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Neurophysiological pain education for patients with symptomatic knee osteoarthritis: A systematic review and meta-analysis☆

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ABSTRACT

Objective: To evaluate the effectiveness of neurophysiological pain education in patients with symptomatic knee osteoarthritis considering pain-related variables.
Methods: A systematic review and meta-analysis was carried out according to the PRISMA guidelines. A search was conducted in PubMed, PEDro Database, Cochrane Library, Scopus, and Web of Science. Only randomized controlled trials enrolling patients ≥ 18 years of age with symptomatic knee osteoarthritis were included. The Downs and Black quality assessment tool was used to assess the quality of the articles, and the risk of bias was evaluated with the Cochrane Risk of Bias Assessment Tool.
Results: A total of 7 studies were included in the study. Most of the studies were rated as "fair" on the Downs and Black quality assessment tool, and in the category of "some concerns" according to the Cochrane Risk of Bias Assessment Tool. Neurophysiological pain education was conducted alone or combined with exercise, joint mobilizations, or self-management programs. The number of sessions ranged from 1 to 10. The meta-analysis results showed significant differences in favor of the intervention group in pain (MD = −0.49; 95% CI = −0.66; −0.32; $p < 0.001$) and catastrophization (MD = −1.81; 95% CI = −3.31, −0.3; p = 0.02).
Conclusion, practice implications: Neurophysiological pain education interventions in isolation or combined with exercise, joint mobilizations, or self-management programs have proven to significantly improve pain and catastrophization in patients with symptomatic knee osteoarthritis. These findings could provide clinicians with more information regarding the management of patients with symptomatic knee osteoarthritis.

1. Introduction

Knee pain is one of the major public health problems affecting most older adults. Its prevalence has increased to 65% of the population over the past 20 years [1]. It is associated with substantial health care utilization, with an estimated 4 million primary care visits per year attributed only to knee pain [2]. One of the most common types of knee pain is osteoarthritis, which is one of the most frequent articular diseases in the developed world and can result in disability, particularly in the elderly population [3].

Knee osteoarthritis is usually associated with stiffness, reduced joint motion, and muscle weakness. It has long-term consequences that include reduced physical activity, deconditioning, impaired sleep, fatigue, depression, and disability [4]. The progression of the disease from episodic/acute to chronic pain has been associated with different factors such as younger age, female sex, obesity, burden of coexisting conditions, psychological factors (e.g., depression, low level of self-efficacy, pain catastrophizing), and pain sensitization [5]. Its identified causes are often joint tissue breakdown and inflammation, but the heterogenous clinical profile has been considered of primary importance in the development of knee pain chronicity [6]. It is now well established that the biomedical model does not successfully explain or treat chronic musculoskeletal pain conditions such as knee osteoarthritis. The pain and associated dysfunctions experienced by osteoarthritis patients appear to have multiple dimensions; as a result, a comprehensive biopsychosocial strategy is required for effective knee osteoarthritis management [7].

Studies indicate that factors such as pain catastrophizing,

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kinesiophobia, and ineffective pain-coping methods play a crucial role in understanding the diversity of pain levels and physical capabilities among individuals with knee osteoarthritis [8]. For these reasons, the importance of a biopsychosocial approach has progressively been highlighted, and the most recent approaches include therapeutic exercise, manual therapy associated with exercise, pharmacological pain management, and patient education [9].

Traditional musculoskeletal education models have mainly relied on biomedical education focused on anatomy, biomechanics, and pathoanatomy. These biomedical educational models have had limited efficacy in alleviating pain and disability. Moreover, it has been shown that they can even increase patient fears, anxiety, and stress, which can have a negative impact on their intended outcomes [10]. Along these lines, neurophysiological pain education has been proposed in recent decades as a key part of rehabilitation from pain, a process that requires the acquisition of new knowledge and skills [11]. Neurophysiological pain education concentrates on enhancing the patient's understanding of pain, the nervous system, and the various influences that affect pain perception. Its goal is to reshape the patient's perspective on pain by imparting the understanding that experiencing pain frequently involves hypersensitivity of the nervous system rather than solely tissue damage [12].

Specifically, several meta-analyses of patient education interventions for different chronic pain aetiologies have shown that education led to decreased disability, increased quality of life, and decreased frequency of pain episodes [13,14]. However, considering the evidence to support patient education not just in general pain management but in specific pain conditions, there are only some healthcare systems in which those interventions have been specifically included.

To the best of our knowledge, no previous reviews have analyzed the effects of neurophysiological pain education programs on patients with symptomatic knee osteoarthritis. Thus, the purpose of the current review was to examine the efficacy of neurophysiological pain education in patients with symptomatic knee osteoarthritis considering pain-related variables.

2. Materials and methods

2.1. Design

A systematic review was performed to identify clinical trials exploring the effects of neurophysiological pain education on care of patients with chronic knee pain. This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the Cochrane Collaboration statement guidelines [15]. It was previously registered at the International Prospective Register of Systematic Reviews (PROSPERO) with number CRD42022372798, available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022372798.2.2.

2.2. Search strategy

Five databases were searched from their inception up to November 2022 without language restrictions. The databases were MEDLINE via PubMed, PEDro Database, Cochrane Library, Scopus, and Web of Science.

A search strategy was created for MEDLINE and then modified to be specific to each database. The search strategy was developed using the following steps: an exploration of the MeSH Database, and the development of keywords by examining relevant key terms used in existing systematic reviews. This search strategy was tested and refined to claim it was the most effective strategy for this review. Next, the strategy was adapted to index across other databases. The full search strategy is described in Appendix I. To find other relevant articles for the study, we reviewed the reference list of other reviews and related articles.

To define the research question, we applied the PICOS (Participants, Interventions, Comparisons, Outcome, and Study design) model. The inclusion criteria were:

i) (P) Participants: adults (≥ 18 years) with symptomatic knee osteoarthritis;

Interventions: face-to-face neurophysiological pain education interventions alone or with other interventions;

i) (C) Comparisons: no intervention, standard treatment, usual care, interventions without neurophysiological pain education, placebo, or control;
ii) (O) Outcomes: pain intensity, and pain-related outcomes.
iii) (S) Study design: clinical trials.

