching exercises (Sañudo et al., 2010) for pain, impact of fibromyalgia and quality of life in the short-term.
- There was also no difference between aerobic exercises and stretching exercises plus relaxation for pain and impact of fibromyalgia in the medium-term, and for impact of fibromyalgia in the long-term (Richards and Scott, 2002).

Land-based aerobic exercise versus Water-based aerobic exercise

- There was no difference between these exercises for impact of fibromyalgia and quality of life in the short- (Assis et al., 2006; Fernandes et al., 2016; Jentoft et al., 2001; Sevimli et al., 2015) and medium-term (Assis et al., 2006; Fernandes et al., 2016; Jentoft et al., 2001).

Muscle strengthening versus Muscle stretching

- Strengthening exercise was superior for the improvement of impact of fibromyalgia in the short-term, but muscle stretching was superior for quality of life in the same time frame (Assumpção et al., 2018).
- There was no difference between these exercises for pressure pain threshold in the short-term (Assumpção et al., 2018; Jones et al., 2002).

Muscle stretching versus Tai Chi

- There was no difference between these exercises for impact of fibromyalgia and quality of life in the short-term (Calandre et al., 2009).

Muscle stretching versus Combined exercise

- There was no difference between isolated muscle stretching exercise and a combination of exercises (stretching plus balance plus coordination exercises) for pain, pressure pain threshold and impact of fibromyalgia in the short- and medium-term (Demir-Göçmen et al., 2013).
- *Combined exercise versus other Combined exercise*

	- There was no difference between muscle strengthening plus aerobic plus stretching exercises and a program of aerobic plus stretching exercises alone for pain, disability, impact of fibromyalgia and quality of life in the short-term (Rooks et al., 2007). - Range of motion plus aerobic plus stretching exercises performed in the water were superior to the same combined exercises performed in the land for pain in the short- and medium-term, but there was no difference between these exercises for impact of fibromyalgia in the short- and medium-term (Evcik et al., 2008).
Duration of the session	- Only one study did not present this information (Ramsay et al., 2000). - The session time ranged from 10 to 60 minutes. - The groups that performed sessions of 10 to 15 minutes also performed exercises at home (Schachter et al., 2003; Sevimli et al., 2015). - One study (Schachter et al., 2003) showed that there was no difference between performing a session of 30 minutes or two sessions of 15 minutes of home aerobic exercises for pain, pressure pain threshold, disability and impact of fibromyalgia in the short-term.
Weekly treatment	- Only one study did not present this information (Ramsay et al., 2000).

frequency	- The weekly exercise frequency ranged from 1 to 7 times a week. - Only one study (Wang et al., 2018) performed exercise once a week, and two studies performed home exercises every day (Genc et al., 2015; Sevimli et al., 2015). - Most of the studies (24 studies, 92%) performed the exercise 2 to 3 times a week (Assis et al., 2006; Assumpção et al., 2018; Bircan et al., 2008; Bjersing et al., 2012; Calandre et al., 2009; Demir-Göçmen et al., 2013; Duruturk et al., 2015; Evcik et al., 2008; Fernandes et al., 2016; Gavi et al., 2014; Genc et al., 2015; Jentoft et al., 2001; Jones et al., 2002; Kayo et al., 2012; Mannerkorpi et al., 2010; McCain et al., 1988; Nørregaard et al., 1997; Richards and Scott, 2002; Rooks et al., 2007; Sañudo et al., 2010; Sevimli et al., 2015; Valim et al., 2003; van Santen et al., 2002; Wang et al., 2018). - One study (Wang et al., 2018) showed that there was no difference between performing Tai Chi once or twice a week for impact of fibromyalgia and quality of life in the short-, medium-, and long-term.
Duration of treatment	- Thirteen studies performed 13 to 24 weeks of treatment (Assis et al., 2006; Bjersing et al., 2012; Gavi et al., 2014; Jentoft et al., 2001; Kayo et al., 2012; Mannerkorpi et al., 2010; McCain et al., 1988; Rooks et al., 2007; Sañudo et al., 2010; Schachter et al., 2003; Valim et al., 2003; van Santen et al., 2002; Wang et al., 2018).

