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## TITLE PAGE

TITLE: Effects of non-pharmacological conservative treatment on pain, range of motion and physical function in patients with mild to moderate hip osteoarthritis. a systematic review.

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**Highlights**

- Manual therapy and exercise decrease pain and improve physical function.
- Manual therapy increases range of motion in hip osteoarthritis at short term.
- Physical therapist could apply patient education and expect positive effects.

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EFFECTS OF NON-PHARMACOLOGICAL CONSERVATIVE TREATMENT ON PAIN, RANGE OF MOTION AND PHYSICAL FUNCTION IN PATIENTS WITH MILD TO MODERATE HIP OSTEOARTHRITIS. A SYSTEMATIC REVIEW.

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**ABSTRACT**

**Objective:** The purpose of this review was to identify the effects of non-pharmacological conservative treatment on pain, range of motion and physical function in patients with mild to moderate hip osteoarthritis.

**Design:** A systematic review based on Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.

**Setting:** We searched MEDLINE, PEDro, Scopus and the Cochrane Library databases for randomized controlled trials related to non-pharmacological conservative treatments for hip osteoarthritis with the following keywords: “hip osteoarthritis,” “therapeutics,” “physical therapy modalities,” and “combined physical therapy”. The PEDro scale was used for methodological quality assessment and the Oxford Centre of Evidence-Based Medicine scale was used to assess the level of evidence. Outcomes measures related to pain, hip range of motion and physical function were extracted from these studies.

**Results:** Twelve studies met the inclusion criteria. Most of the studies showed high level of evidence and only two showed low level of evidence. High quality of evidence showed that manual therapy and exercise therapy are effective in improving pain, hip range of motion and physical function. However, high quality studies based on combined therapies showed controversy in their effects on pain, hip range of motion and physical function.

**Conclusions:** Exercise therapy and manual therapy and its combination with patient education provides benefits in pain and improvement in physical function. The effects of combined therapies remain unclear. Further investigation is necessary to improve the knowledge about the effects of non-pharmacological conservative treatments on pain, hip range of motion and physical function.

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**1.Introduction**

Hip osteoarthritis (OA) is one of the most common chronic degenerative joint disease in the world.<sup>1</sup> People suffering from OA are troubled with chronic pain, loss of mobility,

stiffness around the hip joint which leads to limitations of daily activities.<sup>2,3</sup> The estimated prevalence of hip OA is approximately 3.9% for men and 5.1% for women and is expected to grow greatly and be a major public health problem in the near future.<sup>4</sup>

According to the recommendation of the American College of Rheumatology (ACR), the oral drugs are primarily pain treatment. The limitations of these medications include gastrointestinal upset and dose dependency.<sup>5</sup> Clinical practice guidelines recommend non-pharmacological interventions such as manual therapy (MT), therapeutic exercise and other conservative techniques as a part of the management of patients with mild to moderate hip OA.<sup>5-7</sup> These treatments have been proposed with the aim to reduce pain and improve hip mobility.

However, the effects of conservative treatments in patients with mild to moderate hip OA are still unclear. There is no evidence of the best treatment for patients diagnosed with hip OA with no surgery indications or previous replacements.

Therefore, we carried out this systematic review with the aim of assessing the methodological quality of studies that evaluated non-pharmacological conservative treatments in patients with mild to moderate hip OA and determining the effects of the published techniques on pain, hip range of motion (ROM) and physical function. The information from this review could help the development of rehabilitation programs focused on helping these patients, slowing the progression of the disease<sup>8</sup> and reducing costs.

## **2.Methods**

### *2.1. Design*

This review has been reported based on Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.<sup>9,10</sup> The review protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO) with ID CRD42018103864.

## 2.2. *The review question*

Studies were identified from MEDLINE, Physiotherapy Evidence Database (PEDro), Cochrane Library and SCOPUS databases. The search was performed using combinations of the following Medical Subject Headings (MeSH): “hip osteoarthritis”, “therapeutics”, “physical therapy modalities”, “combined physical therapy” linked with the Boolean operators of AND and OR and with no limits on publication date. The search strategy is shown in detail in Appendix 1.

To be included studies had to meet the following inclusion criteria based on the PICOS method:

- Population: The population of interest was patients with mild to moderate hip OA without surgical indications, diagnosed with primary OA according to ACR criteria or X-Ray.
- Intervention: The interventions of interest were non-pharmacological conservative treatments.
- Comparative intervention (Comparison): Comparison interventions of interest included other non-pharmacological conservative treatments, sham techniques, or no intervention.
- Outcome(s) of the intervention (Outcome): The studies that measured pain, ROM and/or physical function as primary variables using various methods were selected.
- Study design: randomized controlled trials.
- Language: studies published into the English, French or Spanish language were included.



Studies were excluded if they: (1) selected patients with secondary hip OA, previous hip surgery, history of congenital /adolescent hip disease; hip pelvic fracture; rheumatoid arthritis, ankylosing spondylitis or other rheumatic diseases; or intra-articular hip corticosteroid injection within one month; (2) reported patients with musculoskeletal disorders such as low back pain, neck pain, knee OA or ankle OA; (3) reported patients on waiting list for total hip surgery; (4) used pharmacological or surgical treatment as a primary intervention in any group.

### *2.3. Data collection process*

Two authors independently reviewed the titles and abstracts retrieved from all databases and determined if the studies met the inclusion criteria. Eligible full text studies were retrieved and screened again by the same reviewers. To be as inclusive as possible, reference lists of the identified studies were manually checked for inclusion. A third author decided on any disagreement.

Data were extracted from the studies by the same two reviewers independently, including conservative treatment type, single session duration, frequency of the intervention, total number of sessions, duration of care, follow up time frame, outcome measures assessing pain, ROM and/or function and other secondary outcomes relevant for hip OA such as quality of life.