2.3. Study selection and data extraction

One researcher undertook the initial literature search, scanning abstracts to identify eligible studies. If it was unclear whether a study met the selection criteria, advice was sought from a second researcher and a consensus opinion was made. Key data were independently extracted from the identified papers by two researchers using a structured form. Data extraction forms included the key components of general study information (i.e., title, author, and year of publication), study characteristics (i.e., population data, intervention, comparator, and outcomes), and findings, including length of follow-up.

2.4. Assessment of methodological quality and risk of bias

Data extraction and quality assessment were performed when the articles were selected.

We used the Downs and Black quality assessment method to assess the methodological quality of the studies included. This method is composed of 27 items with five subscales (i.e., study quality, external validity, study bias, confounding and selection bias, and study power); Methodological quality is classified as "excellent" if studies have a score of 26 or higher, "good" if scores range between 20 and 25, "fair" if they range between 15 and 19, and "poor" if the score is 14 or lower [16].

In addition to the methodological quality of the articles, the Cochrane Risk of Bias Assessment Tool was used to assess the risk of bias of included studies [17]. This tool assesses seven domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. For each study, the different domains were scored as "high risk of bias", "low risk of bias", or "unclear".

2.5. Statistical analysis

Where appropriate, study results regarding pain and catastrophization were pooled and a meta-analysis was conducted using Review Manager software (Rev-Man version 5.1, updated March 2011) and the Cochrane Collaboration guidelines for reviewing interventions [18].

Post-intervention means and standard deviations were used to perform the meta-analysis. When data were insufficient for a meta-analysis (e.g., no means provided, no standard deviation provided), we contacted the authors of the studies when possible. When standard deviations were missing but p-values or 95% confidence intervals were provided, these were calculated via the embedded Review Manager calculator. If different intervention arms were compared in a trial, they were added separately to the data of the meta-analysis.

Continuous outcomes were analyzed using weighted mean differences when all studies measured outcomes on the same scale. Standardized mean differences were used when all scales were assumed to measure the same underlying symptom or condition, but some studies measured outcomes on different scales. Ninety-five percent confidence intervals were computed for all outcomes.

Overall mean effect sizes were estimated using random effect models or fixed effect models according to statistical heterogeneity I^2 tests. $I^2 >$ 50% is considered a heterogeneous meta-analysis, and a random-effects model was used. A visual inspection of the forest plots for outlier studies was also undertaken. Sources of heterogeneity were explored, and sensitivity analyses were conducted by excluding trials with a high risk of detection or attrition bias.

A sensitivity analysis was conducted to explore potential sources of heterogeneity and to determine how sensitive the conclusions of the study were to the particular method or study design feature used. If the effect and confidence intervals in the sensitivity analysis led to the same conclusion as the primary meta-analysis value, the results are deemed robust.

3. Results

3.1. Search process

An initial search of the electronic databases yielded 322 records. After eliminating duplicates, a total of 246 studies were screened. We excluded those that did not meet the inclusion criteria defined with the PICOS strategy. Screening based on the title resulted in the selection of 38 articles. Screening based on the abstract resulted in the selection of 20 articles. All those studies were available as full-text articles. These retrieved articles were subsequently evaluated further according to the inclusion criteria. After screening the full text of each article, 7 studies were included [19–25].

The PRISMA flow diagram presenting the study selection process is shown in Fig. 1.

3.2. Characteristics of eligible RCTs included for analysis

Information on their characteristics is provided in Table 1.

A total of 7 studies were considered eligible and included for analysis in this study. The oldest included study was published in 2015 [25] and the newest one dated from 2020 [19,20].

A total of 870 adult patients with symptomatic knee osteoarthritis were included in this systematic review and meta-analysis. Sample size ranged from 41 [25] to 300 [20] participants, and mean age ranged from 57 [25] to 74.1 [21] years old. Additionally, the percentage of women included in the studies was higher than the percentage of males in all studies except that of Birch et al., 2020 [19]. There was one article [20] in which mean age and gender were not reported.

3.3. Content and implementation of neurophysiological pain education programs

Information on the neurophysiological pain education interventions conducted in each study is provided in Table 1. Specifically, the table shows the content of the comparison group approach, the content of the experimental interventions, the intervention duration, the outcome measures, the follow-up, and the main results.

Three studies [19–21] compared usual care in addition to neurophysiological pain education with a control group that received usual care. One study [22] compared passive mobilization in addition to neurophysiological pain education with a control group that received passive mobilization in addition to biomedical education. One study [23] compared neurophysiological pain education alone to exercise alone and neurophysiological pain education with exercise to exercise alone. One study [24] compared a treatment including neurophysiological pain education, exercise, dietary advice, insoles, and pain medication to a control group that received usual care. One study [25] compared neurophysiological pain education in addition to a self-management program and exercise to a control group that received a self-management program alone.

The mean duration of the interventions was 5.1 sessions and ranged from 1 session to 10 sessions.

3.4. Outcome analysis

The most frequent outcomes were pain and catastrophization. Pain was analyzed in all the studies included. The most frequently used scale was a Visual Analogue Scale (VAS) [19,23,24]. The Numeric Scale (NS) [21] and the subscales of the Knee Injury and Osteoarthritis Outcome Score (KOOS) [20], Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [19], and Lequesne Algofunctional Index (LAI) [25] were also used. Catastrophization was included in five of the seven studies using the Pain Catastrophizing Scale [19–23].

3.5. Results of the interventions

Data from seven RCTs were included in the meta-analysis. All the studies included analyzed pain and four studies analyzed catastrophization [19,21–23].

Results obtained for pain were analyzed as shown in Fig. 2a.

Comparing neurophysiological pain education with usual care, the mean difference showed a non-significant overall effect (SMD = −0.22, 95% CI = −0.65, 0.22; p = 0.33, four studies [19–21,23].

When comparing neurophysiological pain education combined with exercise to a control group, results showed significant differences in favor of the intervention group (SMD = −0.50, 95% CI = −0.81, −0.19; p = 0.002, three studies [23–25]).

