National Institute for Health and Care Excellence

Draft for consultation

Osteoarthritis: assessment and management (update)

[G] Evidence reviews for the clinical and cost-effectiveness of electrotherapy for the management of osteoarthritis

NICE guideline <number>

Evidence reviews underpinning recommendation 1.3.9 and research recommendations in the NICE guideline

April 2022

Draft for Consultation

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ISBN:

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1.1 Review question

What is the clinical and cost-effectiveness of electrotherapy for the management of osteoarthritis?

1.1.1 Introduction

Electrotherapy can be used to provide pain relief in a range of conditions including osteoarthritis. Although Transcutaneous Electrical Nerve Stimulation (TENS) was recommended as an intervention to consider in NICE Osteoarthritis guideline CG177 it is not thought to be widely used within the NHS. TENS is available over the counter, however, so may be recommended by NHS healthcare professionals. Reviewing and updating the evidence again may help determine whether electrotherapy should be recommended as part of NHS treatment.

This review aims to evaluate the effectiveness of electrotherapeutic interventions (including pulsed short-wave therapy, interferential therapy, laser, transcutaneous electrical nerve stimulation, and ultrasound) in the management of osteoarthritis in adults.

1.1.2 Summary of the protocol

Table 1: PICO characteristics of review question

Population	Inclusion: • Adults (age ≥16 years) with osteoarthritis affecting any joint To note that where evidence for other rare forms of osteoarthritis is identified the committee will stratify into the most appropriate group. Exclusion: • Children (age ≤16 years) • People with conditions that may make them susceptible to osteoarthritis or often occur alongside osteoarthritis (including: crystal arthritis, inflammatory arthritis, septic arthritis, diseases of childhood that may predispose to osteoarthritis, medical conditions presenting with joint inflammation and malignancy). • Studies in people with meniscal injury without osteoarthritis • Studies with an unclear population (e,g, type of arthritis, proportion of participants with osteoarthritis) • Spinal osteoarthritis
Interventions	Non-invasive electrotherapy interventions (minimum intervention duration 1 week), including: • Pulsed short-wave therapy • Interferential therapy • Neuromuscular electrical stimulation • Extracorporeal shockwave therapy • Laser therapy

	• Transcutaneous electrical nerve stimulation (TENS) • Ultrasound • Combination therapy (ultrasound and interferential therapy)

Comparisons	• Compared to each other
	• Sham electrotherapy
	• No intervention (including either):
	  ○ Electrotherapy versus no treatment*
	  ○ Electrotherapy plus additional treatment versus additional treatment alone**
	
	**No treatment defined as either (1) doing nothing or (2) very low intensity intervention such as advice*
	***Inclusion of studies where additional treatment is the same in each arm will be assessed on a case by case basis. Studies including high intensity additional treatment may not be included due to the risk that treatment could have an interaction with the intervention of interest and mask the true treatment effect.*

Outcomes	Stratify by ≤/>3 months (longest time-point in each): • Health-related quality of life [validated patient-reported outcomes, continuous data prioritised] • Pain [validated patient-reported outcomes, continuous data prioritised] • Physical function [validated patient-reported outcomes, continuous data prioritised] • Psychological distress [validated patient-reported outcomes, continuous data prioritised] • Osteoarthritis flares [validated patient-reported outcomes, continuous data prioritised] • Mild adverse events [dichotomous data prioritised] • Moderate/major adverse events [dichotomous data prioritised]
Study design	RCTs or systematic reviews of RCTs

For full details see the review protocol in Appendix A.

1.1.3 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in Appendix A and the methods document.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.4 Effectiveness evidence

1.1.4.1 Included studies

Eighty-one randomised controlled trial studies (eighty-five papers) were included in the review;[6, 8, 10-13, 15-17, 21, 22, 27, 29, 35-38, 40-42, 44, 58, 64, 66, 69, 71, 74, 76, 79, 80, 83, 84, 86, 90-93, 96, 97, 100-102, 107, 115, 118, 120, 121, 124, 126, 131, 132, 142, 146, 148, 150-155, 160, 166-170, 175, 178, 179, 190, 193, 205, 208, 211, 213, 217, 220, 224, 225, 229, 236-238, 240] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 3).

