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SYSTEMATIC REVIEW

Evidence synthesis of types and intensity of therapeutic land-based exercises to reduce pain in individuals with knee osteoarthritis

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Abstract

The objective of this study is to construct an evidence synthesis to identify the types of land-based exercises most investigated in the current literature, the intervention duration, frequency of the programs and the exercises which are most frequently implemented. A search was performed on the reference list of included and excluded studies of one systematic review, on land-based exercises for knee osteoarthritis and, an updated search of The Cochrane Library, Embase, CINAHL and PEDro was completed. Two authors independently selected the studies and a third author was consulted for an additional opinion. The inclusion criteria were male or female with tibiofemoral knee osteoarthritis, land-based exercises, non-exercise control group and randomized clinical trials. The exclusion criteria were mixed diagnosis or comparison to other types of exercise. The data were extracted by two authors. Fifty-five full-text articles were included. Strengthening, proprioception and aerobic exercises resulted in significant pain reduction. The intervention durations which were significant for pain reduction were either the period of 8–11 weeks or 12–15 weeks. The frequency of three times per week was found significant in comparison to a non-exercise control group. The results, which formed an evidence synthesis, demonstrate that there is substantial evidence regarding the benefits of strengthening exercises to reduce pain in knee osteoarthritis patients. Based on the included studies analysis, exercises should be performed three times weekly for a duration of 8–11 or 12–15 weeks. Health professionals working with knee osteoarthritis patients can use this evidence synthesis as a fast and pragmatic instrument to obtain information about several effective types of exercises for pain reduction.

Keywords Therapeutic exercise · Knee osteoarthritis · Evidence-based clinical practice guideline · Recommendations · Rehabilitation · Rheumatology · Management · Systematic review

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Abbreviations

OA	Osteoarthritis
e.g.	"For example"
RCTs	Randomized clinical trials
ACSM	American College of Sports Medicine
i.e.	"That is"
PICOTS	Population, intervention, comparator, outcomes, time, and study design
MDT	Mechanical diagnosis and therapy
min	Minutes
TIDieR	Template for intervention description and replication
CONTENT	Consensus on therapeutic exercise training

Introduction

Osteoarthritis (OA) [1] is the most common chronic joint disease in adults and can be defined as a loss of articular cartilage and other structural changes [2–4]. The symptoms of OA are pain, muscle weakness, instability, joint stiffness and loss of function. These factors could lead to an increased risk of mortality and morbidity [5]. The main intervention goals are pain reduction and improvement of physical function and quality of life (QoL) [6].

In comparison to a control group of healthy individuals, patients with knee OA have been shown to have weakened quadriceps muscles [7–9]. According to Pettee Gabriel et al.'s [10] theoretical framework, therapeutic exercises (e.g., aerobic, muscle strengthening, flexibility), sports, and mind–body exercises (e.g., tai chi, yoga, pilates) have been found to be the best leisure-time physical activity subcategories. These therapeutic exercises have been found effective to improve muscle strength, flexibility and the overall body condition of the patient [11]. Greater muscular condition could lead to an improvement of functional status and QoL [12]. Conditioning exercise in patients with a degenerative joint disease increases flexibility and one's pain threshold [13]. Further, it reduces muscle weakness, muscle atrophy, osteoporosis, depression and fatigue [13]. According to the American College of Sports Medicine (ACSM) [13], some recommendations should be followed for the protection of the joint such as performing low-impact exercises, gradually increasing intensity of strengthening exercises, avoiding overstretching and reducing the intensity of exercises if pain or swelling occurs [13].

Authors of previous studies have showed that land-based exercises can benefit patients with mild to moderate knee OA through pain reduction, increased physical function and increased QoL [14]. Also, land-based exercises are a good cost-effective method for treating knee OA [15]. Strong recommendations have been made for the practice of exercises for patients with knee OA [16–20]. The effectiveness of land-based therapeutic exercise for people with knee OA, hip OA and hip arthroplasty have also been investigated in terms of pain reduction and disability [14, 21, 22]. However, no studies have investigated the specificity about dose, frequency, and intensity of therapeutic land-based exercises for knee OA and their effects on pain reduction. According to Bartholdy [23], to implement evidence into practice, clinicians need to have sufficient information about the details of the exercise interventions including specificity about dose, frequency, and intensity. There is no general consensus about the characteristics of exercises for knee OA regarding the type and intensity of exercises [14]. A better overview of the exercises characteristics is needed to support physiotherapists in their daily practice and facilitate evidence-based decision making. Therefore, our main research questions are:

- What is the effect of different types of land-based exercises to reduce pain?
- What is the effect of different durations of a strengthening exercise program?
- What is the effect of different weekly frequencies of a strengthening exercise program?
- Which exercise characteristics (number of sets and repetitions, equipment used) are most described by the authors?

Methods

The steps to construct this evidence synthesis were: (1) identification of the scope, (2) search and selection of the studies, (3) categorization of the studies according to exercise characteristics and (4) data synthesis. The details are described below.

Identification of the scope

The following aspects of research regarding the articles were considered:

(1) The effect of different types of land-based exercise to reduce pain. (2) The effect of different exercise program durations. (3) The effect of different exercise program weekly frequencies. (4) Description of number of sets and repetitions and device used.

Search and selection of the studies

Our "database" search was based on the reference list of included and excluded studies of one recent Cochrane systematic review [14, 24] on land-based exercises for knee OA (until May 2013) as well as an updated search by Brousseau et al. [18]. The databases searched were: EMBASE (Ovid), the Cochrane library, CINAHL and PEDro. The search strategy included specific keywords and combined Medical Search History (MeSH) headings (Table 1). Two authors independently selected the studies and inserted them in the COVIDENCE platform (https://www.covidence.org/home) to conclude the process. A third author was consulted for an additional opinion. The selection criteria of the studies considered in this paper followed the PICOTS format (i.e., population, intervention, comparator, outcomes, time, and study design):

- Population: male or female with tibiofemoral knee OA diagnosis or chronic knee pain
- Intervention: land-based exercises for knee OA
- Control group: no exercise and wait list
- Type of study: randomized clinical trials (RCTs) published in English language
- Exclusion criteria: mixed diagnosis (e.g., hip osteoarthritis) and a non-exercise control group (e.g., no intervention, education, relaxation, usual care)

Categorization of studies according to exercise characteristics

The types of exercises were categorized into seven categories: (1) strengthening; (2) aerobic; (3) mind–body (4) proprioception; (5) mechanical diagnosis and therapy (MDT) exercises; (6) combination of strengthening and aerobic and (7) combination of strengthening and proprioception. The description of each category corresponds to the following characteristics:

1. *Strengthening exercises* Strength training can be defined as a systematic program of exercises designed to increase an individual's ability to exert or resist force against gravity and/or with use of weights, weight machines or elastic bands [25]. To improve the effectiveness of strengthening exercises, one or more of the following variables could be modified to increase the demands placed upon the body: (1) exercise intensity, (absolute or relative resistance/load for a given exercise/movement); (2) total repetitions performed at the current intensity; (3) repetition speed with submaximal loads; (4) rest periods may be shortened for endurance improvement or lengthened for strength and power training; and (5) training volume (total work represented as the product of the total number of repetitions performed and the resistance) [13]. The types of muscular contractions that can be part of resistance training programs are both concentric (muscle shortening) and eccentric (muscle lengthening) or isometric (no change in muscle length) [13, 26].
2. Aerobic exercise consists of an activity or combination of activities that uses large muscle groups with continu-

Table 1 Updated search strategy (2013–2016) from Fransen et al. [14]

1. EMBASE (Ovid) search strategy
1. exp osteoarthritis/
2. osteoarthr$.tw
3. (degenerative adj2 arthritis).tw
4. arthrosis.tw
5. or/1–4
6. Knee/
7. knee$.tw
8. 6 or 7
9. exp EXERCISE/
10. fitness/
11. exercise test/
12. exercise tolerance/
13. exp Sport/
14. pliability/
15. exp "physical activity, capacity and performance"/
16. exertion$.tw
17. exercis$.tw
18. sport$.tw
19. ((physical or motion) adj5 (fitness or therap$)).tw
20. (physical$ adj2 endur$).tw
21. ((strength$ or isometric$ or isotonic$ or isokinetic$ or aerobic$ or endurance or weight$) adj5 (exercis$ or train$)).tw
22. exp physiotherapy/
23. physiotherap$.tw
24. manipulat$.tw
25. kinesiotherap$.tw
26. exp REHABILITATION/
27. rehab$.tw
28. (skate$ or skating).tw
29. run$.tw
30. jog$.tw
31. treadmill$.tw
32. swim$.tw
33. bicycl$.tw
34. (cycle$ or cycling).tw
35. walk$.tw
36. (row or rows or rowing).tw
37. muscle strength$.tw
38. or/9–37
39. and/5, 8, 38
40. random$.ti,ab
41. factorial$.ti,ab
42. (crossover$ or cross over$ or cross-over$).ti,ab
43. placebo$.ti,ab
44. (doubl$ adj blind$).ti,ab
45. (singl$ adj blind$).ti,ab
46. assign$.ti,ab
47. allocat$.ti,ab
48. volunteer$.ti,ab

Table 1 (continued)

49. crossover procedure.sh
50. double blind procedure.sh
51. randomized controlled trial.sh
52. single blind procedure.sh
53. or/40–52
54. exp animal/ or nonhuman/ or exp animal experiment/
55. exp human/
56. 54 and 55
57. 54 not 56
58. 53 not 57
59. 39 and 58
2. The Cochrane Library (Wiley Interscience) search strategy
1. MeSH descriptor Osteoarthritis explode all trees
2. osteoarthr*:ti,ab
3. (degenerative next arthritis):ti,ab
4. arthrosis:ti,ab
5. (#1 OR #2 OR #3 OR #4)
6. MeSH descriptor Knee explode all trees
7. MeSH descriptor Knee Joint explode all trees
8. knee*:ti,ab
9. (#6 OR #7 OR #8)
10. MeSH descriptor Exercise explode all trees
11. MeSH descriptor Exertion explode all trees
12. MeSH descriptor Physical Fitness explode all trees
13. MeSH descriptor Exercise Test explode all trees
14. MeSH descriptor Exercise Tolerance explode all trees
15. MeSH descriptor Sports explode all trees
16. MeSH descriptor Pliability explode all trees
17. MeSH descriptor Physical Endurance explode all trees
18. exertion*:ti,ab
19. exercis*:ti,ab
20. sport*:ti,ab
21. ((physical or motion) near/5 (fitness or therap*)):ti,ab
22. (physical* near/2 endur*):ti,ab
23. ((strength* or isometric* or isotonic* or isokinetic* or aerobic* or endurance or weight*) near/5 (exercis* or train*)):ti,ab
24. MeSH descriptor Physical Therapy Modalities explode all trees
25. (physical next therap*):ti,ab
26. physiotherap*:ti,ab
27. manipulat*:ti,ab
28. kinesiotherap*:ti,ab
29. MeSH descriptor Rehabilitation explode all trees
30. rehab*:ti,ab
31. (skate* or skating):ti,ab
32. run*:ti,ab
33. jog*:ti,ab
34. treadmill*:ti,ab
35. swim*:ti,ab
36. bicycl*:ti,ab
37. (cycle* or cycling):ti,ab