### *2.4. Data synthesis and analysis*

The PRISMA checklist was used to document the studies and include information on study design, sample size, subject characteristics, treatment protocol, dependent variables, measurement tools and outcomes measures.

Methodological quality of the studies was conducted using PEDro scale checklist. The PEDro scale is based on the Delphi list developed by Verhagen and colleagues at the Department of Epidemiology, University of Maastricht. The Delphi list is a criteria list for quality assessment of clinical trials for conducting systematic reviews developed by Delphi consensus.<sup>11</sup> This scale has 11 items. A total score out of 10 is derived for each study from the number of criteria that are satisfied. A higher score indicates better methodological quality. A score of 7 or above was considered to be “high” quality, 5-6 was considered “fair” quality and 4 or below was considered “poor quality”.<sup>12</sup> The PEDro scale has shown to be a valid measure of methodological quality of clinical trials and to present high internal consistency, (0.53) inter-rater (0.4-0.75) and test-retest (r: 0.99) reliability.<sup>13</sup>

Also, the Oxford Centre of Evidence-Based Medicine (OCEBM) scale was used to assess the level of evidence of each included study. This scale is characterized by making an assessment of the evidence based on the thematic area and the type of the study. It has the advantage of grading the evidence according to the best design for each clinical scenario.<sup>14</sup>

Data extraction and study quality were revised independently by the two same authors and a third author decided on any disagreement.

### **3. Results**

Initial searches identified 2734 studies (2372 MEDLINE, 267 PEDro, 197 SCOPUS and 85 Cochrane Library). After eliminating duplicates, the title and the abstract were screened and a total of 42 studies were considered relevant to full text screening. Finally,

a total of 12 studies that met the inclusion criteria were included. The selection process is shown in Figure 1.

A total of 900 participants were examined in the trials. Marked variability was noted with regard to study participants recruited. Most studies recruited between 60 and 152 participants.<sup>15–22</sup> However, 4 studies recruited fewer than 60 participants.<sup>23–26</sup> Sample size calculation was performed in most of the studies based on determining a minimally clinically relevant difference for one or more of the primary outcomes measures.<sup>15–17,20–22,25,26</sup> The studies were done in Europe,<sup>15–19,21,25</sup> Asia,<sup>23,24,26</sup> America,<sup>20</sup> and Oceania.<sup>22</sup> Recruitment of samples varied widely, with studies recruiting from rheumatology departments, orthopaedic departments<sup>15–17,21,23,24</sup> or private clinics.<sup>20,26</sup> Four studies did not specify the recruitment.<sup>18,19,22,25</sup> The interventions were delivered by physiotherapist except for two studies in which the MT intervention was provided by chiropractors.<sup>17,20</sup>

### *3.1. Methodological quality assessment*

According to PEDro scale, 10 studies showed high quality with a score of 7 or above,<sup>15–22,25,26</sup> no one presented a fair quality and 2 studies presented a poor quality with a score of 4.<sup>23,24</sup> The quality ratings are provided in Table 1. The most part of the studies met the criteria for random allocation, similar baseline characteristics between groups, between group statistical comparisons and point measures and measures of variability for at least one key outcome. Nevertheless, in most studies neither the therapist nor the patients were blinded. This is common in most physical therapy trials because of the nature of physical therapy intervention.<sup>27</sup> Figure 2 provides the risk of bias across studies.

All the studies showed a level of evidence 1b according to Oxford scale. This level corresponds to an advisable level of recommendation, moderate evidence that the measure is effective and the benefits are higher than detriments.

### 3.2. Characteristics of the studies: interventions and outcomes

Most of the studies used MT, supervised or unsupervised exercise therapy (ET) and patient education (PE). Two studies used MT in isolation,<sup>15,25</sup> 3 used MT combined with ET,<sup>16,20,22</sup> 4 used different types of ET,<sup>18,19,23,24</sup> 2 used PE combined with MT or ET<sup>17,21</sup> and 1 ET plus ultrasounds (US).<sup>26</sup>

The frequency and the total number of sessions varied across all studies. MT sessions ranged from 1 to 3 sessions in alternative days when it was applied in isolation.<sup>15,25</sup> When MT was combined with other techniques, the number of sessions ranged from 4 to 12, over 5 to 12 weeks.<sup>16,20,22</sup> Studies in which ET was used in isolation the application varied widely. In some studies, ET was applied daily for 2 months or 3 times a week for 4 months, 60 and 48 sessions in total respectively.<sup>18,19,23,24</sup> When ET was combined with other therapies varied from 6 to 120 sessions over 2 to 9 months.<sup>16,20,22</sup> PE consisted of 5 sessions in both studies.<sup>17,21</sup> The only study that used electrotherapy applied US 5 times a week for 2 weeks, 10 sessions in total.<sup>26</sup>

In relation to the assessment of primary outcomes of the studies, 11 studies assessed pain; 4 studies used a visual analogic scale (VAS);<sup>22-24,26</sup> 7 studies used Western Ontario and McMaster Universities (WOMAC) pain subscale questionnaire<sup>15,16,19-22,26</sup> and 2 studies used the numerical rating scale (NRS).<sup>16,17</sup> 5 studies assessed hip ROM with goniometer.<sup>15-18,25</sup> 8 studies assessed physical function; 6 studies registered physical function with WOMAC physical function subscale questionnaire.<sup>16,19-22,26</sup> Other physical function measures most used were Timed up and go test (TUG)<sup>19,23,25</sup> and 30 seconds chair to stand (30CS).<sup>19,25</sup> Other tests used in the included studies were: timed stairs climbing test (TSC), 6 minutes walking test (6MWT), 15 seconds marching on the spot

test (MOS), 40 meters self-placed (SPW), five times sit to stand and 50 full walk test, 3 minutes walking test (3MWT) and 15 m time walking test.<sup>16,19,23,25,26</sup>