The pooled analyses showed significant results in favor of the intervention groups (SMD = −0.35, 95% CI = −0.63, −0.07; p = 0.01).

Results showed heterogeneity, with a significant variability of I^2 = 61% not attributable to chance. After performing the sensitivity analysis (Fig. 2b), it was possible to reduce the I^2 to 31% and therefore apply a fixed-effect model. The pooled mean difference (MD) showed a significant overall effect of respiratory training compared to the control group (MD = −0.49; 95% CI = −0.66; −0.32; p < 0.001).

Results obtained in catastrophization were analyzed as shown in Fig. 3a.

Comparing neurophysiological pain education alone to a control group, results showed no significant results in favor of the intervention groups (SMD = −1.12, 95% CI = −3.79, 1.55; p = 0.41, three studies [19,21,23]). When neurophysiological pain education combined with exercise was compared to a control group, results showed no significant differences between groups (SMD = −1.30, 95% CI = −5.83, 3.23; p = 0.57, one study [23]). Finally, neurophysiological pain education and joint mobilization led to significant improvements compared to a control group (SMD = −12.00, 95% CI = −19.13, −4.87; p = 0.001, one study [22]).

The pooled analyses obtained no significant results in favor of the intervention groups (SMD = −2.20, 95% CI = −5.53, 0.93; p = 0.17).

Results showed heterogeneity, with a significant variability of I^2 = 63% not attributable to chance. After performing the sensitivity analysis (Fig. 3b), it was possible to reduce the I^2 to 10% and therefore apply a fixed-effect model; the pooled mean difference (MD) showed a significant overall effect of respiratory training compared to the control group (MD = −1.81; 95% CI = −3.31, −0.3; p = 0.02).

3.6. Methodological quality and risk of bias

Seven studies were assessed with the Downs and Blacks checklist for clinical trials. The methodological quality of the 7 articles included is described in Table 2. The average score of studies included in this systematic review was 18.7. Following the cutoff points to grade studies according to their methodological quality, five articles were rated as "fair" (15–19 points) [19,21,22,24,25] and two articles were rated as "good" (20–25 points [20,23].

One item was rated "0" in all the studies, because it was impossible to blind the subjects to the type of intervention undergone.

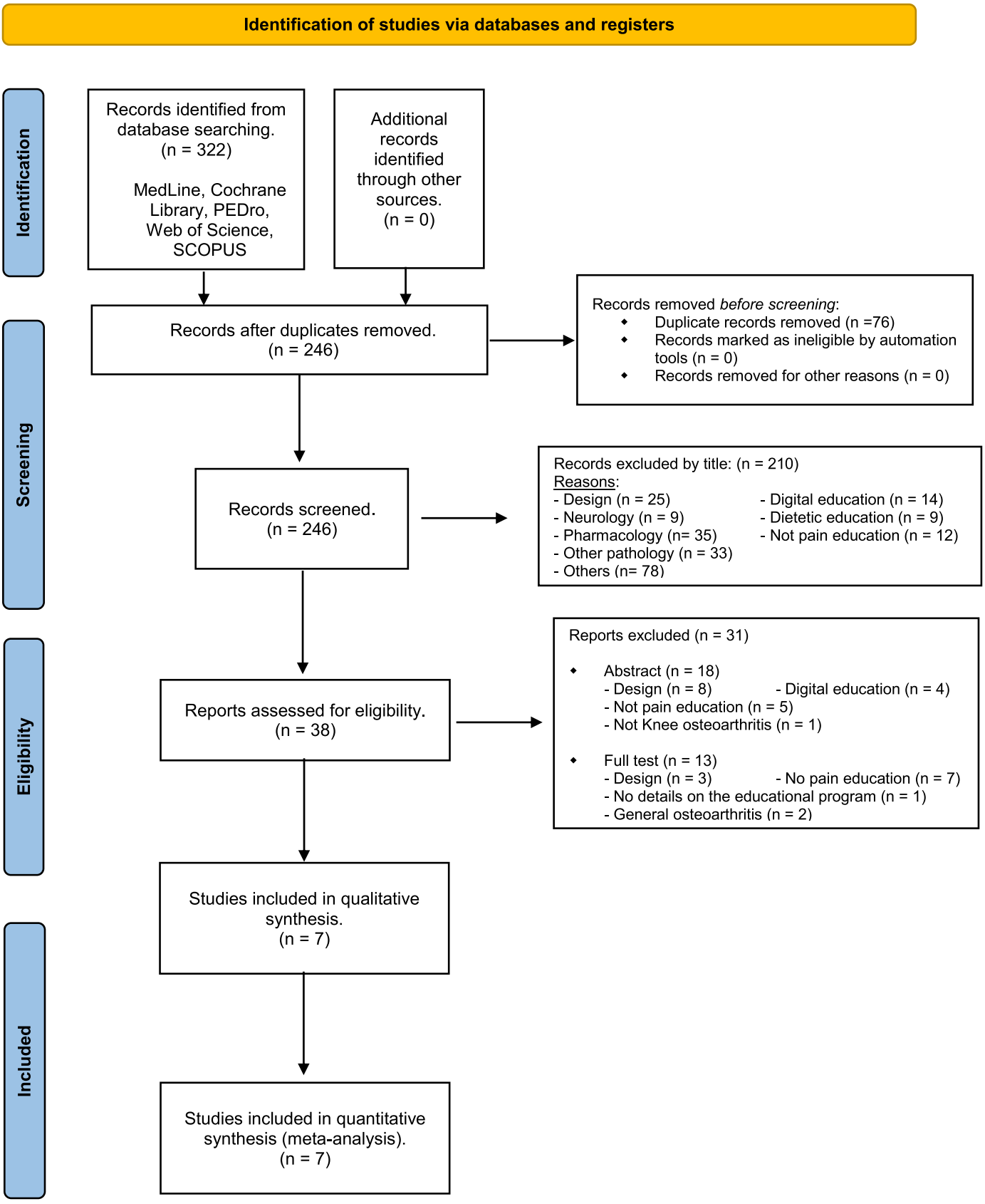


Fig. 1. Flow diagram.