Table 1 (continued)

38. walk*:ti,ab
39. (row or rows or rowing):ti,ab
40. muscle next strength:ti,ab
41. (#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR # 24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR # 39 OR #40)
42. (#5 AND #9 AND #41)
3. CINAHL (EBSCOhost) search strategy
1. S56 S55 and S42
2. S55 S54 or S53 or S52 or S51 or S50 or S49 or S48 or S47 or S46 or S45 or S44 or S43 S54 TI Allocat* random* or AB
Allocat* random*
3. S53 (MH “Quantitative Studies”)
4. S52 (MH “Placebos”)
5. S51 TI Placebo* or AB Placebo*
6. S50 TI Random* allocat* or AB Random* allocat*
7. S49 (MH “Random Assignment”)
8. S48 TI Randomi?ed control* trial* or AB Randomi?ed control* trial*
9. S47 TI singl* mask* or TI doubl* mask* or TI treb* mask* or TI tripl* mask* or AB singl* mask* or AB doubl* mask* or AB
treb* mask* or AB tripl* mask*
10. S46 TI singl* blind* or TI doubl* blind* or TI treb* blind* or TI tripl* blind* or AB singl* blind* or AB doubl* blind* or AB
treb* blind* or AB tripl* blind*
11. S45 TI “clinic* trial*” or AB “clinic* trial*”
12. S44 PT Clinical Trial
13. S43 (MH “Clinical Trials+”)
14. S42 S41 and S40 and S5
15. S41 S39 or S38 or S37 or S36 or S35 or S34 or S33 or S32 or S31 or S30 or S29 or S28 or S27 or S26 or S25 or S24 or S23 or
S22 or S21 or S20 or S19 or S18 or S17 or S16 or S15 or S14 or S13 or S12 or S11 or S10 or S9 or S8 or S7 or S6
16. S40 S8 or S7 or S6
17. S39 (ti “muscle strength*”) or (ab “muscle strength*”)
18. S38 (ti row or rows or rowing) or (ab row or rows or rowing)
19. S37 (ti walk*) or (ab walk*)
20. S36 (ti cycle* or cycling) or (ab cycle* or cycling)
21. S35 (ti bicycl*) or (ab bicycl*)
22. S34 (ti swim*) or (ab swim*)
23. S33 (ti swim*) or (ab swim*)
24. S32 (ti treadmill*) or (ab treadmill*)
25. S31 (ti jog*) or (ab jog*)
26. S30 (ti run*) or (ab run*)
27. S29 (ti skate* or skating) or (ab skate* or skating)
28. S28 (ti rehab*) or (ab rehab*)
29. S27 (MH “Rehabilitation+”)
30. S26 (ti kinesiotherap*) or (ab kinesiotherap*)
31. S25 (ti manipulat*) or (ab manipulat*)
32. S24 (ti physiotherap*) or (ab physiotherap*)
33. S23 (MH “Physical Therapy+”)

Table 1 (continued)

34. S22 TI (strength* or isometric* or isotonic* or isokinetic*or aerobic* or endurance or weight*) or AB (strength* or isometric* or isotonic* or isokinetic*or aerobic* or endurance or weight*)
35. S21 TI physical* n2 endur* or AB physical* n2 endur*
36. S20 TI physical N5 fitness or TI physical N5 therap* or AB physical N5 fitness or AB physical N5 therap* or TI motion n5 therap* or AB motion n5 therap*
37. S19 (ti sport*) or (ab sport*)
38. S18 (ti exercis*) or (ab exercis*)
39. S17 (ti exertion*) or (ab exertion*)
40. S16 (MH "Physical Endurance+")
41. S15 (MH "Pliability)
42. S14 (MH "Sports+")
43. S13 (MH "Exercise Tolerance+")
44. S12 (MH "Exercise Test+")
45. S11 (MH "Physical Fitness")
46. S10 (MH "Exertion+")
47. S9 (MH "Exercise+")
48. S8 (ti knee*) or (ab knee*)
49. S7 (MH "Knee Joint")
50. S6 (MH "Knee")
51. S5 S4 or S3 or S2 or S1
52. S4 (ti arthrosis) or (ab arthrosis)
53. S3 (ti degenerative N2 arthritis) or (ab degenerative N2 arthritis)
54. S2 (ti osteoarthr*) or (ab osteoarthr*)
55. S1 (MH "Osteoarthritis+")
4. PEDro search strategy
1. Advanced search
2. Therapy: Fitness training OR Strength training
3. Body Part: Lower leg or knee

ous contraction, that is rhythmical and aerobic in nature, e.g., walking, running, cycling or aerobic dance [25].

3. Proprioception exercises consist of stimulating the conscious and/or unconscious perception of position and movement of an extremity or a joint in space, e.g., balance exercises [27].
4. Mind–body exercises involve low-impact and low-intensity alternative exercises such as tai chi, yoga or other alternative techniques. Mind–body exercises characteristics include gentle and continuous movement combined with muscle strengthening, balance training, relaxation and mental concentration [28].
5. MDT is a methodology assessment that is derived from a mechanical sub-classification system based on patient history and the response to repeated motions and positioning. Following MDT assessment, patients are classified as having either postural, dysfunction or derangement syndromes. The most prevalent MDT subgroup is derangement syndromes. Following specific therapeutic end range of motion exercises, this subgroup presents a rapid positive change in symptoms, functional status, and/or range of motion, which corresponds to directional preference [29]. A directional preference in the knee can be of either flexion or extension [30].

As a didactic purpose and considering the clinical applicability, the intervention duration was categorized as follows:

4–7 weeks
8–11 weeks
12–15 weeks

More than 16 weeks

The exercise frequency was categorized as follows:

1. once to two times per week
2. three times per week
3. more than three times per week

When available, the exercise program's number of sets and repetitions and also the equipment used for exercise performance in the included studies were reported.

The quality of description of interventions in publications is often remarkably poor. To improve the completeness of reporting, an international group of experts and stakeholders developed the Template for Intervention Description and Replication (TIDieR) [31] checklist and guide. TIDieR is useful for the authors to describe their interventions, for the reviewers and editors to assess completeness of descriptions and for the readers to use the information [31]. Hoogeboom [32] developed the Consensus on Therapeutic Exercise Training (CONTENT) rating scale to assess the therapeutic validity of therapeutic exercise programs. This scale includes four categories: patients' eligibility, competences and settings, rationale for exercise and content and patient adherence. Slade et al. [26] published the Consensus on Exercise Reporting Template (CERT) list, a 16-item checklist designed to improve the description of exercise programs in studies. It contains seven categories: materials, provider, delivery, location, dosage, tailoring, and compliance.

Data synthesis

At the end of the intervention, the pain value (mean and standard deviation), measured with various scales (WOMAC pain, visual analog scale or other quantitative pain questionnaire), was extracted from each study. The standardized mean difference (SMD) was calculated by pooling the outcomes assessed in individual trials (95% CI) according to the Cochrane Handbook [33] recommendation using the Review Manager software (https://community.cochrane.org/help/tools-and-software/revman-5). The effect was calculated using the random effects method. The differences between groups were considered as significant when the 95% CI did not include zero. A subgroup analysis was performed to observe the effect of each type of exercise. The effects of an intervention on pain reduction was analyzed for each program duration category and for each exercise frequency category. The control group was defined as non-exercise intervention, e.g., waiting list, usual care, no intervention, diet and education.

The statistical heterogeneity was quantified by the I^2 statistic that describes the percentage of variability in effect estimates that is due to heterogeneity rather than to chance [34]. According to the Cochrane Handbook [34], the interpretation of I^2 results is as follows: (1) 0–40%: might not be important; (2) 30–60%: may represent moderate heterogeneity; (3) 50–90%: may represent substantial heterogeneity; (4) 75–100%: considerable heterogeneity. Sensitivity analyses were performed based on two domains for risk of bias assessment: random sequence generation and allocation concealment.

Risk of bias assessment

The risk of bias assessment of the included studies was performed according to the tool recommended by Cochrane Collaboration, that considers the following domains: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment, subjective self-reported outcomes (pain, physical function, QoL); (5) blinding of outcome assessment, other outcomes; (6) incomplete outcome data and (7) selective outcome reporting.

The figure generated by the 'Risk of bias' tool was used to provide summary assessments of risk of bias (Fig. 5).

Results

A total of 722 studies were identified from the searched databases. After removing duplicates and reviewing the titles and abstracts of 158 records, the full text of 58 records were reviewed. Finally, 55 RCTs were included in the metanalysis (Fig. 1).

Results of the search

Figure 1 summarizes how the studies were included or excluded in this paper. The total number of included studies was 55. As eight studies have more than one intervention group [35–43], the total number of comparison intervention control comparisons was 66. The included studies characteristics such as type of exercises, intervention duration and exercise frequency can be found in Table 2.

Most common type of exercise for knee OA and their effects on pain reduction

The effectiveness of strengthening exercise was investigated by 26 studies with 33 comparisons (intervention vs. control group) [5, 36–60]. In addition to a non-exercise control group, those studies compared different modes of strengthening exercise: individual and in-group exercise [35], isokinetic, isometric and isotonic exercise [33], high- and low-resistance exercise [37], isometric and concentric–eccentric exercise [38] and isometric and isotonic exercise [41]. Lim [43] compared how different patients (aligned knee vs. mal aligned knee) responded to a quadriceps strengthening program in different knee degrees of flexion (30° and 60° degrees of flexion). The two groups from Lim [43] were included in our synthesis. Four studies investigated the effectiveness of aerobic exercise [36, 58–60] and eight studies investigated the effectiveness of mind–body exercise [42, 61–67]. One study investigated proprioception exercise [57] and one study investigated MDT [29] as therapeutic interventions. The combination of strengthening and aerobic exercise was investigated in 11 studies with 12 comparison intervention control groups [35, 68–77] and the combination of strengthening and proprioception exercise was investigated in seven studies [40, 78–83].