The clinical studies identified included the following comparisons:

- Pulsed short-wave therapy compared to sham electrotherapy[22, 27, 41, 66, 79, 83, 86, 155, 160, 168, 179, 208, 211, 220, 240]
- Pulsed short-wave therapy compared to no treatment[6, 44, 66, 83, 155]
- Pulsed short-wave therapy compared to laser therapy[66]
- Interferential therapy compared to pulsed short-wave therapy[22, 66]
- Interferential compared to laser therapy [15, 66]
- Interferential therapy compared to sham electrotherapy[15, 22, 66, 91]
- Interferential therapy compared to no treatment[66]
- Neuromuscular electrical stimulation compared to no treatment[21, 36, 76, 131, 154, 170]
- Extracorporeal shockwave therapy compared to sham electrotherapy[58, 217, 236-238]
- Extracorporeal therapy compared to no treatment [74, 90]
- Laser therapy compared to neuromuscular electrical stimulation[152]
- Laser therapy compared to sham electrotherapy[10, 13, 15, 29, 35, 37, 42, 66, 84, 92, 93, 96, 97, 100, 120, 146, 148, 150, 193, 229]
- Laser therapy compared to no treatment[8, 64, 66, 97]
- Transcutaneous electrical nerve stimulation compared to pulsed short-wave therapy[22, 44]
- Transcutaneous electrical nerve stimulation compared to interferential therapy[22, 38]
- Transcutaneous electrical nerve stimulation compared to sham electrotherapy[17, 22, 107, 132, 169, 175, 178]
- Transcutaneous electrical nerve stimulation compared to no treatment[44, 151, 175, 178]
- Ultrasound compared to pulsed short-wave therapy[44]
- Ultrasound compared to neuromuscular electrical stimulation[69]
- Ultrasound compared to transcutaneous electrical nerve stimulation[44, 151]
- Ultrasound compared to sham electrotherapy[40, 71, 115, 118, 124, 126, 142, 166, 167, 205, 213, 224, 225]
- Ultrasound compared to no treatment[12, 44, 101, 102, 151]
- Combination therapy compared to neuromuscular electrical stimulation[152]
- Combination therapy compared to laser therapy[15, 152]
- Combination therapy compared to ultrasound[124, 190]
- Combination compared to interferential therapy[15]
- Combination therapy compared to sham electrotherapy[15, 124]
- Combination therapy compared to transcutaneous electrical nerve stimulation[121]
- Combination therapy compared to no treatment[16, 74]

Evidence was available for each intervention stated in the protocol. However, there was no evidence for the following comparison to sham electrotherapy:

- Neuromuscular electrical stimulation

See also the study selection flow chart in Appendix C, study evidence tables in Appendix D, forest plots in Appendix E and GRADE tables in Appendix F.

A network meta-analysis was not conducted for this review. This was due to the heterogeneity identified in the studies and outcomes, including heterogeneity in the types of interventions (including the intensity of therapy delivered) and in comparisons (different types of sham therapy devices, some studies delivering different levels of concomitant care being combined in the no treatment group). Given this, the committee agreed it would be difficult to draw conclusions from the results of a network meta-analysis and so used the evidence from pairwise meta-analysis instead.

1.1.4.1.1 Combination therapy

The combinations of therapy reported in the studies included:

- Laser therapy combined with neuromuscular electrical stimulation[152]
- Ultrasound combined with transcutaneous electrical nerve stimulation[16, 74, 121, 124, 190],
- Interferential combined with laser therapy[15]

No other combinations were reported.

1.1.4.1.2 Inconsistency

Heterogeneity was seen in outcomes in the following comparisons:

- Pulsed short-wave therapy compared to sham electrotherapy (quality of life, pain and physical function)
- Interferential therapy compared to sham electrotherapy (pain and physical function)
- Neuromuscular electrical stimulation compared to no treatment (physical function)
- Laser therapy compared to sham electrotherapy (pain and physical function)
- Laser therapy compared to no treatment (quality of life, pain and physical function)
- Transcutaneous electrical nerve stimulation compared to interferential therapy (pain and physical function)
- Transcutaneous electrical nerve stimulation compared to sham electrotherapy (pain and physical function)
- Transcutaneous electrical nerve stimulation compared to no treatment (pain and physical function)

In these scenarios, there was either an insufficient number of studies to form valid subgroups or subgroup analysis did not resolve the heterogeneity, therefore outcomes were downgraded for inconsistency and analysed using a random effects model.

1.1.4.1.3 Indirectness

The majority of evidence was direct in most cases and therefore only one outcome was downgraded for indirectness. However, some outcomes included indirect components.

- Cho 2016[58] included people with osteoarthritis who had also had a stroke and so was noted as having serious population indirectness.
- Marquina 2012[150] did not define the population as having knee osteoarthritis, but included people with chronic knee pain so was noted as having serious population indirectness.
- Thamsborg 2005[208] included a sham intervention that sounded like it could have an active effect (a device applying a magnetic field with a DC current rather than a pulse generating therapy) and so was noted as having serious intervention indirectness.