Table 1
Description of the appraised studies.

Author, year	Participants	Intervention protocols and controls	Frequency and duration	Outcomes (Measure) Follow-up	Results
Birch, 2020	N = 60 Mean age: IG: 66 CG: 66 Female (%): IG: 29 CG: 38 Severity (% grade 4) IG: NR CG: NR	**Intervention group: Pain Education** Standard information about surgical intervention + 6 sessions of pain education. **Control group: Usual care** Standard information about surgical intervention.	7 individual sessions of approximately 45 minutes, 3 sessions preoperatively and 4 sessions postoperatively.	**Pain**: VAS **Catastrophization:** PCS **Self-Efficacy**: PSEQ **Follow-up:** 3 months 12 months	No significant differences were found between groups at the end of the intervention in any of the variables. At 3 months follow-up and at 12 months follow-up, no significant differences were found between groups in any of the variables.
Foo, 2020	N = 300 Mean age: IG: NR CG: NR Female (%): IG: NR CG: NR Severity (% grade 4) IG: NR CG: NR	**Intervention group: Pain Education** Physiotherapy sessions + Knee Book + Three sessions of group cognitive behavioral-based therapy. **Control group: Usual care** Physiotherapy sessions + Knee Book.	3 group sessions (8 to 12 participants) for two-and-a-half-hour total time.	**Pain intensity**: VAS **Pain Catastrophizing:** PCS **Self-Efficacy:** PSEQ **Follow-up:** 1 month 6 months	IG improved significantly in pain at the end of the intervention compared to baseline and CG. At 1 month follow-up, IG improved significantly in pain and catastrophization compared to baseline and CG. At 6 months follow-up, IG improved significantly compared to baseline in all the variables.
Louw, 2019	N = 103 Mean age: IG: 74.1 ± 10.6 CG: 74.1 ± 9.5 Female (%): IG: 65 CG: 57 Severity (% grade 4) IG: NR CG: NR	**Intervention group: Pain Education** Traditional hospital preoperative program + Education covering anatomy, information about the surgery, pain medication and postoperative rehabilitation + Booklet + Additional 30-minutes Pain Neuroscience Education adapted from the PNE program for lumbar surgery. **Control group:** Traditional hospital preoperative program + Education covering anatomy, information about the surgery, pain medication and postoperative rehabilitation + Booklet.	1 group session (8 to 10 participants) of 30-minutes	**Pain:** NS **Catastrophization**: PCS **Self-Efficacy:** PSEQ **Follow-up:** 1 month 3 months 6 months	IG improved significantly in pain catastrophizing and self-efficacy at the end of the intervention compared to baseline. At 1 month follow-up, IG improved significantly in pain intensity and pain catastrophizing compared to baseline and GC. At 6 months follow-up, IG improved significantly compared to baseline in all the variables. IG improved significantly in pain intensity and pain catastrophizing compared to GC.
Lluch, 2018	N = 44 Mean age: IG: 67.7 ± 7.8 CG: 72.8 ± 5.6 Female (%): IG: 59 CG: 68 Severity (% grade 4) IG: 27.3 CG: 22.7	**Intervention group: Pain Education + Mobilization** 4 Pain Neuroscience Education sessions based on the book *Explain Pain* (One 60-minutes session and three 30-minutes sessions) + Knee mobilization. **Control group: Biomedical Education + Mobilization** Biomedical education, including anatomy and biomechanics of the knee and etiology, symptoms, recommended treatments and surgical procedure for KOA + Knee mobilization.	4 sessions: the first lasted 50 to 60 min and the three others 20 to 30 min.	**Pain:** WOMAC **Catastrophization**: PCS **Follow-up:** 1 month 3 months	IG improved significantly in catastrophization at the end of the intervention compared to baseline and CG. At 1 month follow-up, IG and CG improved significantly in catastrophization compared to baseline. At 3 months follow-up, IG and CG improved significantly in pain compared to baseline. IG improved significantly in catastrophization compared to baseline and CG.
Bennell, 2016	N = 222 Mean age: IG1: 63.0 ± 7.9 IG2: 64.6 ± 8.3 CG: 62.7 ± 7.9 Female (%): IG1: 61 IG2: 60 CG: 59 Severity (% grade 4) IG1: 27 IG2: 32CG: 35	**Intervention group 1: Pain Education** 10 physical therapist-delivered modules covering pain education and training in cognitive and behavioral pain coping skills. **Intervention group 2: Pain Education + Exercise** 10 physical therapist-delivered modules covering pain education and training in cognitive and behavioral pain coping skills + 6 exercises to strengthen the quadriceps, hamstrings, and hip abductors muscles. **Control group: Exercise** 6 exercises to strengthen the quadriceps, hamstrings, and hip abductors muscles.	IG 1: 10 individual sessions of 45 min for 12 weeks IG2: 10 individual sessions of 70 min for 12 weeks CG: 10 individual sessions of 25 min for 12 weeks	**Pain:** VAS **Catastrophization**: PCS **Self-Efficacy:** ASES and CSQ **Follow-up:** 12 weeks 32 weeks 52 weeks	All groups improved significantly in all variables at the end of intervention compared to baseline, except for self-efficacy (CSQ) in CG. At 32 weeks follow-up, all groups improved significantly in all variables compared to baseline, except for self-efficacy (CSQ) in IG1 and CG. IG2 improved significantly in pain and self-efficacy compared to CG and IG1 improved significantly in self-efficacy compared to CG. At 52 weeks follow-up, all groups improved significantly in all variables compared to baseline, except for catastrophization in CG and for self-efficacy (CSQ) in CG and IG1.
Skou, 2016	N = 100 Mean age: IG: 64.8 CG: 67.1 Female (%): IG: 52	**Intervention group: MEDIC Treatment** 3 months program including pain education, Exercise, Dietary advice, Insole, Pain medication. **Control group: Usual care** Two standardized information leaflets,	Two 60-minutes sessions for 3 months	**Pain**: VAS **Follow-up:** 3 months	IG improved significantly in pain compared to baseline. At 3 months follow-up, no significant difference was found in pain compared to CG.