The SMD analysis for the overall effect of all types of exercises (Fig. 2) in comparison to a control group showed significance in favor of all types of exercise for pain reduction (SMD −0.64 [95% CI − 0.86, − 0.43]), $I^2 = 71.2\%$ (4368 patients). The subgroup analysis showed a statistical difference for pain reduction compared to a control group in favor of: (1) strengthening exercise (SMD −0.84 [95% CI − 1.23, − 0.46], $I^2 = 94\%$, 28 studies [36–39, 41–47, 49–51, 53–57, 59, 84, 85], 2197 patients); (2) proprioception (SMD −1.02 [95% CI − 1.52, − 0.53], one study [57], 72 patients) and (3) aerobic exercises (SMD −0.63 [95% CI − 0.91, − 0.35], $I^2 = 0\%$, four studies [39, 86–88], 204 patients). There was no significant difference for the following types of exercise: (1) mind–body (SMD −0.15 [95% CI − 0.45, 0.16], $I^2 = 41\%$, six studies [42, 61, 62, 65–67], 367 patients); (2) MDT (SMD −0.32 [95% CI − 0.65, 0.00], one study [29], 158 patients) and (3) strengthening combined with aerobic exercises (SMD −0.15 [95% CI − 0.37, 0.08], $I^2 = 64\%$, nine studies [35, 68, 70, 71, 73, 74, 76, 77], 103 patients) compared to a control group. The high heterogeneity ($I^2 = 94\%$) of the analysis regarding strengthening exercises could be explained by the different modes of strengthening exercises of the included studies: isometric, isotonic and isokinetic strengthening, home-based exercises as well as the different number of sets and repetitions and the different equipment used to produce resistance.

Strengthening [5, 40, 52, 58, 60], mind–body [63, 64] and strengthening combined with aerobic [69, 72] studies were

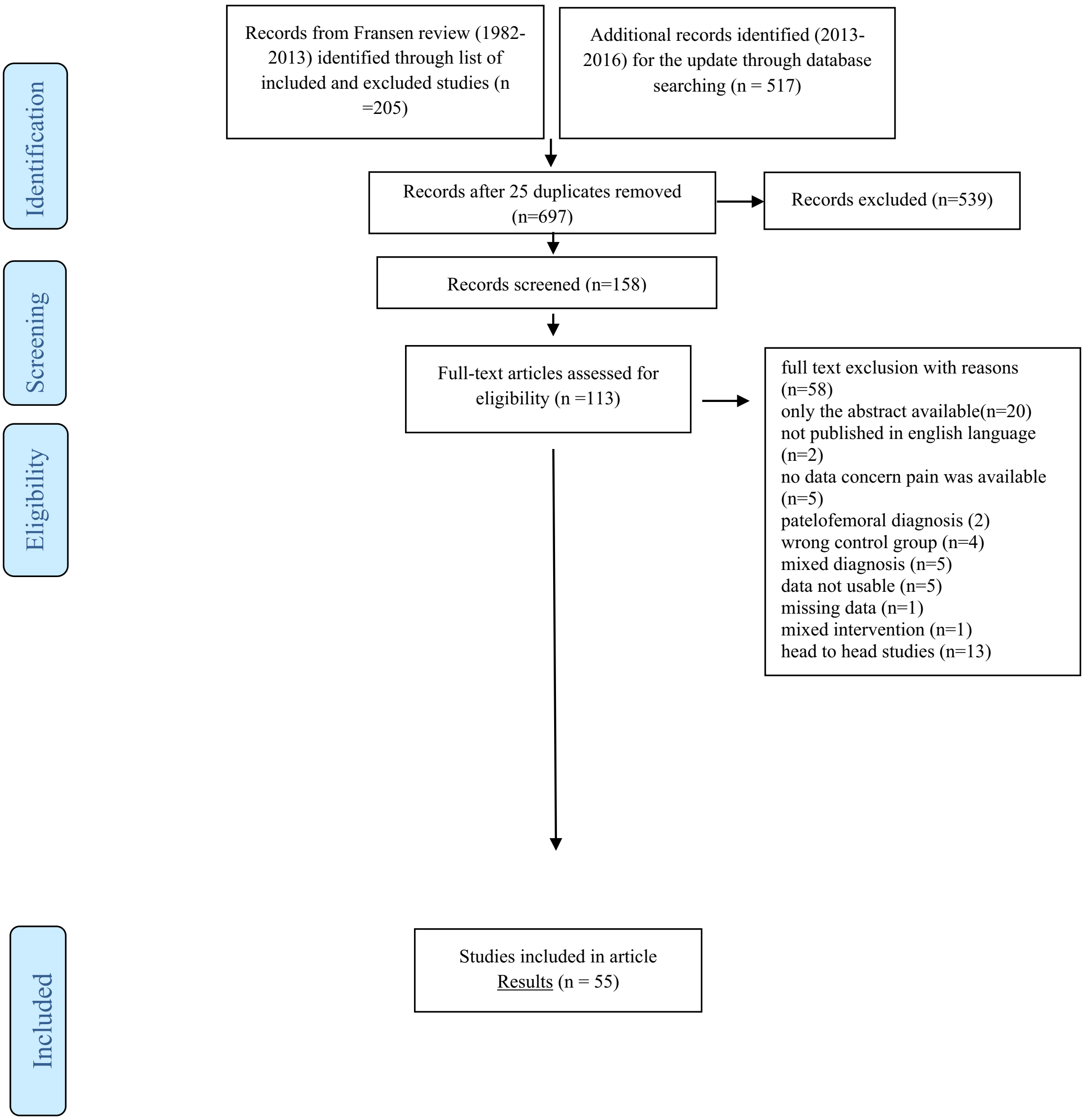


Fig. 1 PRISMA flow diagram

not included in the metanalysis, because the outcome values of the end of intervention (mean and SD) pain outcome were not available.

Effects of intervention duration and weekly frequency on pain reduction

The intervention duration of 8–11 weeks (SMD − 1.27 [95% CI − 1.74, − 0.81], $I^2 = 90\%$, 14 studies [36–38, 42, 47, 49, 51, 55, 57, 84], 1007 patients) and 12–15 weeks (SMD − 0.80 [95% CI − 1.27, − 0.33], $I^2 = 70\%$, six studies [43–45, 58, 85], 510 patients), showed significance in pain reduction (Figs. 3, 4) compared to a control group. However, there was no statistical significance for the intervention duration of 4–7 weeks (SMD − 0.07 [95% CI -0.82, 0.67], $I^2 = 88\%$, four studies [39, 46, 56, 60], 344 patients), and for more than 16 weeks (SMD − 0.94 [95% CI -1.90, 0.02], $I^2 = 98\%$), four studies [41, 50, 53, 59], 319 patients, compared to a control group.

In fourteen studies [5, 36, 38, 39, 41, 44, 47, 49, 50, 52–54, 85, 89], the frequency of three times per week [SMD − 1.22 (95% CI [− 1.67, − 0.77]), $I^2 = 90\%$, 1039 patients] showed significance in favor of exercise compared to a control group. In five studies [42, 46, 55, 56, 58, 60, 84], 375 patients, the frequency of one or two times per week [SMD − 0.46 (95% CI [− 1.36, 0.44], $I^2 = 93\%$] did not show significance for pain reduction.

Table 2 Characteristics of included studies

Study	Type of exercise category	Length of the program (weeks) category	Weekly frequency (times per week) category
An 2008	Mind–body	8–11	More than 3
Baker 2001	Strengthening	12–15	3
Bautch 1997	Strengthening and aerobic	12–15	3
Bennell 2005	Strengthening and proprioception	12–15	More than 3
Bennell 2010	Strengthening	12–15	Not reported
Bezalel 2010	Strengthening	4–7	1–2
Brismée 2007	Mind–body	12–15	3
Bruce-Brand 2012	Strengthening	8–11	3
Chang 2012	Strengthening	8–11	1–2
Chen 2014	Strengthening	8–11	3
Cheung 2014	Mind–body	≥ 16	1–2
Christensen 2015	Strengthening	≥ 16	3
Deyle 2000	Strengthening and aerobic	4–7	1–2
Doi 2008	Strengthening	8–11	Not reported
Foley 2003	Strengthening	4–7	3
Foroughi 2011	Strengthening	≥ 16	3
Fransen 2001a	Strengthening and aerobic	8–11	Not reported
Fransen 2001b	Strengthening and aerobic	8–11	Not reported
Hay 2006	Strengthening and aerobic	8–11	More than 3
Henrikssen 2014	Strengthening	12–15	3
Huang 2003a	Strengthening (isokinetic)	8–11	3
Huang 2003b	Strengthening (isometric)	8–11	3
Huang 2003c	Strengthening (isometric)	8–11	3
Huang 2005	Strengthening	8–11	
Hughes 2006	Strengthening and aerobic	8–11	3
Jan 2008a	Strengthening (high resistance)	8–11	3
Jan 2008b	Strengthening (low resistance)	8–11	3
Jenkinson 2009	Strengthening and aerobic	≥ 16	More than 3
Jorge 2015	Strengthening	8–11	1–2
Kao 2012	Strengthening	4–7	1–2
Keefe 2004	Strengthening and aerobic	12–15	3
Kim 2013	Strengthening and proprioception	12–15	1–2
Kovar 1992	Aerobic	8–11	3
Lee 2009	Mind–body	8–11	1–2
Lim 2008a	Strengthening (neutral alignment knee)	12–15	More than 3
Lim 2008b	Strengthening (malalignment knee)	12–15	More than 3
Lin 2009a	Proprioception	8–11	3
Lin 2009b	Strengthening	8–11	3
Lund 2008	Strengthening and proprioception	8–11	1–2
Maurer 1999	Strengthening	8–11	3
Messier 2004	Strengthening and aerobic	≥ 16	3
Messier 2013	Strengthening and aerobic	≥ 16	3
Mikesky 2006	Strengthening	12–15	1–2
O'Reilly 1999	Strengthening	≥ 16	More than 3
Peloquin 1999	Strengthening and aerobic	≥ 16	3
Rogind 1998	Strengthening and proprioception	12–15	More than 3
Rosedale 2014	Mckenzie	12–15	3
Salacinski 2012	Aerobic	12–15	1–2
Salli 2010a	Strengthening (isometric)	8–11	3

Table 2 (continued)

Study	Type of exercise category	Length of the program (weeks) category	Weekly frequency (times per week) category
Salli 2010b	Strengthening (concentric–eccentric)	8–11	3
Samut 2015a	Strengthening	4–7	3
Samut 2015b	Aerobic	4–7	3
Segal 2015	Aerobic	≥ 16	1–2
Silva 2015	Strengthening and proprioception	8–11	1–2
Simao 2012a	Strengthening and proprioception	12–15	3
Simao 2012b	Strengthening	12–15	3
Skou 2015	Strengthening and proprioception	12–15	1–2
Song 2003	Mind–body	12–15	3
Thorstensson 2005	Strengthening	4–7	1–2
Topp 2002a	Strengthening (isometric)	≥ 16	3
Topp 2002b	Strengthening (dynamic)	≥ 16	3
Tsai 2013	Mind–body	≥ 16	3
Wang 2011	Strengthening and aerobic	12–15	3
Wortley 2013a	Mind–body	8–11	1–2
Wortley 2013b	Strengthening	8–11	1–2
Yip 2007	Mind–body	4–7	1–2

In three studies [43, 45, 59] with 195 patients, where exercise was performed more than three times per week (SMD − 0.53, 95% CI [− 0.81, − 0.24], $I^2 = 0\%$), there was no significance for pain reduction.