### *3.3. Effects of interventions*

#### *3.3.1. Pain*

Two studies showed a high quality of evidence that MT could relieve pain in the short term.<sup>15,25</sup> High quality of evidence suggested that Nordic Walking (NW) improved pain more than supervised or not strength training at 4 months of follow-up.<sup>19</sup> Low quality of evidence showed unclear outcomes about the effectiveness of low and high velocity training to relieve pain.<sup>23,24</sup> Low velocity resistance seemed to be more effective than high-velocity resistance training.<sup>24</sup> High quality evidence suggested that ET was more effective combined with hot packs and US at 1 and 3 months of follow-up.<sup>26</sup> High quality evidence showed that PE combined with MT was effective in reducing pain in the long term.<sup>17</sup> Three studies showed controversy about combined treatments; MT plus ET did not show better benefits than full kinetic chain treatment or ET in isolation or a sham treatment.<sup>16,20,22</sup>

#### *3.3.2. Range of motion*

High quality evidence was presented, showing that MT increased hip ROM in the short-term.<sup>15,25</sup> High quality of evidence suggested that NW seemed to improve ROM more than strength training, but without statistical differences between them at 4 months of follow-up.<sup>18</sup> The combination of MT plus ET did not show better benefits in hip ROM at

4 months of follow-up.<sup>16</sup> Poulsen et al.,<sup>17</sup> did not show differences in hip ROM between PE, PE plus MT and a control group.

### 3.3.3. *Function*

High quality of evidence showed that MT could improve physical function immediately after treatment.<sup>25</sup> ET based on high velocity training seemed to be more effective than low velocity training in improving physical function after 8 weeks.<sup>23</sup> High quality evidence showed that NW had better effects on physical function, measured by TUG test, 30CS, TSC and MOS, than strengthening or unsupervised exercises at 4 and 12 months of follow-up.<sup>19</sup> The combination of ET plus PE showed better benefits than PE at 10 and 16 months of follow-up<sup>21</sup> and the combination of ET plus hot packs and US showed better benefits than ET at 1 and 3 months of follow-up.<sup>26</sup> The combination of MT plus PE did not show better benefits in physical function at 4 months of follow-up.<sup>16</sup> Bennell et al.,<sup>22</sup> showed that MT plus home exercises and PE had no better benefits than a sham technique. Brantingham, et al.,<sup>20</sup> did not show differences between the application of MT in the hip joint or in the entire lower limb.

Table 2 shows the results of the selected studies.

### 3.3.4. *Effect Size*

Only 4 studies reported effect size results. ET showed a small effect size for reducing pain.<sup>24</sup> MT reported a large effect size on pain, ROM and physical function.<sup>25</sup> PE plus MT showed a large effect size on pain but a small effect size on ROM.<sup>17</sup> PE plus ET showed a small to moderate effect size for reducing pain and disability.<sup>21</sup> Results are shown in detail in Table 3.

#### 4. Discussion

This systematic review assessed the effects of non-pharmacological conservative treatments on pain, hip ROM and physical function in mild to moderate hip OA patients. Our review found high quality evidence that MT, ET and MT combined with PE reduced pain intensity at post-treatment<sup>15,25</sup> and follow-up.<sup>17,19,21</sup> The combination of MT and ET had shown unclear results about the effects on pain variable.<sup>16</sup>

According to the authors of these studies, the improvements of MT could be related to a biomechanical and neurophysiological effects. MT might provide an improvement of elasticity of the joint capsule and a stretching effect on the muscles surrounding the hip joint. In addition, the mechanical stimulus could initiate a physiological response that activates the descending pain inhibitory system as well as potentially central pain processing mechanism.<sup>28,29</sup>

The improvement achieved in pain variable with ET has been explained by two ways. One way suggests the systematic desensitization or graded repeated exposure to generate a new memory of safety in the brain replacing the maladaptive movement-related pain memories.<sup>30</sup> Another approach, directly targets to the increase of intraarticular and perisynovial concentrations of interleukin-10 and anti-inflammatory cytokine that protects chondrocytes and may be responsible for the benefits for OA shown with exercise.<sup>31</sup> However, there is a lack of evidence about which type, frequency, volume and intensity of exercise is better.

PE combined with MT<sup>17</sup> or with ET<sup>21</sup> have shown to be better than education isolated for pain.<sup>17</sup> Patients suffering some chronic pain condition used strategies to manage their pain and develop coping strategies, defined as the thoughts and actions in which people engage in their efforts to manage pain on a daily basis.<sup>32</sup> Pain education tries to increase patients'

beliefs in their own ability to control their situation, and thereby potentially improve their coping strategy.<sup>33</sup>

High quality evidence of studies showed that combined treatment with ET plus hot packs plus US is better than ET plus hot packs for intensity of pain at post-treatment and at one and three months of follow-up.<sup>26</sup> However, the effectiveness of US combined with other techniques should be interpreted with caution as this is based on the significant benefits demonstrated by only one study.

The results of our review on hip ROM showed high quality evidence that MT increases ROM in hip OA patients at post-treatment.<sup>15,25</sup> Nevertheless, the effects of ET on hip ROM still remained unclear.<sup>34,35</sup>

As previously was explained, MT might produce different effects on hip capsule and surrounding muscles that could explain the increase in hip ROM restoring the normal hip arthrokinematics.<sup>15,25</sup> Estébanez-de-Miguel et al.,<sup>15</sup> showed that a specific intensity of force mobilization appears to be necessary for increasing ROM in these patients.