(*continued on next page*)

Table 1 (*continued*)

Author, year	Participants	Intervention protocols and controls	Frequency and duration	Outcomes (Measure) Follow-up	Results
	CG: 50 Severity (% grade 4) IG: 17 CG: 14	including information on KOA with regards to etiology, symptoms, common functional limitations and recommended treatments.			
Da Silva, 2015	N = 41 Mean age: IG: 57 ± 6.0 CG: 60 ± 7.8 Female (%): IG: 87 CG: 87 Severity (% grade 4) IG: NR CG: NR	**Intervention group: Self-Management Education + Rehabilitation Program (Pain Education + Exercise)** General information about OA + Rehabilitation program including pain educational aspect about KOA (15 min) and exercise (45 min). **Control group: Self-Management Education + Booster educational information** 90 min containing general information about OA + 8 weeks of booster educational information about the disease and how to improve quality of life.	90 min containing general information about OA + 8 weeks of rehabilitation program (IG) or booster educational information (CG).	**Pain:** LAI **Follow-up:** 8 weeks	No significant differences were found between groups at the end of the intervention in pain intensity. At 8 weeks follow-up, IG improved significantly in pain intensity compared to baseline and CG.

CG: Control Group; IG: Intervention Group; NR: Not Reported; KOA: Knee Osteoarthritis; OA: Osteoarthritis; ASES: Arthritis Self-Efficacy Scale; CSQ: Coping Strategies Questionnaire; KOOS: Knee Injury and Osteoarthritis Outcome Score; LAI: Lequesne Algofunctional Index; NS: Numeric Scale; PCS: Pain Catastrophization Scale; PSEQ: Pain Self-Efficacy Questionnaire; PRSS: Pain-related Self Statements; VAS: Visual Analogue Scale. WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

As shown, the Downs and Black score ranged from 17 to 23. Two studies [20,23] showed good quality and the rest showed fair quality.

Fig. 4 shows the detailed scores of the studies on the different items of the Cochrane Risk of Bias Tool for randomized trials.

Fig. 4 shows that two studies obtained high risk of bias [19,21], one study showed low risk of bias [23], and most studies showed some concerns.

4. Discussion

The objective of this systematic review and meta-analysis was to evaluate the effectiveness of neurophysiological pain education in patients with symptomatic knee osteoarthritis.

In the articles included in this systematic review and meta-analysis, the sample was mainly composed of females. Osteoarthritis is expressed differently in women than in men [26]. Apart from the affected anatomical region, women typically exhibit more advanced stages of the condition compared to men, display distinct gait patterns, and report higher levels of pain and disability [27]. The cause may be multifactorial and include anatomical differences (i.e., more slender femurs, thinner patellae, increased quadriceps angles, or variations in tibial condylar size), previous trauma, and genetic and hormonal issues [28,29].

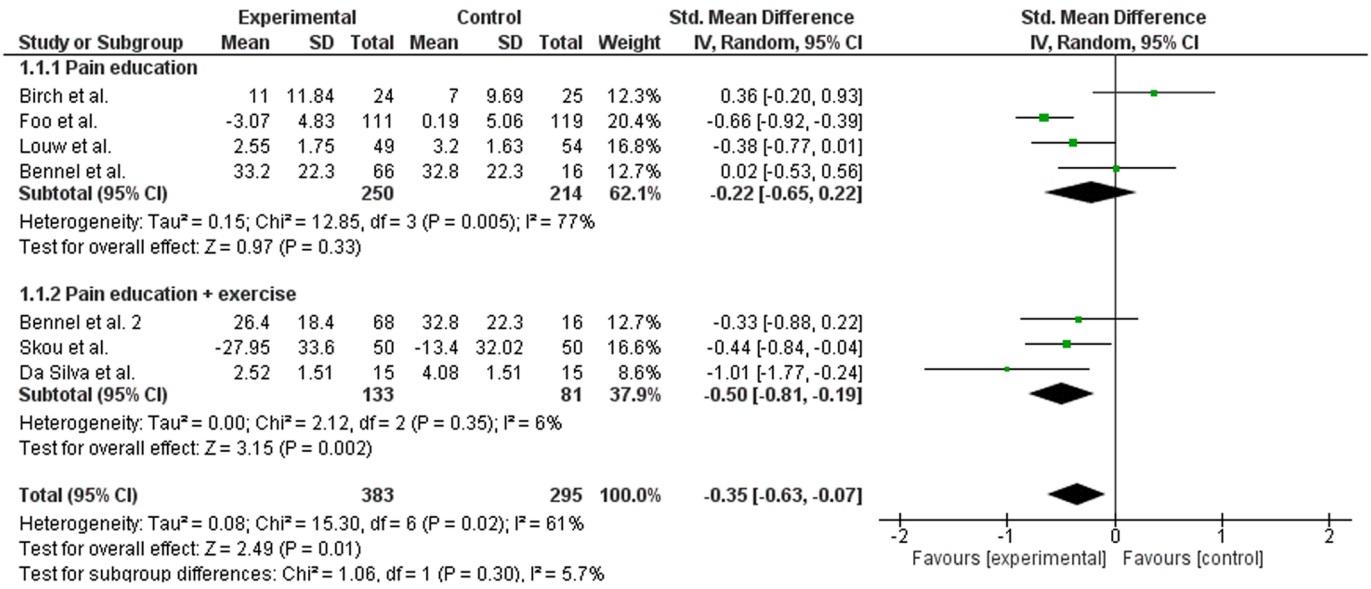
Educational interventions are very important in the treatment of knee osteoarthritis. The goal of these programs is to improve functionality and reduce pain by getting patients to make changes in their lifestyle such as being more active or losing weight [30,31]. Such treatments have proven to be effective but require changes in the patient's behavior, which are difficult to obtain [32].

Nevertheless, the purpose of neurophysiological pain education is to change patients' pain perceptions to reconceptualize and reconfigure the way they feel pain [33]. Patient education and active participation regarding pain and pain treatment are one of the cornerstones of effective pain management [34].