Exercise characteristics (number of sets and repetitions, equipment used)

Out of 55 studies which included strengthening exercises, 18 [35, 38, 46, 50, 56, 60, 63–67, 69–71, 73, 75, 80, 88] did not report the number of sets and repetitions and the others had a wide variation ranging from 1 set of 5 repetitions to 15 sets of 15 repetitions [5, 29, 36, 37, 39–45, 47, 49, 51–55, 57–59, 61, 62, 68, 72, 74, 76–79, 82–85, 90]. In the studies which included aerobic exercise, Salacinsky [86] reported that patients used a bicycle for 60 min, Samut [87] reported that patients used a treadmill for 45 min, Segal [87] reported that patients used treadmill for 45 min and Kovar [88] instructed walking for 30 min.

In terms of the equipment used to increase the resistance during exercise, nine studies [46, 50, 56, 65, 69, 70, 73, 75, 88] did not report the information, five did not use a device [40, 61, 68, 77, 78] and nine did not require devices (yoga, tai chi and MDT) [29, 42, 61–67]. The equipment applied in the studies were free weights, elastic bands, combinations of free weights and elastic bands, gym machines, isokinetic machines and a combination of gym machines and elastic bands [5, 35–39, 41–45, 47–49, 51–55, 57–59, 71, 72, 74, 76, 79, 80, 82, 83, 85, 90]. Lin [57] applied the proprioception intervention with a previously designed computer game foot-stepping exercise that predominantly involves knee movement in a sitting position. A description of the exercise characteristics of each included study above can be found in Table 3.

Risk of bias

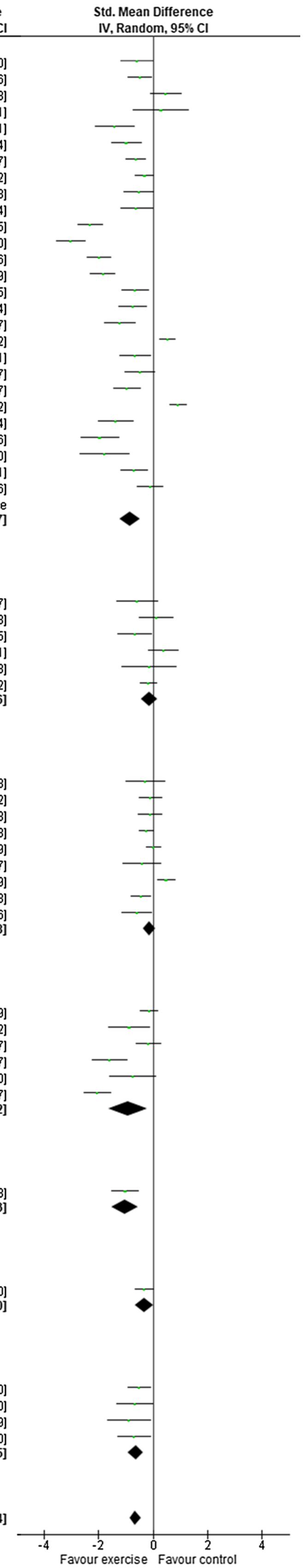
The number of studies assessed as low risk of bias for the domain "sequence generation" was 37 [29, 35, 37, 43–45, 47, 49–51, 55, 57, 59, 62, 65–67, 70, 71, 74, 76–80, 82, 83, 85–88, 90, 91], for the domain "concealment of allocation" was 23 [29, 35, 43–45, 49–51, 55, 57, 65, 74, 77, 78, 80, 82, 83, 85, 87] and for the domain "incomplete outcome data addressed" was 23 [35, 37, 38, 43, 45–47, 54, 57, 62, 65, 70, 74, 76–78, 80, 90] (Fig. 5). In most of the studies, blinding of participants was not feasible. Therefore, assessment of "blinding of participants and personnel" resulted in low risk in only three studies [61, 78, 84]. The domains "blinding of outcome assessment" and "selective reporting" was addressed as low risk in 11 studies [50, 53, 55, 61, 66, 78, 79, 82–85] and 32 studies [29, 35, 37–39, 42–46, 49, 50, 57, 59, 62, 70, 74, 77–80, 82, 83, 85, 87], respectively (Fig. 5).

Sensitivity analysis

For the sensitivity analysis, the effects of the type of studies were pooled according to two domains for risk of bias assessment (Fig. 5). Only the effects of the studies with a random sequence generation and allocation

Fig. 2 Effects of type exercise in pain reduction

Study or Subgroup	Exercises Mean	Exercises SD	Exercises Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.1.1 Strenghtening Exercises								
Baker 2001	128	101.54	23	189	101.54	23	1.8%	-0.59 [-1.18, 0.00]
Bennell 2010	4.9	3.3	45	6.5	3.3	44	2.0%	-0.48 [-0.90, -0.06]
Bezalel 2010	6.6	1.12	25	5.5	3.11	25	1.8%	0.46 [-0.10, 1.03]
Bruce-Brand 2012	9.6	4.14	10	8.33	4.08	6	1.4%	0.29 [-0.73, 1.31]
Chang 2012	2	0.9	24	3.7	1.5	17	1.7%	-1.41 [-2.11, -0.71]
Chen 2014	4.2	0.9	30	5.2	1.1	30	1.9%	-0.98 [-1.52, -0.44]
Christensen 2015	38	5.1	64	41.2	5.02	64	2.0%	-0.63 [-0.98, -0.27]
Doi 2008	22.55	20.68	73	29.59	23.94	70	2.0%	-0.31 [-0.64, 0.02]
Foroughi 2011	3.83	2.7	26	5.5	3.6	28	1.9%	-0.51 [-1.06, 0.03]
Henriksen 2014	37.5	3.46	25	39.5	2.85	23	1.8%	-0.62 [-1.20, -0.04]
Huang 2003a	2.5	1.8	56	6.1	1.3	66	1.9%	-2.31 [-2.77, -1.85]
Huang 2003b	2	1.4	58	6.1	1.3	66	1.9%	-3.02 [-3.54, -2.50]
Huang 2003c	3.2	1.6	60	6.1	1.3	66	1.9%	-1.99 [-2.42, -1.56]
Huang 2005	3.9	1.4	52	6.6	1.5	56	1.9%	-1.85 [-2.30, -1.39]
JAN 2008a	4.8	3.5	34	7.1	3.4	30	1.9%	-0.66 [-1.16, -0.15]
JAN 2008b	4.8	2.7	34	7.1	3.4	30	1.9%	-0.75 [-1.25, -0.24]
Jorge 2015	4.9	4.2	29	9.5	3.2	31	1.8%	-1.22 [-1.78, -0.67]
Kao 2012	70	16.7	114	60.5	18.5	91	2.0%	0.54 [0.26, 0.82]
Lim 2008a	22.8	16.9	27	33.6	15.4	27	1.9%	-0.66 [-1.21, -0.11]
Lim 2008b	28.5	15.4	26	36.2	16.2	26	1.9%	-0.48 [-1.03, 0.07]
Lin 2009	4.2	3	36	7.3	3.4	36	1.9%	-0.96 [-1.45, -0.47]
O'Reilly 1999	7.9	0.89	78	7.17	0.72	113	2.0%	0.92 [0.61, 1.22]
Salli 2010a	3.9	1.9	24	6.3	1.5	24	1.8%	-1.38 [-2.01, -0.74]
Salli 2010b	3.1	1.7	24	6.3	1.5	24	1.7%	-1.96 [-2.66, -1.26]
Samut 2015a	2.57	1.49	15	6.19	2.39	13	1.5%	-1.80 [-2.69, -0.90]
Topp 2002a	10.38	0.56	32	10.77	0.54	35	1.9%	-0.70 [-1.20, -0.21]
Topp 2002b	10.71	0.53	35	10.77	0.54	35	1.9%	-0.11 [-0.58, 0.36]
Wortley 2013a	0.71	1	13	1.57	0.96	6		Not estimable
Subtotal (95% CI)			**1079**			**1099**	**50.1%**	**-0.85 [-1.23, -0.47]**
Heterogeneity: Tau² = 0.92; Chi² = 430.29, df = 26 (P < 0.00001); I² = 94%								
Test for overall effect: Z = 4.42 (P < 0.00001)								
1.1.2 Mind body								
An 2008	71.1	110.1	14	138.2	112.6	14	1.7%	-0.59 [-1.34, 0.17]
Brismée 2007	3.46	2.45	22	3.19	1.97	19	1.8%	0.12 [-0.50, 0.73]
Song 2003	-2.45	3.9	22	0.61	5.1	21	1.8%	-0.66 [-1.28, -0.05]
Tsai 2013	9.56	0.83	28	8.67	3.21	27	1.9%	0.38 [-0.16, 0.91]
Wortley 2013b	141	107	12	157	96	6	1.5%	-0.15 [-1.13, 0.83]
Yip 2007	38.58	22.01	94	42.5	23.67	88	2.0%	-0.17 [-0.46, 0.12]
Subtotal (95% CI)			**192**			**175**	**10.6%**	**-0.15 [-0.45, 0.16]**
Heterogeneity: Tau² = 0.06; Chi² = 8.43, df = 5 (P = 0.13); I² = 41%								
Test for overall effect: Z = 0.95 (P = 0.34)								
1.1.3 Strengthening combined with Aerobic exercises								
Bautch 1997	2.71	2.51	15	3.51	2.82	15	1.7%	-0.29 [-1.01, 0.43]
Fransen 2001a	60.7	21.3	43	62.7	18.4	43	2.0%	-0.10 [-0.52, 0.32]
Fransen 2001b	60.7	21.3	40	62.7	18.4	43	1.9%	-0.10 [-0.53, 0.33]
Hay 2006	7.41	4.4	109	8.49	4.5	108	2.0%	-0.24 [-0.51, 0.03]
Hughes 2004	5.39	3.72	115	5.31	4.42	100	2.0%	0.02 [-0.25, 0.29]
Keefe 2004	3.19	1.85	16	4.03	2.08	18	1.7%	-0.42 [-1.10, 0.27]
Messier 2004	6.24	0.47	80	6.02	0.45	78	2.0%	0.48 [0.16, 0.79]
Peloquin 1999	3.09	1.54	59	3.94	2.22	65	2.0%	-0.44 [-0.80, -0.08]
Wang 2011	24	15	28	34	18	28	1.9%	-0.60 [-1.13, -0.06]
Subtotal (95% CI)			**505**			**498**	**17.3%**	**-0.15 [-0.37, 0.08]**
Heterogeneity: Tau² = 0.07; Chi² = 22.40, df = 8 (P = 0.004); I² = 64%								
Test for overall effect: Z = 1.28 (P = 0.20)								
1.1.4 Strenghtening AND Proprioception								
Bennell 2005	3.2	1.67	73	3.5	2.39	67	2.0%	-0.15 [-0.48, 0.19]
Da Silva 2015	2.6	1.55	15	4	1.56	15	1.7%	-0.88 [-1.63, -0.12]
Kim 2013	33.77	21.91	37	37.86	22.58	37	1.9%	-0.18 [-0.64, 0.27]
Lund 2008	51.5	4.1	25	58.1	4	27	1.8%	-1.61 [-2.24, -0.97]
Rogind 1998	4	4.53	11	7	3.09	12	1.6%	-0.75 [-1.60, 0.10]
Skou 2015	29.7	3.64	50	37.1	3.49	50	1.9%	-2.06 [-2.55, -1.57]
Subtotal (95% CI)			**211**			**208**	**10.9%**	**-0.93 [-1.64, -0.22]**
Heterogeneity: Tau² = 0.70; Chi² = 53.42, df = 5 (P < 0.00001); I² = 91%								
Test for overall effect: Z = 2.56 (P = 0.01)								
1.1.5 Proprioception								
Lin 2009b	4.3	2.3	36	7.3	3.4	36	1.9%	-1.02 [-1.52, -0.53]
Subtotal (95% CI)			**36**			**36**	**1.9%**	**-1.02 [-1.52, -0.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.07 (P < 0.0001)								
1.1.6 MDT								
Rosedale 2014	21	10	99	24	8	59	2.0%	-0.32 [-0.65, 0.00]
Subtotal (95% CI)			**99**			**59**	**2.0%**	**-0.32 [-0.65, 0.00]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.94 (P = 0.05)								
1.1.8 Aerobic only								
Kovar 1992	3.77	1.73	47	4.77	2.12	45	2.0%	-0.51 [-0.93, -0.10]
Salacinski 2012	12.4	10.7	19	23.9	21.5	18	1.8%	-0.67 [-1.33, -0.00]
Samut 2015a	3.78	2.83	14	6.19	2.39	13	1.6%	-0.89 [-1.69, -0.09]
Segal 2015	29.9	4.59	29	33.2	4.84	19	1.8%	-0.69 [-1.29, -0.10]
Subtotal (95% CI)			**109**			**95**	**7.2%**	**-0.63 [-0.91, -0.35]**
Heterogeneity: Tau² = 0.00; Chi² = 0.76, df = 3 (P = 0.86); I² = 0%								
Test for overall effect: Z = 4.35 (P < 0.0001)								
Total (95% CI)			**2231**			**2170**	**100.0%**	**-0.65 [-0.86, -0.44]**
Heterogeneity: Tau² = 0.55; Chi² = 583.59, df = 53 (P < 0.00001); I² = 91%								
Test for overall effect: Z = 6.01 (P < 0.00001)								
Test for subgroup differences: Chi² = 24.12, df = 6 (P = 0.0005), I² = 75.1%								