The effects of ET on the three planes of hip ROM are unclear,<sup>34,35</sup> high quality evidence showed that exercise based on NW and strengthening exercises for hip and knee muscles improve different movements of hip ROM at post-treatment.<sup>18</sup> The combination of MT and ET or PE showed no better benefits.<sup>16,17</sup> This fact could be related with the interaction between both therapies or because the combined intervention spent less time on each intervention compared to isolated interventions.

For physical function outcomes, high quality evidence reflected the benefits of ET and MT in isolation in any of the tests used in the studies.<sup>19,25</sup> Combined therapies such as ET plus PE, showed better benefits than ET isolated.<sup>16</sup>



Improvements achieved in physical function by MT and ET are not explained clearly by the authors. Improvements achieved in pain intensity and ROM by MT and ET could be related to a better physical function. Although muscular training may contribute to a better physical function, it cannot be ruled out that improvements in hip ROM also played a role for improvements in functional performance.<sup>36</sup>

Although ET and MT showed positive effects on physical function, their combination showed no better benefits. French et al.,<sup>16</sup> suggested that these results were due to the fact that the intervention had not a psychological impact. These findings agree with high quality evidence that showed better benefits on physical function when ET was combined with PE.<sup>21</sup> PE combined with ET could improve the coping strategy of the patients, which, in turn, could influence an improvement in physical function.<sup>37</sup> Nevertheless, clinical guidelines recommend the combination of ET and MT,<sup>5</sup> so further investigation is necessary to describe the effects of this intervention and the results of this study should be interpreted with caution.

High quality evidence indicates that combined treatment with ET plus hot packs plus US is better than ET plus hot packs for physical function at post-treatment.<sup>26</sup> It is assumed that US have thermal and mechanical effects on the target tissue resulting in an increased local metabolism, circulation, extensibility of connective tissue and tissue regeneration.<sup>38</sup> But the results are based on only one study and most of studies about US are poor quality and not well designed. Moreover, hot therapy applied to warm up the muscles for exercise might obtain positive effects.

The results of the present review suggest that MT reduces pain, increases hip ROM and improves physical function in hip OA population in a short term. Our results also show that ET improves pain intensity and physical function and the combination of MT or ET with PE is beneficial in terms of improvement pain and physical function in hip OA

population in short and long term. These findings are in agreement with previous systematic reviews which found that MT improve physical function.<sup>39</sup> Also, therapeutic exercise based on aquatic exercise have shown decreasing pain and improving physical function in short term<sup>40</sup> and other approaches as Tai-Chi have shown decreasing pain and improving physical function in short and long term in hip and knee OA.<sup>41,42</sup> However, a definitive conclusion cannot be made due to insufficient data and limitations of the studies.

Given the demonstrated positive effects, we believe that non-pharmacological conservative treatment such as MT and ET will improve the prognosis of patients in the mild and moderate phases of hip OA. Also, the combination of MT and ET with other therapies like viscosupplementation could be a promising approach for hip OA.<sup>43</sup> This has a very important clinical application, since if this approach is undertaken at an early stage it could delay progression of the hip OA and thereby prevent the need for surgery and avoid complications and risks.

This review has several limitations. First, the heterogeneity of measurements and tools used to assess physical function, lack of power and internal and external validity of the studies. Second, although we conducted an extensive literature search because resources were limited we extracted data only from studies published in the English, Spanish and French language, potentially excluding other important evidence. And finally, we included only hip OA studies, previous reviews have included studies of OA affecting other joints as well which could explain the difference in the findings.

## **5. Conclusion**

The result of this review provides high quality evidence that MT, ET and its combination with PE decrease pain and improve physical function in patients with hip OA. There is

high quality evidence that MT increases ROM in hip OA, However the effects of ET on hip ROM are unclear. The combination of MT plus ET needs further investigation to establish the effects. We are unable to make a definitive conclusion due to the insufficient studies and limitations listed previously. Future studies should consider better methodological aspects, therapies combined, homogeneous outcome measurements and analyse effect size.

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**DECLARATION OF INTEREST:**

None

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ACCEPTED MANUSCRIPT

Figure 1. Flowchart diagram.