The results of the meta-analysis showed significant improvements in pain and catasptrophization in patients with symptomatic knee osteoarthritis that underwent a neurophysiological pain education program. Our results are consistent with other systematic reviews and meta-analyses that conducted neurophysiological pain education in other musculoskeletal pain states [35–42]. Three of these reviews, focused on chronic pain conditions, suggested that neurophysiological pain education may have a positive impact on kinesiophobia, pain catastrophizing, and healthcare utilization [37,39,40]. Regarding chronic low back pain, one review [41] noted very limited evidence supporting the beneficial effects of neurophysiological pain education on pain, physical, psychological, and social function. Furthermore, two reviews focused on chronic low back pain conducted in 2018 [35,36] highlighted moderate-quality evidence indicating that neurophysiological pain education had a slight to moderate influence on pain and disability. They also suggested that neurophysiological pain education in conjunction with physiotherapy was able to decrease pain and disability in the short term, but not in the long term. In addition, Tegner et al. (2018) [35] conducted a systematic review and meta-analysis to evaluate the effects of neurophysiological pain education in patients with low back pain. They concluded that there were significant improvements in pain and disability after the intervention and at 3-month follow-up. In addition, the systematic review by Marris et al. (2021) [43] concluded that combining neurophysiological pain education strategies with interventions provided by physical therapists had a moderate to large effect size regarding pain and disability in patients with chronic musculoskeletal pain.

When analyzing the results obtained in the meta-analysis regarding pain variables, the mean standard difference (MSD) was − 0.49 for the studies included. Such changes were not clinically relevant since they were less than one point on a 0–10 scale, which is the minimal clinically important difference [44]. Regarding catastrophization, all the studies included used the Patient Catastrophizing Scale. The MSD obtained in the meta-analysis was − 1.81, which was lower than the minimal clinically important difference of this scale (6.48 points) [45]. Some limitations should be considered in this systematic review and meta-analysis. First, the number of articles included and the methodological quality were low. In addition, the heterogeneity of the studies makes it difficult to draw solid conclusions, and further studies are needed to delve deeper into this topic. Nevertheless, the sensitivity analysis showed similar results that make the conclusion more solid. The lack of consistent reporting on the severity of the pathology in most studies is another limitation. A more consistent and comprehensive reporting of this information across all studies is something the authors of future articles should consider. Finally, another limitation is that the scale used to assess the methodological quality of the studies was not the most updated modified version of the Downs and Black scale.

(a)



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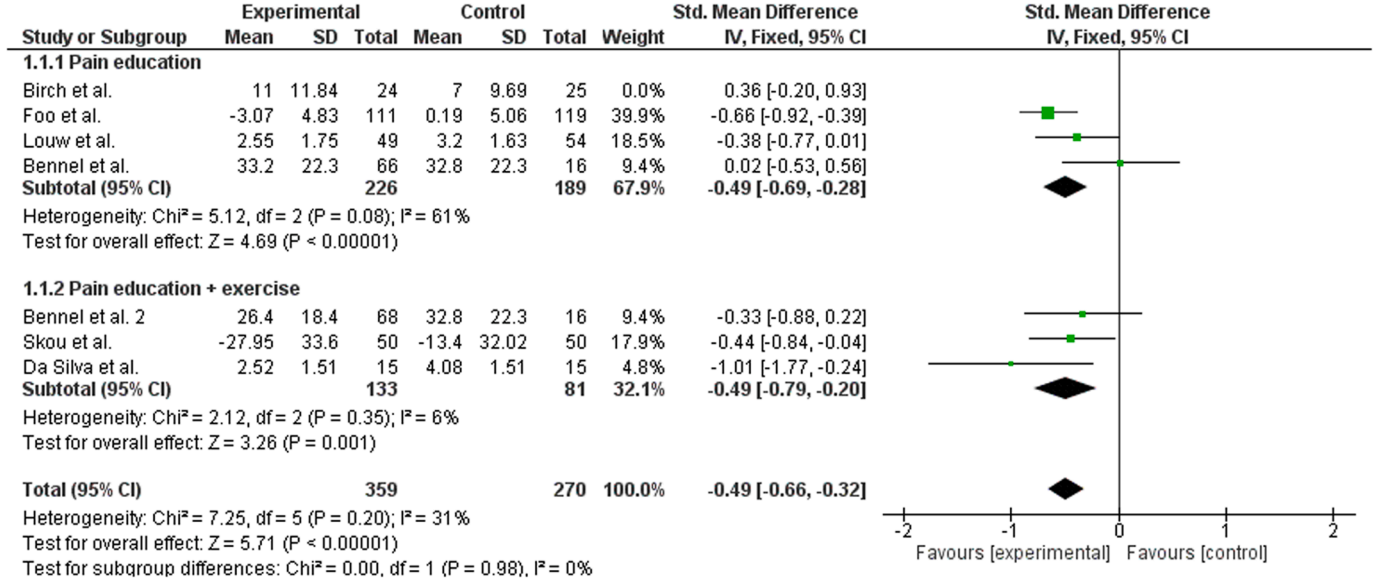


Fig. 2. a. Standardized mean difference and 95% confidence interval for pain. b. Standardized mean difference and 95% confidence interval for pain with a sensitivity analysis.

5. Conclusion

Results suggest that neurophysiological pain education interventions isolated or combined are effective in reducing pain and catastrophization in patients with symptomatic knee osteoarthritis. This review provides a comprehensive synthesis of evidence related to patient education for syntomatic knee osteoarthritis, which can inform guidelines, clinical practice, and future research.