Study or Subgroup	Exercises Mean	Exercises SD	Exercises Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.2.1 4-7 weeks								
Bezalel 2010	6.6	1.12	25	5.5	311	25	3.5%	0.00 [-0.55, 0.56]
Kao 2012	70	16.7	114	60.5	18.5	91	3.7%	0.54 [0.26, 0.82]
Samut 2015a	2.57	1.49	15	6.19	2.39	13	3.0%	-1.80 [-2.69, -0.90]
Thorstensson 2005	36.9	1.59	30	34.9	4.84	31	3.5%	0.54 [0.03, 1.06]
Subtotal (95% CI)			**184**			**160**	**13.7%**	**-0.07 [-0.82, 0.67]**
Heterogeneity: Tau² = 0.49; Chi² = 25.60, df = 3 (P < 0.0001); I² = 88%								
Test for overall effect: Z = 0.20 (P = 0.84)								
1.2.2 8-11 weeks								
Bruce-Brand 2012	9.6	4.14	10	8.33	4.08	6	2.9%	0.29 [-0.73, 1.31]
Chang 2012	2	0.9	24	3.7	1.5	17	3.3%	-1.41 [-2.11, -0.71]
Chen 2014	4.2	0.9	30	5.2	1.1	30	3.5%	-0.98 [-1.52, -0.44]
Doi 2008	22.55	20.68	73	29.59	23.94	70	3.7%	-0.31 [-0.64, 0.02]
Huang 2003a	2.5	1.8	56	6.1	1.3	66	3.6%	-2.31 [-2.77, -1.85]
Huang 2003b	2	1.4	58	6.1	1.3	66	3.5%	-3.02 [-3.54, -2.50]
Huang 2003c	3.2	1.6	60	6.1	1.3	66	3.6%	-1.99 [-2.42, -1.56]
JAN 2008a	4.8	3.5	34	7.1	3.4	30	3.5%	-0.66 [-1.16, -0.15]
JAN 2008b	4.8	2.7	34	7.1	3.4	30	3.5%	-0.75 [-1.25, -0.24]
Jorge 2015	4.9	4.2	29	9.5	3.2	31	3.5%	-1.22 [-1.78, -0.67]
Lin 2009	4.2	3	36	7.3	3.4	36	3.5%	-0.96 [-1.45, -0.47]
Salli 2010a	3.9	1.9	24	6.3	1.5	24	3.4%	-1.38 [-2.01, -0.74]
Salli 2010b	3.1	1.7	24	6.3	1.5	24	3.3%	-1.96 [-2.66, -1.26]
Wortley 2013a	0.71	1	13	1.57	0.96	6	2.9%	-0.83 [-1.84, 0.18]
Subtotal (95% CI)			**505**			**502**	**47.5%**	**-1.27 [-1.74, -0.81]**
Heterogeneity: Tau² = 0.68; Chi² = 132.28, df = 13 (P < 0.00001); I² = 90%								
Test for overall effect: Z = 5.39 (P < 0.00001)								
1.2.3 12-15 weeks								
Baker 2001	128	101.54	23	189	101.54	23	3.4%	-0.59 [-1.18, 0.00]
Bennell 2010	4.9	3.3	45	6.5	3.3	44	3.6%	-0.48 [-0.90, -0.06]
Henriksen 2014	37.5	3.46	25	39.5	2.85	23	3.4%	-0.62 [-1.20, -0.04]
Lim 2008a	22.8	16.9	27	33.6	15.4	27	3.5%	-0.66 [-1.21, -0.11]
Lim 2008b	28.5	15.4	26	36.2	16.2	26	3.5%	-0.48 [-1.03, 0.07]
Mikesky 2006	0.8	0.3	113	1.2	0.3	108	3.7%	-1.33 [-1.62, -1.04]
Subtotal (95% CI)			**259**			**251**	**21.1%**	**-0.72 [-1.08, -0.37]**
Heterogeneity: Tau² = 0.13; Chi² = 16.82, df = 5 (P = 0.005); I² = 70%								
Test for overall effect: Z = 3.97 (P < 0.0001)								
1.2.4 more than 16 weeks								
Christensen 2015	38	5.1	64	41.2	5.02	64	3.6%	-0.63 [-0.98, -0.27]
Foroughi 2011	3.83	2.7	26	5.5	3.6	28	3.5%	-0.51 [-1.06, 0.03]
O'Reilly 1999	5	0.89	78	7.17	0.72	113	3.6%	-2.72 [-3.12, -2.32]
Topp 2002a	10.38	0.56	32	10.77	0.54	35	3.5%	-0.70 [-1.20, -0.21]
Topp 2002b	10.71	0.53	35	10.77	0.54	35	3.5%	-0.11 [-0.58, 0.36]
Subtotal (95% CI)			**235**			**275**	**17.8%**	**-0.94 [-1.90, 0.02]**
Heterogeneity: Tau² = 1.14; Chi² = 93.92, df = 4 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 1.92 (P = 0.05)								
Total (95% CI)			**1183**			**1188**	**100.0%**	**-0.93 [-1.28, -0.58]**
Heterogeneity: Tau² = 0.83; Chi² = 415.44, df = 28 (P < 0.00001); I² = 93%								
Test for overall effect: Z = 5.25 (P < 0.00001)								
Test for subgroup differences: Chi² = 7.88, df = 3 (P = 0.05), I² = 61.9%								

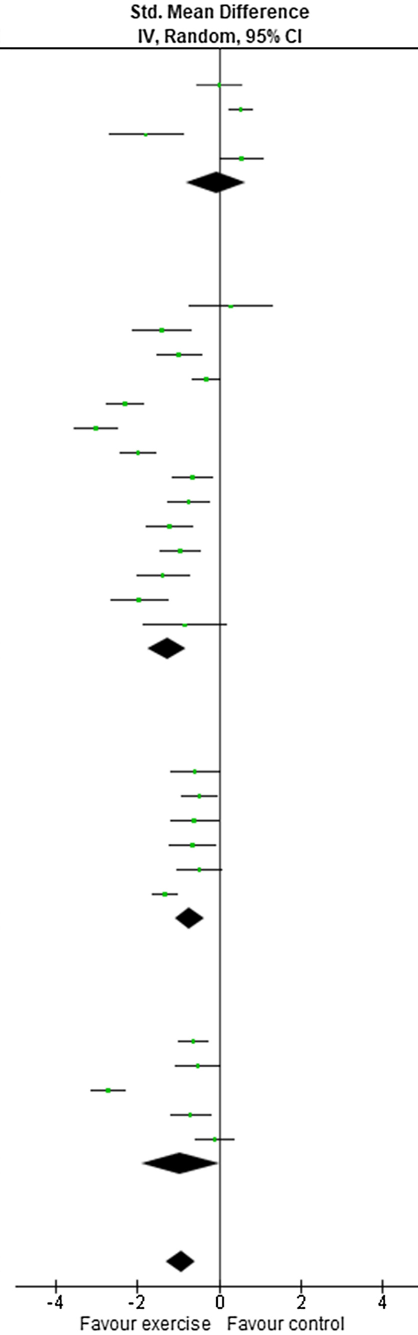


Fig. 3 Effects of intervention duration in pain reduction

concealment adequately met were pooled. The pooled effects restricted to those studies indicated a significant reduction in pain for exercise group [SMD − 0.66; 95% CI (− 0.88, − 0.44)], $I^2 = 81\%$. The subgroup analysis showed significance for the following types of exercise: strengthening [SMD − 0.64; 95% CI (− 0.77, − 0.5)], $I^2 = 4\%$, mind–body [SMD − 0.66; 95% CI (− 1.28, − 0.05)], strengthening and proprioception [SMD − 1.16; 95% CI (− 2.18, − 0.15)], $I^2 = 94\%$, proprioception [SMD − 1.02; 95% CI (− 1.52, − 0.53)] and aerobic [SMD − 0.69; 95% CI (− 1.29, − 0.10)]. The between-study heterogeneity for the strengthening exercises was reduced to $I^2 = 4\%$. However, the heterogeneity was still high for strengthening combined with aerobic ($I^2 = 78\%$) and proprioception ($I^2 = 94\%$). For mind–body, proprioception, MDT and aerobic, the heterogeneity calculation was not applicable because of the low number of studies.