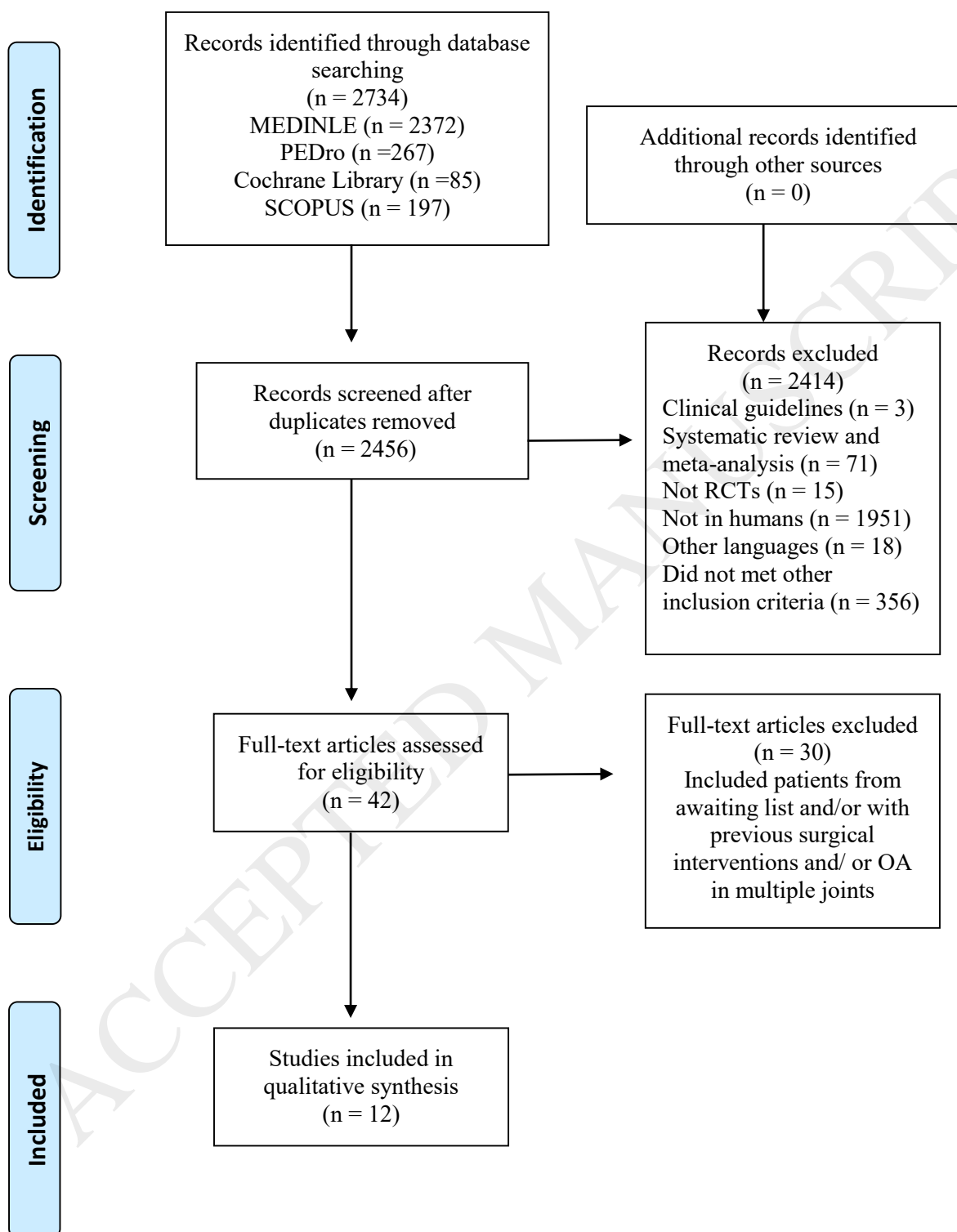


Figure 2. Risk of bias across studies presented by percent that met the PEDro scale criteria.

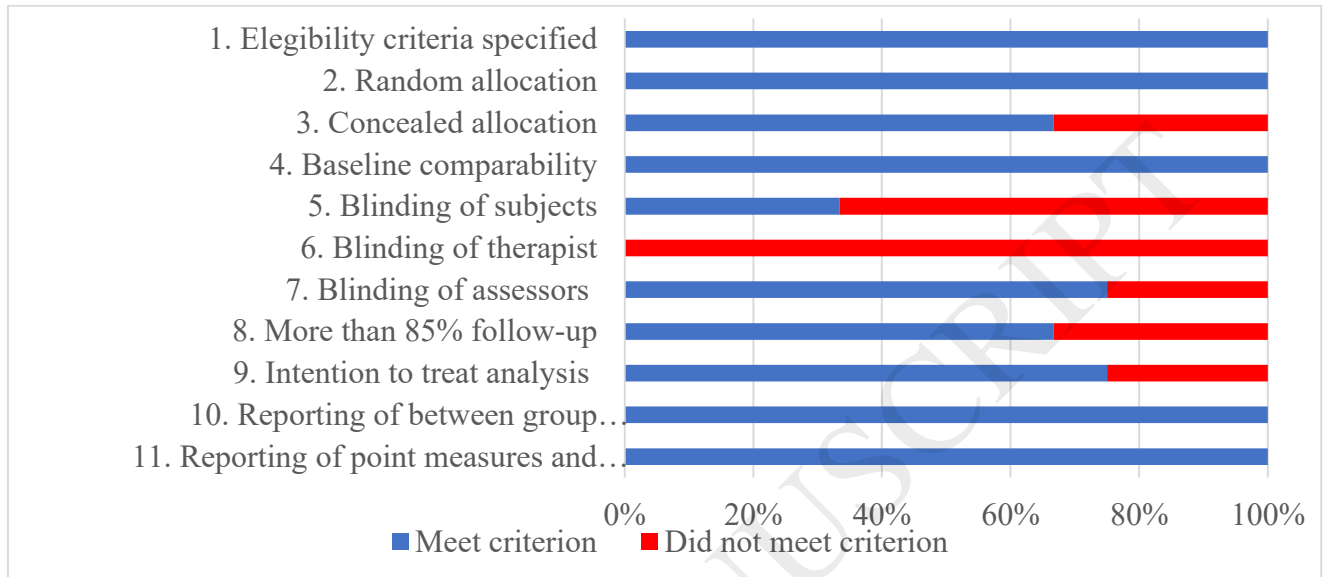


Table 1. PEDro scores for included studies.

Reference	Item											Total Score	Study quality
	1	2	3	4	5	6	7	8	9	10	11		
Bennell et al., <sup>22</sup>	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	9	High
Poulsen et al., <sup>17</sup>	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8	High
Brantingham et al., <sup>20</sup>	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	7	High
Fernandes et al., <sup>21</sup>	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8	High
Köybasi et al., <sup>26</sup>	Y	Y	Y	Y	Y	N	Y	Y	N	Y	Y	8	High
Bieler et al., <sup>18</sup>	Y	Y	Y	Y	N	N	Y	N	Y	Y	Y	7	High
Bieler et al., <sup>19</sup>	Y	Y	Y	Y	N	N	Y	N	Y	Y	Y	7	High
Fukumoto et al., <sup>23</sup>	Y	Y	N	Y	N	N	N	N	N	Y	Y	4	Poor
Fukumoto et al., <sup>24</sup>	Y	Y	N	Y	N	N	N	N	N	Y	Y	4	Poor
French et al., <sup>16</sup>	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8	High
Estébanez de Miguel et al., <sup>15</sup>	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	8	High
Beselga et al., <sup>25</sup>	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	8	High

\*1, Eligibility criteria were specified.