	- Ten studies performed 7 to 12 weeks of treatment (Assumpção et al., 2018; Bircan et al., 2008; Demir-Göçmen et al., 2013; Fernandes et al., 2016; Jones et al., 2002; Nørregaard et al., 1997; Ramsay et al., 2000; Richards and Scott, 2002; Sevimli et al., 2015; Wang et al., 2018). - Only four studies performed 4 to 6 weeks of treatment (Calandre et al., 2009; Duruturk et al., 2015; Evcik et al., 2008; Genc et al., 2015). - One study (Wang et al., 2018) showed that performing Tai Chi for 12 or 24 weeks was not different for impact of fibromyalgia in the short- (12 weeks) and long-term (52 weeks), but was different in the medium-term (24 weeks), in favor of the group that performed 24 weeks of treatment. The 12-week group did not receive any treatment in the 12 weeks before the 24-week assessment, whereas the group that underwent treatment for 24 weeks had finished treatment just before the medium-term assessment.
Intensity of the exercise	- Seven studies did not present information about intensity of the exercise (Bjersing et al., 2012; Calandre et al., 2009; Demir-Göçmen et al., 2013; Evcik et al., 2008; Jones et al., 2002; Ramsay et al., 2000; Richards and Scott, 2002). - There was no difference between high and low intensity aerobic exercises for pressure pain threshold and impact of fibromyalgia in the short-term, and for pain and pressure pain threshold in the medium-

	term (Bjersing et al., 2012; Mannerkorpi et al., 2010; van Santen et al., 2002). - High-intensity exercise was more effective to improve function in the short-term (Mannerkorpi et al., 2010). - **Aerobic exercises** were performed at an intensity of 40 to 80% of maximum heart rate (Bircan et al., 2008; Duruturk et al., 2015; Genc et al., 2015; Jentoft et al., 2001; Kayo et al., 2012; Rooks et al., 2007; Sañudo et al., 2010; Schachter et al., 2003; Sevimli et al., 2015; van Santen et al., 2002; Wang et al., 2018), and between 9 and 15 in the Rated Perceived Exertion (RPE) Scale (Mannerkorpi et al., 2010). - **Strengthening exercises** were performed at an intensity of 45 to 50% of the maximal repetition (Gavi et al., 2014; Rooks et al., 2007). - **Stretching exercises** were performed until a moderate discomfort (Assumpção et al., 2018).
- EXERCISE PRESCRIPTION PARAMETERS FOR CHRONIC IDIOPATHIC NECK PAIN	
Type of therapeutic exercise	*Muscle strengthening versus Muscle stretching* - There was no difference between these exercises for pain and disability in the short- and long-term (Karlsson et al., 2014; Kietrys et al., 2007). *Muscle strengthening versus Active range of motion exercises*

- There was no difference between these exercises for pain in the short- and medium-term, and for disability in the medium-term (Khan et al., 2014; O'Leary et al., 2012).
- Muscle strengthening was superior for disability in the short-term (Khan et al., 2014).

Muscle strengthening versus Muscle endurance

- There was no difference between muscular strengthening exercise with focus on strength or endurance for pain, disability and quality of life in the long-term (Salo et al., 2010; Ylinen et al., 2003).

Muscle strengthening versus Motor control

- There was no difference between motor control exercises and muscle strengthening plus muscle endurance exercises for pain and disability in the short-term. However, the combination of these three exercises was superior for pain reduction in the short-term (Borisut et al., 2013).
- There was no difference between motor control exercises and nonspecific strengthening for pressure pain threshold, disability and quality of life in the short-term (Javanshir et al., 2015; Kim and Kwag, 2016; O'Leary et al., 2012). However, one study (Kim and Kwag, 2016) showed a statistically significant improvement in disability, in favor of motor control exercises, after eight weeks of treatment.

Motor control versus Aerobic exercise

- Motor control exercise was superior for pain reduction in the short-term (Andersen et al., 2008).

Motor control versus Active range of motion exercises

- There was no difference between these exercises for pain and disability in the short- and medium-term (O'Leary et al., 2012).

Motor control versus Proprioceptive exercises

- There was no difference between these exercises for pain, pressure pain threshold and disability in the short-term (Izquierdo et al., 2016).

Motor control versus Combined exercises

- Motor control exercise was superior compared to motor control exercises plus isometric exercise plus active range of motion for disability in the short-term (Senthil et al., 2016).

Mind-body exercises (Qigong and Tai Chi) versus Combined exercise

- There was no difference between mind-body exercises and different combined exercise modalities (aerobic, strengthening, stretching, active range of motion, and proprioceptive exercises) for disability and quality of life in the short- and medium-term (Lansinger et al., 2013; Lansinger et al., 2007; Lauche et al., 2016; Rendant et al., 2011; von Trott et al., 2009).

	- There was no difference between these exercises for pain in the medium-term (Lansinger et al., 2007; Lauche et al., 2016; Rendant et al., 2011; von Trott et al., 2009). *Yoga versus Combined exercise* - Yoga presented a superior and clinically relevant effect compared with strengthening plus stretching combination performed at home for pain, pressure pain threshold, disability and quality of life in the short-term (Cramer et al., 2013). *Muscle stretching versus Combined exercise* - There was no difference between strengthening plus stretching exercise and stretching exercise alone for pain and disability in the short- and long-term (Häkkinen et al., 2008), and for quality of life in the long-term (Salo et al., 2012).
Supervision of the exercise	- Four studies did not present this information (Borisut et al., 2013; Karlsson et al., 2014; Kim and Kwag, 2016; Senthil et al., 2016). - Nine studies performed supervised exercise (Andersen et al., 2008; Izquierdo et al., 2016; Javanshir et al., 2015; Khan et al., 2014; Lansinger et al., 2013; Lansinger et al., 2007; Lauche et al., 2016; Rendant et al., 2011; von Trott et al., 2009).