	Exercises			Control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
1.3.1 Once to two times per week								
Bezalel 2010	6.6	1.12	25	5.5	3.11	25	4.0%	0.46 [-0.10, 1.03]
Chang 2012	2	0.9	24	3.7	1.5	17	3.8%	-1.41 [-2.11, -0.71]
Jorge 2015	4.9	4.2	29	9.5	3.2	31	4.0%	-1.22 [-1.78, -0.67]
Kao 2012	70	16.7	114	60.5	18.5	91	4.3%	0.54 [0.26, 0.82]
Mikesky 2006	0.8	0.3	113	1.2	0.3	108	4.2%	-1.33 [-1.62, -1.04]
Thorstensson 2005	36.9	1.59	30	34.9	4.84	31	4.1%	0.54 [0.03, 1.06]
Wortley 2013a	0.71	1	13	1.57	0.96	6	3.4%	-0.83 [-1.84, 0.18]
Subtotal (95% CI)			**348**			**309**	**27.9%**	**-0.45 [-1.24, 0.34]**
Heterogeneity: Tau² = 1.04; Chi² = 120.80, df = 6 (P < 0.00001); I² = 95%								
Test for overall effect: Z = 1.11 (P = 0.27)								
1.3.2 Three times per week								
Baker 2001	128	101.54	23	189	101.54	23	4.0%	-0.59 [-1.18, 0.00]
Bruce-Brand 2012	9.6	4.14	10	8.33	4.08	6	3.4%	0.29 [-0.73, 1.31]
Chen 2014	4.2	0.9	30	5.2	1.1	30	4.0%	-0.98 [-1.52, -0.44]
Christensen 2015	38	5.1	64	41.2	5.02	64	4.2%	-0.63 [-0.98, -0.27]
Foley 2003	0	0	0	0	0	0		Not estimable
Foroughi 2011	3.83	2.7	26	5.5	3.6	28	4.0%	-0.51 [-1.06, 0.03]
Henriksen 2014	37.5	3.46	25	39.5	2.85	23	4.0%	-0.62 [-1.20, -0.04]
Huang 2003a	2.5	1.8	56	6.1	1.3	66	4.1%	-2.31 [-2.77, -1.85]
Huang 2003b	2	1.4	58	6.1	1.3	66	4.1%	-3.02 [-3.54, -2.50]
Huang 2003c	3.2	1.6	60	6.1	1.3	66	4.1%	-1.99 [-2.42, -1.56]
Huang 2005	3.9	1.4	52	6.6	1.5	56	4.1%	-1.85 [-2.30, -1.39]
JAN 2008a	4.8	3.5	34	7.1	3.4	30	4.1%	-0.66 [-1.16, -0.15]
Maurer 1999	0	0	0	0	0	0		Not estimable
Salli 2010a	3.9	1.9	24	6.3	1.5	24	3.9%	-1.38 [-2.01, -0.74]
Samut 2015a	2.57	1.49	15	6.19	2.39	13	3.6%	-1.80 [-2.69, -0.90]
Topp 2002a	10.38	0.56	32	10.77	0.54	35	4.1%	-0.70 [-1.20, -0.21]
Subtotal (95% CI)			**509**			**530**	**55.8%**	**-1.22 [-1.67, -0.77]**
Heterogeneity: Tau² = 0.65; Chi² = 132.11, df = 13 (P < 0.00001); I² = 90%								
Test for overall effect: Z = 5.28 (P < 0.00001)								
1.3.3 More than three times per week								
Bennell 2010	4.9	3.3	45	6.5	3.3	44	4.2%	-0.48 [-0.90, -0.06]
Lim 2008a	22.8	16.9	27	33.6	15.4	27	4.0%	-0.66 [-1.21, -0.11]
Lim 2008b	28.5	15.4	26	36.2	16.2	26	4.0%	-0.48 [-1.03, 0.07]
O'Reilly 1999	5	0.89	78	7.17	0.72	113	4.2%	-2.72 [-3.12, -2.32]
Subtotal (95% CI)			**176**			**210**	**16.4%**	**-1.09 [-2.29, 0.10]**
Heterogeneity: Tau² = 1.43; Chi² = 77.00, df = 3 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 1.79 (P = 0.07)								
Total (95% CI)			**1033**			**1049**	**100.0%**	**-0.98 [-1.39, -0.57]**
Heterogeneity: Tau² = 0.99; Chi² = 411.99, df = 24 (P < 0.00001); I² = 94%								
Test for overall effect: Z = 4.72 (P < 0.00001)								
Test for subgroup differences: Chi² = 2.76, df = 2 (P = 0.25), I² = 27.6%								

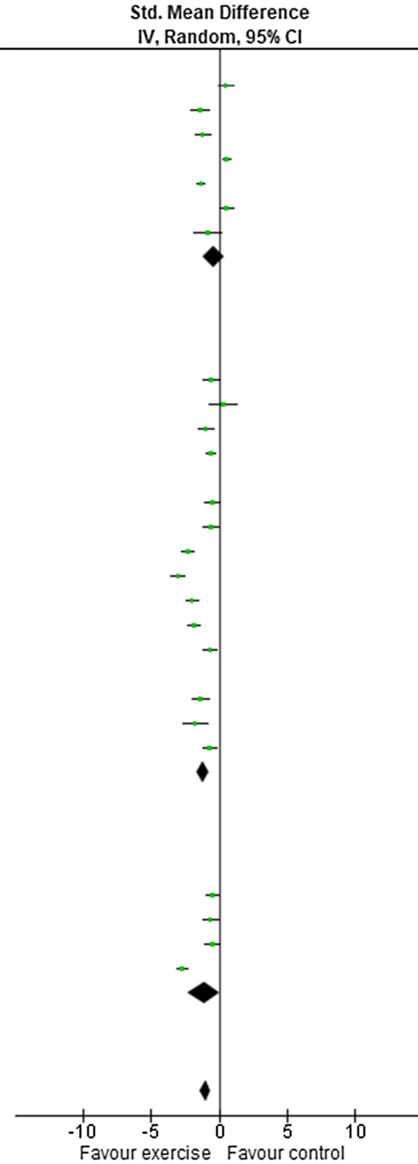


Fig. 4 Effects of exercise weekly frequency in pain reduction

Discussion

This evidence synthesis showed that strengthening exercises are the most common land-based exercises used in RCTs for patients with knee OA. The synthesis demonstrated that different types of strengthening, proprioception and aerobic exercises have significant effects on pain reduction in knee OA. The number of studies researching strengthening exercises is substantially higher than studies investigating other types of intervention.

Effective pain reduction following strengthening exercises is justified because strengthening exercises act on the quadriceps weakness, which is one of the major osteomuscular consequences of knee OA [92, 93]. The accessibility and popularity of this type of exercise could be due to the fact there is an extensive number of positive recommendations on strengthening exercise programs for knee OA management [19]. Due to the higher number of studies and popularity, the categorization regarding intervention duration and weekly frequency was carried out for strengthening exercises only. The strengthening program duration of 8–11 weeks and 12–15 weeks showed statistical significance on pain reduction compared to control group, while the program duration of 4–7 weeks and more than 16 weeks were not significant. The program duration of 4–7 weeks is assumed to be too short to produce a statistical effect on pain reduction. The program duration of 8–11 weeks and 12–15 weeks is a reasonable amount of time

Table 3 Exercise prescription and device used in the included studies

Type of exercise category	Author	Exercise prescription	Device used
Strengthening	Baker 2001	2 sets of 12 repetitions	Free weights
	Bennell 2010	3 sets of 10 repetitions	Free weights and elastic band
	Bezalel 2010	Not reported	Not reported
	Bruce-Brand 2012	3 sets of 10 repetitions	Elastic band
	Chang 2012	3 sets of 10 repetitions	Isokinetic machine
	Chen 2014	6 sets of 20 repetitions	Isokinetic machine
	Christensen 2015	Not reported	Not reported
	Doi 2008	4 sets of 20 repetitions	Free weights
	Foroughi 2011	3 sets of 8 repetitions	Gym machine
	Henriksen 2014	2–3 sets of 6–10 repetitions	Free weights and elastic band
	Huang 2005	5 sets of 20 repetitions	Isokinetic machine
	Foley 2003	1 set of 10 repetitions	Gym machines
	Huang 2003a, b, c	1 set of 20 repetitions	Isokinetic machine
	JAN 2008a	3 sets of 8 repetitions	Gym machine
	JAN 2008b	3 sets of 8 repetitions	Gym machine
	Jorge 2015	2 sets of 8 repetitions	Free weights and gym machine
	Kao 2012	Not reported	Not reported
	Lim 2008a	2–3 sets of 10 repetitions	Free weights and elastic band
	Lim 2008b	2–3 sets of 10 repetitions	Free weights and elastic band
	Lin 2009	4 sets of 6 repetitions	Isokinetic machine
	Maurer 1999	3 sets of 9 repetitions	Isokinetic machine
	Mikesky 2006	3 sets of 10 repetitions	Isokinetic machine
	O'Reilly 1999	1 set of 20 repetitions	Elastic band
	Salli 2010a	Not reported	Isokinetic machine
	Salli 2010b	Not reported	Isokinetic machine
	Samut 2015a	1–6 sets of 20 repetitions	Isokinetic machine
	Simão 2012b	1 set of 6–8 repetitions	No device
	Thorstensson 2005	Not reported	No device
	Topp 2002a	3 sets of 12 repetitions	Elastic band
	Topp 2002b	3 sets of 12 repetitions	Elastic band
	Wortley 2013b	2–3 sets of 8–12 repetitions	Free weights
Aerobic	Kovar 1992	30 min	No device (walking)
	Salacinski 2012	60 min	Bicycle
	Segal 2015	45 min	Treadmill
	Samut 2015(aerobic group)	Not reported	Treadmill
Mind–body	Song 2003	Not reported	No device
	Yip 2007	Not reported	No device
	Brismée 2007	1 set of 5 repetitions	No device
	An 2008	1 set of 20 repetitions	No device
	Lee 2009	Not reported	No device
	Wortley 2013a	2–3 sets of 8–12 repetitions	No device
	Tsai 2013	Not reported	No device
	Cheung 2014	Not reported	No device
Mechanical Diagnosis and Therapy (MDT)	Rosedale 2014	1–3 sets of 10 repetitions	No device
Proprioception	Lin 2009	20 min for each lower extremity, with a 10-min break between sides	Computer game foot-stepping exercise that predominantly involves knee movement in a sitting position was utilized