Not calculated in overall score.

Out of ten; Y = criterion satisfied and N = criterion not satisfied.

2, Subjects randomly allocated to groups.

3, Allocation was concealed.

4, Groups similar at baseline regarding most important prognostic indicators.

5, Blinding of subjects.

6, Blinding of all therapists.

7, Blinding of all assessors who measured at least one key outcome.

8, Measures of key outcomes obtained from more than 85% of those initially allocated to groups.

9, All subjects for whom outcome measures were available received the treatment or control condition as allocated or where this was not the case, data was analysed by "intention to treat".

10, Results of between group statistical comparisons are reported for at least one key outcome.

11, Study provides both point measures and measures of variability for at least one key outcome.

Table 2. Results of the included studies.

Study	Sample (N)	Intervention	Total number of session /Frequency / Single session duration	Variables	Results (p-value)	Follow-up time frame (p-value)
Estébanez de Miguel et al., <sup>15</sup>	G1: 61.8 ± 9.6 years (N=20) G2: 66 ± 9.5 years (N=20)  G3: 61.1 ± 9.5 years (N=20)	G1: MT low force  G2: MT medium force  G3: MT high force	3 sessions of 10 minutes of duration each one.	WOMAC pain, ROM	Greater ROM after treatment in G3 compared to G1 (p<0.05). No differences were found between G2 and G3 (p>0.05)  Greater WOMAC pain was found in G1 (p=0.002) and G3 (p=0.03). No differences were found between groups in WOMAC pain (p>0.05)	No data
Bieler et al., <sup>18</sup>	G1: 69.6 ± 5.4 years (N=50)  G2: 70.0 ± 6.3 years (N=50)  G3: 69.3 ± 6.4 years (N=52)	G1: Strength training  G2: Nordic Walking  G3: Unsupervised home-based exercise	12 sessions. 3 times weekly. Progressive strength training 1 hour, 4 weeks 50% of maximum voluntary contraction to 75% of MVC NW 12-14 intensity on Borg scale. 3 km 4 weeks to 4.3km.	ROM	No differences were found between groups after treatment (p>0.05)  G1 improved external rotation ROM after treatment (p<0.05)  G2 improved flexion ROM (p<0.01) and internal rotation	No differences were found between groups at 4 and 12 months follow-up (p>0.05)  G1 improved external and internal rotation at 4 months of follow-up  G2 improved flexion ROM at 4 and 12 months (p<0.05), external rotation at

					(p<0.05) after treatment	12 months (p<0.05) and internal rotation at 4 months (p<0.05)  G3 improved internal and external rotation ROM at 4 months of follow up (p<0.05) and external rotation at 12 months (p<0.05)
Bieler et al., <sup>19</sup>	G1: 69.6 ± 5.4 years (N=50)  G2: 70.0 ± 6.3 years (N=50)  G3: 69.3 ± 6.4 years (N=52)	G1: Strength training  G2: Nordic Walking  G3: Unsupervised home-based exercise	12 sessions. 3 times weekly. 4 weeks. Progressive strength training 1 hour, 50% of maximum voluntary contraction to 75% of MVC NW 12-14 intensity on Borg scale. 3 km 4 weeks to 4.3km.	30CS, TSC, 6MWT, TUG, MOS, WOMAC	No differences were found between groups in WOMAC pain and physical function (p>0.05)  Greater physical function after treatment in G2 compared to G1 and G3 (p<0.05)  G1 improved TUG and MOS after treatment (p<0.05)	Decreased WOMAC pain intensity in G2 compared to G1 and G3 at 4 months follow-up (p<0.05)  Greater physical function in G2 compared to G1 and G3 at 4 and 12 months follow-up (p<0.05)  G1 improved 30CS and TUG at 4 months of follow-up. G3 improved 30CS at 4 and 12 months of follow up (p<0.05) and TUG at 4 months (p<0.01).
Fukumoto et al., <sup>23</sup>	G1: 51.9 ± 7.0 years (N=15)	G1: High-velocity resistance training	Eight-week daily home-based resistance training programme. Two sets of 10	VAS, HHS,	Greater HHS scores after treatment in G1 (p<0.05) and G2 (p<0.01). No	No data

	G2: 53.1 ± 10.2 years (N=17)	G2: Low-velocity resistance training	concentric and eccentric repetitions 2 weeks. 3 sets 6 weeks. HVT as rapidly as possible and 3s eccentric phase. LHY 3s concentric an eccentric phase		differences were found between groups after treatment (p>0.05).  G2 improvement VAS after treatment (p<0.05)	
Beselga et al. <sup>25</sup>	G1: 78.3 ± 6.1 years (N=20)  G2: 77.5 ± 6.9 years (N=20)	G1: MT (Mobilization with movement)  G2: Sham MT	1 session. 3 series of 10 repetitions each with 10 minutes break.	NRS, ROM, TUG, SPW, 30CS	Greater ROM, physical function and less symptoms were found in G1 (p<0.01) and the improvements were superior to G2 (p<0.01).	No data
Bennell et al., <sup>22</sup>	G1: 64.5 ± 8.6 years (N=49)  G2: 62.7 ± 6.4 years (N = 53)	G1: MT (hip thrust manipulation + hip-lumbar spine mobilization + deep tissue massage + stretching) + home exercises + education  G2: Inactive ultrasounds	10 sessions over 12 weeks. Two initial sessions 45-60 minutes. The remainder 30 minutes.	VAS, WOMAC	Greater physical function and less symptoms after treatment in the G1 and G2 (p<0.05). No differences were found between groups (p<0.05).	After 36 weeks there were no differences between groups (p<0.05).