Practice implications

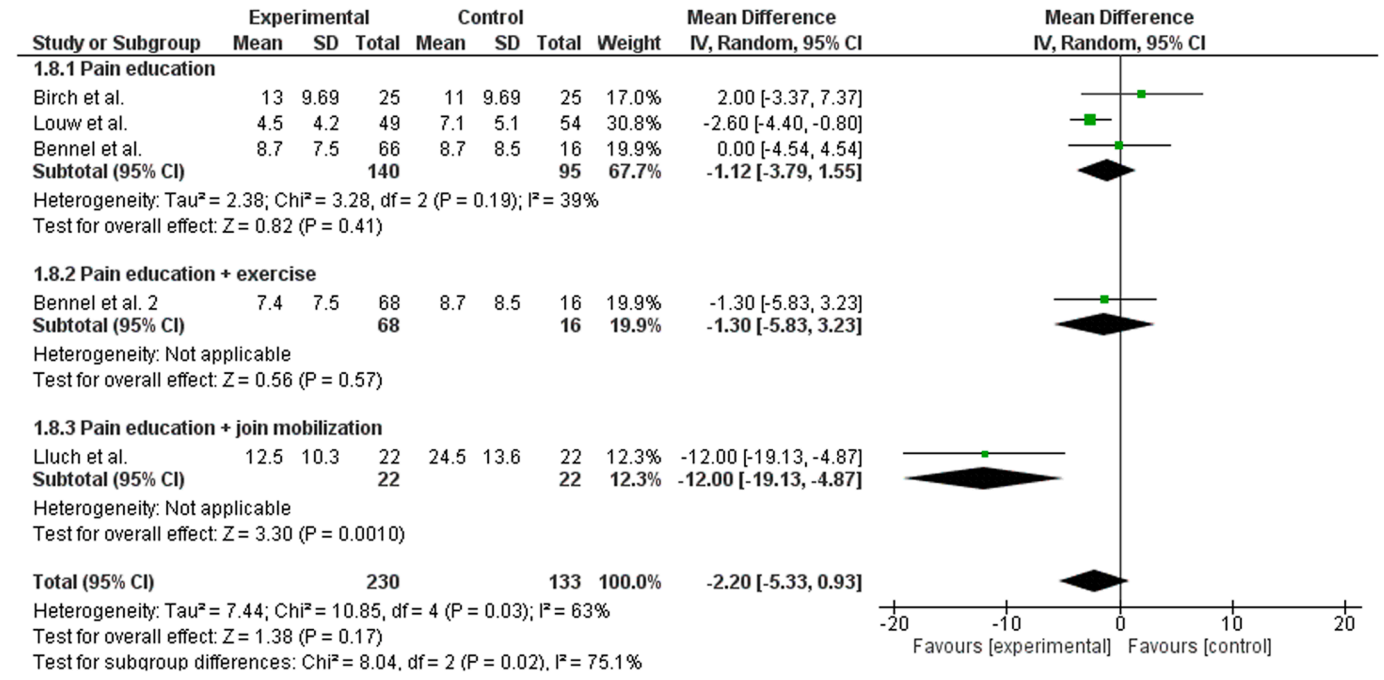
Our findings contribute to the growing evidence on the effectiveness of neurophysiological pain education interventions in patients with symptomatic knee osteoarthritis. Neurophysiological pain education is a feasible and practical strategy that can decrease participants' pain and catastrophization.

These findings can provide clinicians with more information on the management of patients with symptomatic knee osteoarthritis.

Author contributions

IL had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. LLL contributed substantially to the study design, data analysis and interpretation, and the writing of the manuscript. MCV had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. ACM contributed substantially to the study design, data analysis and interpretation, and the writing of the manuscript. AHC contributed substantially to the study design, data analysis and interpretation, and the writing of the manuscript. JMN and ANO had full access to all the data in the study and takes responsibility for the integrity of the data.

(a)



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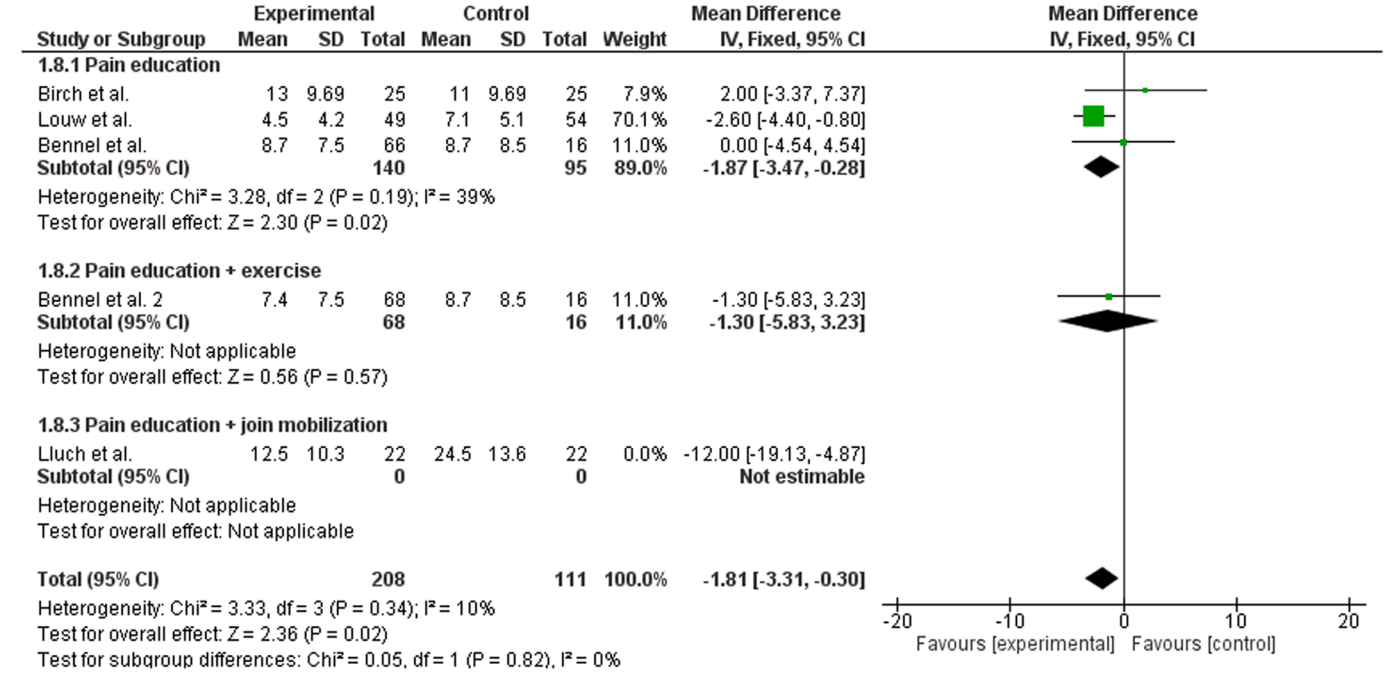

Fig. 3. a. Standardized mean difference and 95% confidence interval for catastrophization. b. Standardized mean difference and 95% confidence interval for catastrophization with a sensitivity analysis.