Table 3 (continued)

Type of exercise category	Author	Exercise prescription	Device used
Combination of strengthening and aerobic	Bautch 1997	1 set of 10 repetitions	No device
	Peloquin 1999	1–3 sets of 3–15 repetitions	Elastic band
	Deyle 2000	Not reported	Not reported
	Fransen 2001a	Not reported	Gym machine
	Fransen 2001b	Not reported	Gym machine
	Hughes 2006	Not reported	Free weights and elastic band
	Keefe 2004	Not reported	Not reported
	Messier 2004	2 Sets of 12 repetitions	Free weights
	Hay 2006	Not reported	Not reported
	Jenkinson 2009	1 set of 5–20 repetitions	Free weights and gym machine
	Messier 2013	Not reported	Not reported
	Wang 2011	15 sets of 10–15 repetitions	No device
Combination of strengthening and proprioception	Bennell 2005	3 sets of 5 repetitions	No device
	Kim 2013	8 repetitions	Free weights and elastic band
	Lund 2008	Not reported	Machine and elastic band
	Rogind 1998	1 set of 10 repetitions	Free weights
	Da Silva 2015	1–3 sets of 10–15 repetitions	Free weights and elastic band
	Simão 2012a	1 set of 6–8 repetitions	No device
	Skou 2015	2–3 sets of 10–15 repetitions	Free weights and elastic band

for an intervention performed at a rehabilitation center and gives the patient enough time to learn the exercises and continue them after the end of intervention. However, the traditional assumption that ‘more exercise is better’ is not reflected in our study. It seems there is a decrease in effect size after 16 weeks. Our hypothesis is that there is a lack of exercise compliance if the rehabilitation program is longer than 16 weeks, rather than the intervention effects diminish with time. Krauss [94] reported that one important reason for not adhering to an exercise regime is a decline in incentive to continue the exercise after the symptoms improve.

In regard to weekly frequency, the three times per week was effective in pain reduction, while the frequency of once, two or more than three times per week were not. Our results partially agree with the findings of Juhl [95] and Bartholdy [96] as the frequency of three times per week yielded a higher number of positive results than lower weekly frequencies. Some studies [14, 95] used the number of 12 sessions to categorize the duration of intervention. However, depending on how many times a week the patient performs the exercises, the intervention effectiveness can vary significantly. Although there was no standard protocol of exercise, the majority of the studies were compliant with the exercise recommendations in terms of weekly exercise duration of the ACSM guidelines [13].

Even with a low number of studies, aerobic exercises were found effective in pain reduction. The Ottawa panel guidelines on aerobic exercises for knee OA patients revealed that any type of aerobic exercises is effective for pain reduction [19]. Some authors showed that aerobic exercises can produce a hypoalgesic effect and reduce the magnitude of late pain sensation [97].

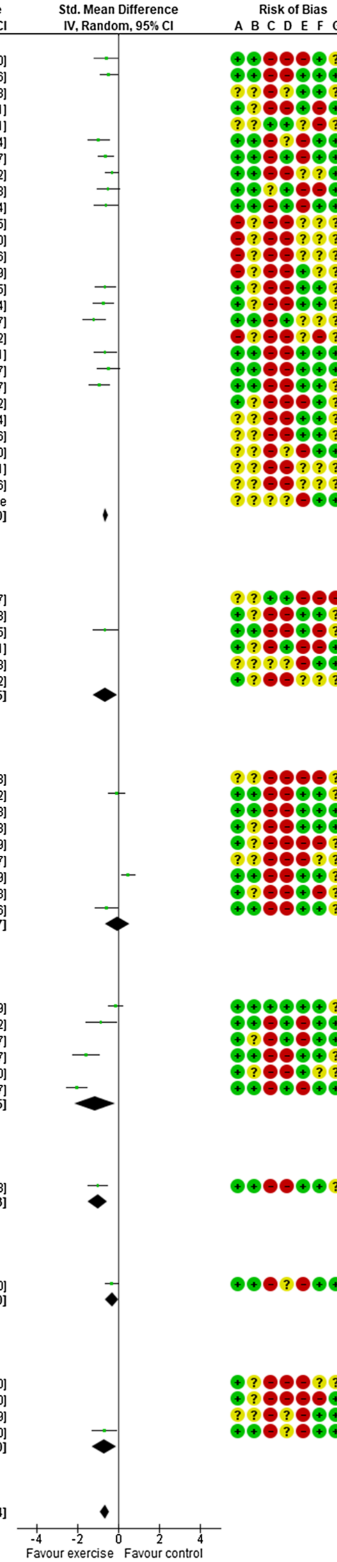
Proprioception exercises and multifaceted activities (such as tai chi and yoga) can improve or maintain physical function, and reduce falls in older people [98]. According to Brosseau [18], yoga or tai chi affects biological, psychological and social factors, particularly if these mind–body exercises are performed in a group setting. The low number of studies investigating mind–body interventions showed no statistical difference for pain reduction compared to a control group. Hence, there is insufficient evidence to support any recommendations for these types of exercises.

One study [29] investigated the use of MDT for knee OA and it did not show statistical significance. To date, there is evidence on the usefulness of MDT for low back pain [99]. However, only a handful studies have investigated its effects on other joints such as shoulder, hip, knee and ankle [100–103]. One of the classifications based on MDT assessment tool is the “derangement” classification that has been associated with positive change in pain, function, and/or range of motion as a response to specific end-range exercises. In case of the knee joint, the specific end-range exercises are flexion or extension [29]. It is worth investigating this method in further studies [30].

Based on the included studies and according to Juhl [95] and Fransen [14], different types of exercises are clinically and statistically significant in pain reduction. Fransen [14]

Fig. 5 Effects of type exercise according to two risk of bias domains in pain reduction and risk of bias assessment