Fukumuto et al., <sup>24</sup>	G1: 52.4 ± 9.2 years (N=19)  G2: 52.5 ± 10.1 years (N=20)	G1: High-velocity resistance training  G2: Low-velocity resistance training	Eight-week daily home-based resistance training programme. Two sets of 10 concentric and eccentric repetitions 2 weeks. 3 sets 6 weeks. HVT as rapidly as possible and 3s eccentric phase. LHY 3s concentric an eccentric phase	3MWT, TUG, HHS, VAS	Greater physical function after treatment in G1 respect G2 (p<0.05)  No differences were found in the rest of variables between groups after treatment (p>0.05)	No data
French et al. <sup>16</sup>	G1: 62.44 ± 9.09 years (N=43)  G2: 61.43 ± 10.7 years (N=45)  G3: No data (N=43)	G1: Therapeutic exercise  G2: Therapeutic exercise + Manual therapy (translatory or rotatory techniques)  G3: control	Therapeutic exercise 6 to 8 individual sessions over 8 weeks. 30 minutes.  15 minutes of manual therapy for G2.	WOMAC, NRS, SF-36, ROM, 5 times sit to stand, 50 foot-walk test	No differences were found between G1 and G2 for any variables (p>0.05)  Greater ROM, WOMAC and physical function in G1 and G2 compared to G3 (p<0.05)  No differences were found in G1 and G2 compared to G3 for the rest variables (p>0.05)	No differences were found between G1 and G2 18 weeks follow-up (p>0.05)
Poulsen, et al., <sup>17</sup>	G1: 65.5 ± 7.3 years (N=37)  G2: 65.8 ± 8.5 years	G1: Patient Education (home stretching exercises)  G2: MT (trigger point release therapy + muscular stretching +	5 sessions (45 to 90 minutes)	NRS, ROM, HOOS pain, HOOS ADL, HOOS QoL,	G2 showed better outcomes in HOOS pain and quality of life respect G1 and G3 (p>0.05)	The improvements in G2 are maintained at 12 weeks follow-up (p<0.05)

	(N=38)  G3: 62.5 ± 9.4 years (N=36)	joint manipulation) + Patient Education  G3: Control	12 sessions. 2 times a week. 6 weeks. 15 – 25 minutes  1 session. 5 to 10 minutes.		G2 showed better outcomes for NRS and HOOS respect G3 (p<0.05)  No differences were found between groups in the rest of variables (p>0.05)	
Brantingham et al., <sup>20</sup>	G1: 62.8 ± 10.3 years (N=58)  G2: 63.3 ± 10.7 years (N=53)	G1: MMT (Hip HVLA manipulation) + exercise  G2: Kinematic chain MMT (low back, hip, knee and ankle HVLA manipulation) + exercise	9 treatments over a 5 – week period. 30 minutes each session.	WOMAC, HHS	No differences were found between groups after treatment (p>0.05)	No differences were found between groups 3 months follow-up (p>0.05)
Fernandes et al., <sup>21</sup>	G1: 57.2 ± 9.8 years (N=54)  G2: 58.4 ± 10.0 years (N=55)	G1: Patient education  G2: Patient education + supervised exercise (strengthening, functional and flexibility exercises)	PE comprised 3 group sessions and one individual 2 months later. Exercise therapy started a week after completing the education sessions twice a week for 12 weeks.	WOMAC pain, WOMAC physical function, SF-36	No differences were found between groups in WOMAC pain after 4 months. (p>0.05)  No differences were found between groups in SF-36 after 4 months (p>0,05)	Greater WOMAC physical function was found in G2 compared to G1 after 10 and 16 months (p=0.01)  No differences were found between groups in WOMAC pain at 10 and 16 months follow-up (p>0.05)  No differences were found between groups in SF-36 after 10 and 16 months (p>0,05)

Köybasi et al., <sup>26</sup>	<p>G1: 64.3 ± 6.0 years (N=15)</p> <p>G2: 64.9 ± 6.0 years (N=15)</p> <p>G3: 66.9 ± 8.2 years (N=15)</p>	<p>G1: Exercise + hot packs</p> <p>G2: Exercise + hot packs + sham US</p> <p>G3: Exercise + hot packs + US</p>	<p>2 weeks 5 session per week.</p> <p>Hot packs for 20 minutes before therapy. 20 minutes of strengthening and lengthening exercises</p>	<p>VAS on activity, VAS rest, WOMAC, 15-m timed walking test</p>	<p>Decreased pain intensity and greater physical function in G1, G2 and G3 (p&lt;0.05) and G3 showed after treatment better outcomes in VAS and WOMAC than G1 and G2 (p&lt;0.01)</p>	<p>The improvements were better in G3 than G2 and G1 in pain intensity and WOMAC questionnaire and physical function measurement by 15 timed walking test at 1 and 3 months of follow-up. (p&lt;0.001)</p>
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3MWT: 3 Minutes Walking Test; 6MWT: 6 Minutes Walking Test; 30CS: 30 seconds chair to stand; AD: Activities of daily living; G: Group; HOOS: Hip Osteoarthritis Outcome Scale; HHS: Harris Hip Score; HVLA: High Velocity Low Amplitude; MMT: Manual and Manipulative Therapy; MOS: 15 second Marching on the Spot test; MT: Manual Therapy; NPRS: Numerical Pain Rating Score; NRS: Numerical Rating Score; PE: Patient Education; QoL: Quality of life; ROM: Range of Motion; SF-36: The Short Form Health Survey; SPW: 40 meters Self-Placed; TSC: Timed Stair Climbing Test; TUG: Timed Up and Go; US: Ultrasounds; VAS: Visual Analogic Scale; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

Table 3. Data effect size between groups.