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Table 2
Methodological quality of the included studies.

Authors	Reporting	External validity	Internal validity (bias)	Confounding and selection bias	Power	Total
Birch et al. (2020)	6/11	3/3	5/7	3/6	1/1	17/28
Foo et al. (2020)	9/11	3/3	5/7	3/6	1/1	20/28
Louw et al. (2019)	7/11	2/3	5/7	3/6	1/1	17/28
Lluch et al. (2018)	7/11	3/3	6/7	2/6	1/1	18/28
Bennell et al. (2016)	9/11	3/3	6/7	5/6	1/1	23/28
Skou et al. (2016)	9/11	2/3	5/7	1/6	1/1	17/28
Da Silva et al. (2015)	7/11	3/3	6/7	3/6	1/1	19/28

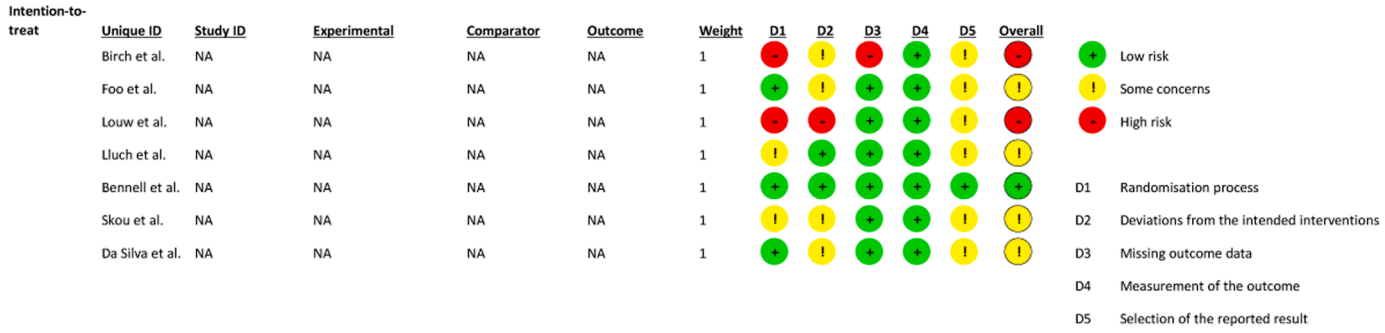

Fig. 4. Results of the Cochrane Risk of Bias Tool for randomized trials.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix I

Databases	Search equation	Number of hits
Pub Med	((knee osteoarthritis[MeSH Terms]) OR (knee osteoarthritides[MeSH Terms])) AND ("pain education" OR "pain neurophysiology" OR "neuroscience education" OR "pain neuroscience education" OR "neurophysiology education" OR "pain neuro-physiology" OR "pain neuro-science" OR "neurobiology education" OR "pain neurobiology" OR "therapeutic neuroscience" OR "therapeutic neurophysiology" OR "therapeutic neurobiology" OR "explain pain" OR "cognitive education" OR "pain biology education" OR "pain science" OR "therapeutic patient education")	78
	((pain[MeSH Terms]) AND ("neurophysiology" OR "neuroscience" OR "neurophysiology" OR "neuro-physiology" OR "neuro-science" OR "neurobiology" OR "therapeutic" OR "explain pain" OR "cognitiv*" OR "science") AND (education)) AND ((knee[MeSH Terms]) OR (knee osteoarthrit*[MeSH Terms])) AND (clinicaltrial[Filter] OR randomizedcontrolledtrial[Filter])	77
Cochrane	(“pain education” OR “pain neurophysiology” OR “neuroscience education” OR “pain neuroscience education” OR “neurophysiology education” OR “pain neuro-physiology” OR “pain neuro-science” OR “neurobiology education” OR “pain neurobiology” OR “therapeutic neuroscience” OR “therapeutic neurophysiology” OR “therapeutic neurobiology” OR “explain pain” OR “cognitive education” OR “pain biology education” OR “pain science” OR “therapeutic patient education”) AND ("knee osteoarthritis")	24
PEDro	Advanced search Problem: pain Title, Abstract: “Knee osteoarthritis” Body part: lower leg or knee Therapy: education Subdiscipline: Musculoskeletal	71
Web of Science	TS = ((“pain education” OR “pain neurophysiology” OR “neuroscience education” OR “pain neuroscience education” OR “neurophysiology education” OR “pain neuro-physiology” OR “pain neuro-science” OR “neurobiology education” OR “pain neurobiology” OR “therapeutic neuroscience” OR “therapeutic neurophysiology” OR “therapeutic neurobiology” OR “explain pain” OR “cognitive education” OR “pain biology education” OR “pain science” OR “therapeutic patient education”) AND ("knee osteoarthritis"))	38
SCOPUS	TITLE-ABS-KEY ((("pain education" OR "pain neurophysiology" OR "neuroscience education" OR "pain neuroscience education" OR "neurophysiology education" OR "pain neuro-physiology" OR "pain neuro-science" OR "neurobiology education" OR "pain neurobiology" OR "therapeutic neuroscience" OR "therapeutic neurophysiology" OR "therapeutic neurobiology" OR "explain pain" OR "cognitive education" OR "pain biology education" OR "pain science" OR "therapeutic patient education") AND ("knee chronic pain" OR "knee osteoarthritis" OR knee AND osteoarthr* OR osteo-arthr* OR "osteoarthritis, knee")))	34
TOTAL		322

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