Study or Subgroup	Exercises Mean	Exercises SD	Exercises Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.1.1 Strenghtening Exercises								
Baker 2001	128	101.54	23	189	101.54	23	3.8%	-0.59 [-1.18, 0.00]
Bennell 2010	4.9	3.3	45	6.5	3.3	44	4.5%	-0.48 [-0.90, -0.06]
Bezalel 2010	6.6	1.12	25	5.5	3.11	25	0.0%	0.46 [-0.10, 1.03]
Bruce-Brand 2012	9.6	4.14	10	8.33	4.08	6	0.0%	0.29 [-0.73, 1.31]
Chang 2012	2	0.9	24	3.7	1.5	17	0.0%	-1.41 [-2.11, -0.71]
Chen 2014	4.2	0.9	30	5.2	1.1	30	4.0%	-0.98 [-1.52, -0.44]
Christensen 2015	38	5.1	64	41.2	5.02	64	4.7%	-0.63 [-0.98, -0.27]
Doi 2008	22.55	20.68	73	29.59	23.94	70	4.8%	-0.31 [-0.64, 0.02]
Foroughi 2011	3.83	2.7	26	5.5	3.6	28	4.0%	-0.51 [-1.06, 0.03]
Henriksen 2014	37.5	3.46	25	39.5	2.85	23	3.9%	-0.62 [-1.20, -0.04]
Huang 2003a	2.5	1.8	56	6.1	1.3	66	0.0%	-2.31 [-2.77, -1.85]
Huang 2003b	2	1.4	58	6.1	1.3	66	0.0%	-3.02 [-3.54, -2.50]
Huang 2003c	3.2	1.6	60	6.1	1.3	66	0.0%	-1.99 [-2.42, -1.56]
Huang 2005	3.9	1.4	52	6.6	1.5	56	0.0%	-1.85 [-2.30, -1.39]
JAN 2008a	4.8	3.5	34	7.1	3.4	30	4.2%	-0.66 [-1.16, -0.15]
JAN 2008b	4.8	2.7	34	7.1	3.4	30	4.1%	-0.75 [-1.25, -0.24]
Jorge 2015	4.9	4.2	29	9.5	3.2	31	4.0%	-1.22 [-1.78, -0.67]
Kao 2012	70	16.7	114	60.5	18.5	91	0.0%	0.54 [0.26, 0.82]
Lim 2008a	22.8	16.9	27	33.6	15.4	27	4.0%	-0.66 [-1.21, -0.11]
Lim 2008b	28.5	15.4	26	36.2	16.2	26	4.0%	-0.48 [-1.03, 0.07]
Lin 2009	4.2	3	36	7.3	3.4	36	4.2%	-0.96 [-1.45, -0.47]
O'Reilly 1999	7.9	0.89	78	7.17	0.72	113	0.0%	0.92 [0.61, 1.22]
Salli 2010a	3.9	1.9	24	6.3	1.5	24	0.0%	-1.38 [-2.01, -0.74]
Salli 2010b	3.1	1.7	24	6.3	1.5	24	0.0%	-1.96 [-2.66, -1.26]
Samut 2015a	2.57	1.49	15	6.19	2.39	13	0.0%	-1.80 [-2.69, -0.90]
Topp 2002a	10.38	0.56	32	10.77	0.54	35	0.0%	-0.70 [-1.20, -0.21]
Topp 2002b	10.71	0.53	35	10.77	0.54	35	0.0%	-0.11 [-0.58, 0.36]
Wortley 2013a	0.71	1	13	1.57	0.96	6		Not estimable
Subtotal (95% CI)			**472**			**462**	**54.2%**	**-0.64 [-0.77, -0.50]**
Heterogeneity: Tau² = 0.00; Chi² = 12.44, df = 12 (P = 0.41); I² = 4%								
Test for overall effect: Z = 9.27 (P < 0.00001)								
1.1.2 Mind body								
An 2008	71.1	110.1	14	138.2	112.6	14	0.0%	-0.59 [-1.34, 0.17]
Brismée 2007	3.46	2.45	22	3.19	1.97	19	0.0%	0.12 [-0.50, 0.73]
Song 2003	-2.45	3.9	22	0.61	5.1	21	3.8%	-0.66 [-1.28, -0.05]
Tsai 2013	9.56	0.83	28	8.67	3.21	27	0.0%	0.38 [-0.16, 0.91]
Wortley 2013b	141	107	12	157	96	6	0.0%	-0.15 [-1.13, 0.83]
Yip 2007	38.58	22.01	94	42.5	23.67	88	0.0%	-0.17 [-0.46, 0.12]
Subtotal (95% CI)			**22**			**21**	**3.8%**	**-0.66 [-1.28, -0.05]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.11 (P = 0.03)								
1.1.3 Strengthening combined with Aerobic exercises								
Bautch 1997	2.71	2.51	15	3.51	2.82	15	0.0%	-0.29 [-1.01, 0.43]
Fransen 2001a	60.7	21.3	43	62.7	18.4	43	4.5%	-0.10 [-0.52, 0.32]
Fransen 2001b	60.7	21.3	40	62.7	18.4	43	0.0%	-0.10 [-0.53, 0.33]
Hay 2006	7.41	4.4	109	8.49	4.5	108	0.0%	-0.24 [-0.51, 0.03]
Hughes 2004	5.39	3.72	115	5.31	4.42	100	0.0%	0.02 [-0.25, 0.29]
Keefe 2004	3.19	1.85	16	4.03	2.08	18	0.0%	-0.42 [-1.10, 0.27]
Messier 2004	6.24	0.47	80	6.02	0.45	78	4.8%	0.48 [0.16, 0.79]
Peloquin 1999	3.09	1.54	59	3.94	2.22	65	0.0%	-0.44 [-0.80, -0.08]
Wang 2011	24	15	28	34	18	28	4.0%	-0.60 [-1.13, -0.06]
Subtotal (95% CI)			**151**			**149**	**13.3%**	**-0.04 [-0.65, 0.57]**
Heterogeneity: Tau² = 0.24; Chi² = 12.72, df = 2 (P = 0.002); I² = 84%								
Test for overall effect: Z = 0.14 (P = 0.89)								
1.1.4 Strenghtening AND Proprioception								
Bennell 2005	3.2	1.67	73	3.5	2.39	67	4.8%	-0.15 [-0.48, 0.19]
Da Silva 2015	2.6	1.55	15	4	1.56	15	3.3%	-0.88 [-1.63, -0.12]
Kim 2013	33.77	21.91	37	37.86	22.58	37	0.0%	-0.18 [-0.64, 0.27]
Lund 2008	51.5	4.1	25	58.1	4	27	3.7%	-1.61 [-2.24, -0.97]
Rogind 1998	4	4.53	11	7	3.09	12	0.0%	-0.75 [-1.60, 0.10]
Skou 2015	29.7	3.64	50	37.1	3.49	50	4.2%	-2.06 [-2.55, -1.57]
Subtotal (95% CI)			**163**			**159**	**15.9%**	**-1.16 [-2.18, -0.15]**
Heterogeneity: Tau² = 1.00; Chi² = 46.26, df = 3 (P < 0.00001); I² = 94%								
Test for overall effect: Z = 2.24 (P = 0.03)								
1.1.5 Proprioception								
Lin 2009b	4.3	2.3	36	7.3	3.4	36	4.2%	-1.02 [-1.52, -0.53]
Subtotal (95% CI)			**36**			**36**	**4.2%**	**-1.02 [-1.52, -0.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.07 (P < 0.0001)								
1.1.6 MDT								
Rosedale 2014	21	10	99	24	8	59	4.8%	-0.32 [-0.65, 0.00]
Subtotal (95% CI)			**99**			**59**	**4.8%**	**-0.32 [-0.65, 0.00]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.94 (P = 0.05)								
1.1.8 Aerobic only								
Kovar 1992	3.77	1.73	47	4.77	2.12	45	0.0%	-0.51 [-0.93, -0.10]
Salacinski 2012	12.4	10.7	19	23.9	21.5	18	0.0%	-0.67 [-1.33, -0.00]
Samut 2015a	3.78	2.83	14	6.19	2.39	13	0.0%	-0.89 [-1.69, -0.09]
Segal 2015	29.9	4.59	29	33.2	4.84	19	3.8%	-0.69 [-1.29, -0.10]
Subtotal (95% CI)			**29**			**19**	**3.8%**	**-0.69 [-1.29, -0.10]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.28 (P = 0.02)								
Total (95% CI)			**972**			**905**	**100.0%**	**-0.66 [-0.88, -0.44]**
Heterogeneity: Tau² = 0.23; Chi² = 118.42, df = 23 (P < 0.00001); I² = 81%								
Test for overall effect: Z = 5.95 (P < 0.00001)								
Test for subgroup differences: Chi² = 10.49, df = 6 (P = 0.11), I² = 42.8%								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

reported that quadriceps strengthening only, lower limb strengthening, combination of strengthening and aerobic exercise, walking programs and 'other programs' (e.g., tai chi) significantly reduce pain. However, no significant differences were noted between the various types of exercise programs to reduce pain [14]. Based on Brosseau [19], one hypothesis is that the type of exercise is not the fundamental aspect to reduce pain, but actually the movement itself. A person with knee OA is frequently unconditioned, therefore starting any exercise program (e.g., aerobic) reinforces the muscles at the initial stage of training. Bartholdy [96] demonstrated that quadriceps knee extensor strength was positively associated to changes in pain and disability and that these clinical outcomes seem unrelated to the choice of strengthening exercises or other type of exercise interventions. The authors explained that other factors such as neuromuscular function, general fitness and health, and psychosocial factors can cause pain reduction and improvement in physical function. In agreement to Juhl [95], the combination of strengthening and aerobic exercises was not significantly better than a control group in reducing pain.

The systematic review of Fransen [14] reported that studies with comparable exercise regimes were not influenced by different exercise's intensities. Therefore, specific recommendations cannot be made concerning optimal dosage (frequency, intensity, duration). The systematic review from Regnaux [24] reported that no strong recommendations related to exercise intensity can be made, since the comparison between low intensity and high intensity was inconclusive. According to Juhl [95], the intensity of the exercise does not change its effectiveness. That assumption should be viewed with caution because the report of intensity is not frequently described by the authors.

In terms of the equipment used for strengthening exercises, the elastic bands were most used throughout the studies. It is an accessible low-cost device and offers a possibility of resistance change according to the color of the band. According to the load input and the number of sets and repetitions, it is possible to increase resistance which would lead to greater muscle strength. In addition, it is an inexpensive device in comparison to others equipment such as gym or isokinetic machines [104]. On the other hand, the effectiveness of muscle strength gained with an elastic band in comparison to other equipment (gym or isokinetic machines) is not known. The included studies that reported the number of sets and repetitions of strengthening exercises, demonstrated a variation between 1 set of 20 repetitions and 5 sets of 20 repetitions. The recommendation from ACSM is 2–4 sets of 10–15 repetitions, a rest interval of 2–3 min and a gradual progression in resistance, number of repetitions and frequency [13]. For better muscle development, the load of an exercise should follow a protocol of gradual increased resistance. The included studies showed that there was no standard or adequate report of exercise prescription in the number of sets and repetitions and no mention of a load increment protocol. Therefore, it makes it difficult to analyze different results or to replicate the same exercise protocol. It would be useful to reach a consensus on an ideal number of sets and repetitions to be implemented in the guidelines and protocols. Although there is high heterogeneity between studies, Bartholdy [96] verified that a muscle strength increase of at least 30% is necessary for beneficial pain reduction. There are strong recommendations [16, 18] for strengthening exercises for knee OA patients. The significant number of studies included in this evidence synthesis, combined with the recommendations of experts, show that there is enough evidence to demonstrate that strengthening exercises are beneficial [14].

With the aim to be more precise than other studies [14, 95] regarding the categories and to emphasize other types of exercise, this evidence synthesis considered the mix of strengthening exercises with aerobic or proprioception exercises, only mind–body exercises and only proprioception exercises as distinctive categories. The extraction of the number of sets and repetitions from each study was missing in some of the previous studies. It emphasized the need for a better description of the protocol from the authors. According to Bartholdy [23], even if exercise is the intervention of choice for knee OA, there is a barrier to implement evidence into practice, because the guidelines lack specific recommendations about the exercise type, duration frequency, intensity, etc.

This evidence synthesis is focused on pain. While physical function and QoL are important elements, integrating all outcomes was beyond the purpose of this paper. As the outcome of this study is pain assessment, there are serious concerns over the risk of bias assessment of the included studies. The random sequence generation and allocation concealment were unclear in most of them. According to Schulz 1995, trials with inadequate sequence generation and allocation concealment, produce overestimated intervention effects in comparison to trials with adequate sequence generation and allocation concealment. The high heterogeneity involved when subgrouping the studies according to type of exercises, reflects the large differences in the exercise program characteristics. Also, the control group was not equal between the included studies. There were variations according to studies description (e.g., "no intervention", diet, waitlist, patient health education, physiotherapy modalities, sham exercise). It could be considered a potential bias and impact the effect size [19]. Nevertheless, the majority of the included studies were considered positive. Considering the knee OA grade of the patients included in the studies, there is no guarantee that all the included RCTs are recruiting participants with mild to moderate knee OA. The adherence to exercises is difficult to measure and can affect greatly the effectiveness of a program. Thus, the execution of home-based exercises in some studies is questionable, as it cannot be assured that the patient really performed the exercises fully. The qualitative study of Ledingham [105] about exercises' adherence in knee OA patients showed that the participants who reported low adherence were uncertain about the benefits of exercise and those who reported high adherence, i.e., more than 12 months, had more autonomy.

Conclusion

According to this evidence synthesis, there is substantial evidence regarding the benefits of strengthening exercises for knee OA. Some interventions such as mind–body and, proprioception should be more investigated.

Based on the included studies analysis, the duration of an exercise program should be 8–11 or 12–15 weeks performed three times weekly. The health professionals working with knee OA patients can use this study as a fast and pragmatic instrument to obtain information about several types of exercises for knee OA used in RCTs. Also, the researchers can use the evidence synthesis to identify the research gaps such as: the ideal and recommended exercise intensity, the type of muscle contraction and the effectiveness of mind–body exercises, proprioception exercises and MDT.

Author contributions AMI: Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. JPP: substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. LB: Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. JT: substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. OT: substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. EF: substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. SP: Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Compliance with ethical standards

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