Study	Variable	Effect size (95% CIs)	
Fukmoto et al., <sup>24</sup>		High-velocity resistance training (G1) VS Low-velocity resistance training (G2)	
	HHS VAS	0.01 (-6.7 to 7.0) 0.10 (-14.8 to 11.3)	
Beselga et al., <sup>25</sup>	NPRS Hip ROM <ul style="list-style-type: none"> <li>• Flexion</li> <li>• IR</li> </ul> TUG 30CS SPW	MT (Mobilization with movement) VS Sham  1.9  3.0 1.4 1.0 1.7 1.5	
Poulsen, et al., <sup>17</sup>	NRS HOOS <ul style="list-style-type: none"> <li>• HOOS Pain</li> <li>• HOOS symptoms</li> <li>• HOOS function ADL</li> <li>• HOOS QoL</li> </ul> Hip ROM <ul style="list-style-type: none"> <li>• Flexion</li> <li>• Abd-add</li> </ul> IR-ER	Patient Education (home stretching exercises) VS Control  -0.02 (-0.49 to 0.46)  0.01 (-0.47 to 0.49) -0.13 (-0.61 to 0.34) -0.05 (-0.53 to 0.42) 0.04 (-0.44 to 0.52)  -0.54 (-1.03 to 0.04) -0.29 (-0.77 to 0.20) -0.29 (-0.78 to 0.20)	MT (trigger point release therapy + muscular stretching + joint manipulation) + Patient Education VS Control  -0.92 (-1.42 to -0.41)  1.08 (0.56 to 1.59) 0.75 (0.25 to 1.25) 0.85 (0.34 to 1.36) 0.88 (0.37 to 1.38)  -0.26 (-0.75 to 0.23) 0.25 (-0.25 to 0.74) -0.28 (-0.78 to 0.22)
Fernandes et al., <sup>21</sup>	WOMAC pain 4 months 10 months	Patient education VS Patient education + supervised exercise (strengthening, functional and flexibility exercises) -0.26 (-0.64 to 0.11) -0.35 (-0.77 to 0.07)	

	16 months	-0.30 (-0.75 to 0.15)	
	WOMAC physical function 4 months	-0.29 (-0.67 to 0.09)	
	10 months	-0.48 (-0.91 to 0.06)	
	16 months	-0.47 (-0.93 to -0.02)	

Abbreviations: 30CS: 30 seconds chair to stand; HHS: Harris Hip Score; HOOS: Hip Osteoarthritis Outcome Scale; NPRS: Numeric Pain Rating Score; NRS: Numeric Rating

Score; ROM: Range of motion; SPW: 40 meters Self-Placed; TUG: Timed Up and Go; VAS: Visual Analogic Scale.

**Appendix 1. Search strategy.**

MEDLINE (Pubmed) database: "osteoarthritis, hip"[MeSH Terms] AND (("physical therapy modalities"[MeSH Terms] OR ("physical"[All Fields] AND "therapy"[All Fields] AND "modalities"[All Fields]) OR "physical therapy modalities"[All Fields]) OR ("combined modality therapy"[MeSH Terms] OR ("combined"[All Fields] AND "modality"[All Fields] AND "therapy"[All Fields]) OR "combined modality therapy"[All Fields]) OR "therapeutics"[MeSH Terms])

Cochrane database: (hip osteoarthritis) AND (physical therapy modalities OR combined modality therapy OR therapeutics): ("osteoarthritis, hip"[MeSH Terms] OR ("osteoarthritis"[All Fields] AND "hip"[All Fields]) OR "hip osteoarthritis"[All Fields] OR ("hip"[All Fields] AND "osteoarthritis"[All Fields])) AND (("physical therapy modalities"[MeSH Terms] OR ("physical"[All Fields] AND "therapy"[All Fields] AND "modalities"[All Fields]) OR "physical therapy modalities"[All Fields]) OR ("combined modality therapy"[MeSH Terms] OR ("combined"[All Fields] AND "modality"[All Fields] AND "therapy"[All Fields]) OR "combined modality therapy"[All Fields]) OR ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields]))

Scopus database: ("hip osteoarthritis"[MeSH Terms]) AND "physical therapy modalities"[MeSH Terms]: "osteoarthritis, hip"[MeSH Terms] AND "physical therapy modalities"[MeSH Terms]

PEDro database: "hip osteoarthritis": "osteoarthritis, hip"[MeSH Terms]



## PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Page 1
<b>ABSTRACT</b>			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Page 1
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Page 1-2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Page 1
<b>METHODS</b>			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Page 2
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Page 2-3
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Page 2-3



Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Page 2-4 and Appendix 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Page 2-3
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Page 3
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Page 4
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Page 4-5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$ ) for each meta-analysis.	Page 5

Page 1 of 2

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Fig 2 and Table 1
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	No applicable
<b>RESULTS</b>			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Page 5-6 and Fig.1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Page 6-7

Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Page 6 and Fig.2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Pag 8-9
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Table 2-3
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Page 6 and Fig.2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Table 2-3
<b>DISCUSSION</b>			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Page 9-10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Page 10-13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Page 10-13
<b>FUNDING</b>			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	No applicable

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