	- Five studies performed unsupervised exercise (Falla et al., 2006; Kietrys et al., 2007; Salo et al., 2012; Salo et al., 2010; Ylinen et al., 2003). - Three studies started treatment with supervised exercise and progressed to unsupervised exercise (Cramer et al., 2013; Häkkinen et al., 2008; O'Leary et al., 2012).
Duration of the session	- Nine studies did not present this information (Borisut et al., 2013; Häkkinen et al., 2008; Karlsson et al., 2014; Khan et al., 2014; Kietrys et al., 2007; Kim and Kwag, 2016; O'Leary et al., 2012; Salo et al., 2012; Senthil et al., 2016). - The session time ranged from 10 to 90 minutes. - The groups that performed sessions of 10-minute duration also performed sessions at home (Cramer et al., 2013; Falla et al., 2006). - The groups that performed 90-minute sessions performed Qigong (Rendant et al., 2011), Tai Chi (Lauche et al., 2016) and Yoga (Cramer et al., 2013) exercises. - Most treatment sessions lasted from 30 to 60 minutes (8 studies, 36%) (Bobos et al., 2016; Izquierdo et al., 2016; Javanshir et al., 2015; Lansinger et al., 2013; Lansinger et al., 2007; Salo et al., 2010; von Trott et al., 2009; Ylinen et al., 2003).

Weekly treatment frequency	- One study did not present this information (Izquierdo et al., 2016). - The weekly exercise frequency ranged from 1 to 7 times a week between studies. - Five studies performed exercise once a week (Cramer et al., 2013; Lansinger et al., 2013; Lansinger et al., 2007; Lauche et al., 2016; Rendant et al., 2011). - Five studies performed home exercises every day (Borisut et al., 2013; Cramer et al., 2013; Falla et al., 2006; Kietrys et al., 2007; O'Leary et al., 2012). - Most of the studies (14 studies, 63%) performed exercise 2 to 3 times a week (Andersen et al., 2008; Bobos et al., 2016; Häkkinen et al., 2008; Javanshir et al., 2015; Karlsson et al., 2014; Khan et al., 2014; Kim and Kwag, 2016; Lansinger et al., 2013; Lansinger et al., 2007; Salo et al., 2012; Salo et al., 2010; Senthil et al., 2016; von Trott et al., 2009; Ylinen et al., 2003).
Duration of treatment	- Six studies performed 13 to 24 weeks of treatment (Häkkinen et al., 2008; Karlsson et al., 2014; Rendant et al., 2011; Salo et al., 2012; Salo et al., 2010; Ylinen et al., 2003). - Eleven studies performed 7 to 12 weeks of treatment (Andersen et al., 2008; Borisut et al., 2013; Cramer et al., 2013; Izquierdo et al., 2016; Javanshir et al., 2015; Khan et al., 2014; Lansinger et al., 2013; Lansinger et al., 2007; Lauche et al., 2016; O'Leary et al., 2012; von Trott et al., 2009).

	- Five studies performed 4 to 6 weeks of treatment (Bobos et al., 2016; Falla et al., 2006; Kietrys et al., 2007; Kim and Kwag, 2016; Senthil et al., 2016).
Intensity of the exercise	- Nine studies did not present this information (Bobos et al., 2016; Cramer et al., 2013; Karlsson et al., 2014; Khan et al., 2014; Kietrys et al., 2007; Lauche et al., 2016; Rendant et al., 2011; Senthil et al., 2016; von Trott et al., 2009). - **Aerobic exercise** was performed at an intensity of 50 to 75% of VO_2max (Andersen et al., 2008). - **Strengthening exercises** were performed at an intensity of 20 to 80% of the maximum voluntary contraction/maximal isometric contraction or 8 to 15 maximum repetitions (Andersen et al., 2008; Borisut et al., 2013; Falla et al., 2006; Häkkinen et al., 2008; Javanshir et al., 2015; Lansinger et al., 2013; Lansinger et al., 2007; O'Leary et al., 2012; Salo et al., 2012; Salo et al., 2010; Ylinen et al., 2003). - **Motor control exercises** were performed with 10 seconds of isometric contraction ranging from 20 to 33 mmHg in pressure biofeedback (Borisut et al., 2013; Izquierdo et al., 2016; Javanshir et al., 2015; Kim and Kwag, 2016; O'Leary et al., 2012).

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