1.1.4.2 Excluded studies

Cochrane reviews were identified but could not be included due to using interventions not stated in the protocol (Rutjes 2010[188], Zammit 2010[231]), using comparisons not stated in the protocol and different outcome measures being used (Li 2013[138], Osiri 2000[164]). The references were checked any studies that fulfilled the inclusion criteria were included.

See the excluded studies list in Appendix J.

1.1.5 Summary of studies included in the effectiveness evidence

1.1.5.1 Pulsed short-wave therapy compared to sham electrotherapy

Table 2: Summary of studies included in the pulsed short-wave therapy compared to sham electrotherapy comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Atamaz 2012[22]	**Transcutaneous electrical nerve stimulation** (n=37) TENS (frequency 80Hz, 10-30mA intensity) for 20 minutes three times a week for 3 weeks **Interferential therapy** (n=31) Interferential currents (frequency 100Hz generated by 4kHz sinusoidal waves) for 3 weeks **Pulsed short-wave therapy** (n=32) Pulsed short-wave diathermy (10cm diameter condenser plate, frequency 27.12mHz, input 300W, mean output 3.2W) for 3 weeks **Sham electrotherapy (TENS)** (n=37) Sham TENS **Sham electrotherapy (interferential therapy)** (n=35) Sham interferential therapy	**Knee osteoarthritis** Mean age (SD): 61.5 (7.5) years N = 203 Definition: People with knee osteoarthritis according to the American College of Rheumatology criteria with radiologically confirmation with a Kellgren Lawrence grade of 2 or 3 Severity: Kellgren Lawrence grade 2-3 Duration of symptoms (mean [SD]): 43.7 (49.1) months. Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months and >3 months Physical function at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Sham electrotherapy (pulsed short-wave therapy) (n=31) Sham pulsed short-wave therapy **Concomitant therapy:** All people had an exercise program conducted in groups of 4-5 people three times a week for 3 weeks involving stretching, isometric quadriceps exercises and chair lift/minisquats. This was supplemented with additional instruction for home exercise. All people also attended an education program consisting of one 1 hour session discussing the functional anatomy of the knee, ergonomic principles, and understanding of osteoarthritis.			
Bagnato 2016[27]	**Pulsed short-wave therapy** (n=33) Pulsed electromagnetic field therapy (frequency 27.12MHz, pulse rate 100Hz, 100μs burst width, peak burst power 0.0098W covering a surface area of 103cm2) for 4 weeks **Sham electrotherapy** (n=33) Sham electrotherapy (device that did not emit a field) **Concomitant therapy:**	**Knee osteoarthritis** Mean age (SD): 67.7 (10.9) years N = 66 Definition: A diagnosis of primary osteoarthritis of the knee according to the American College of Rheumatology criteria, including radiological evidence of osteoarthritis Severity: Not stated	Quality of life at ≤3 months Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	No additional information.	Duration of symptoms (mean [SD]): 12.1 (8.2) years Presence of multimorbidities: Not stated/Unclear		
Callaghan 2005[41]	**Pulsed short-wave therapy** (n=20) Pulsed short-wave therapy (active high frequency (27 mHz) pulsed shortwave for 20 minutes to the affected knee joint using a dose of 200 microseconds and 400 pulses per second with an output of 10W or active high frequency (27mHz) pulsed shortwave for 20 minutes at a dose of 400 microseconds and 400 pulses per second, with an output of 20W) for 2 weeks **Sham electrotherapy** (n=10) Sham electrotherapy **Concomitant therapy:** No additional information.	**Knee osteoarthritis** Mean age (SD): 60.4 (7.7) years N = 30 Definition: Primary generalised osteoarthritis and a diagnosis of osteoarthritis knee with radiographic evidence (Kellgren Lawrence grade 3-4) Severity: Kellgren Lawrence grade 3-4 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Quality of life at ≤3 months Pain at ≤3 months	
De Paula Gomes 2020[66]	**Interferential therapy** (n=20) The sessions were held three times a week, over 8 weeks (24 sessions), on alternate days, lasting approximately 90 minutes each treatment session. Interferential therapy (n=20) ICT was performed using a premodulated tetrapolar method with a carrier frequency of	**Knee osteoarthritis** Mean age (SD): Exercise group: 67.85 (4.49) years, exercise+placebo group: 69.4 (4.45) years, exercise+ICT group: 71.85 (2.62) years, exercise+SDT group: 68.45 (4.62) years, exercise+PHOTO group: 65.75 (4.48) years	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	4KHz, 1/1s sweep mode, 75 Hz frequency modulation amplitude, 25Hz delta frequency modulation amplitude, and automatic vector mode for 40 minutes. **Short wave therapy** (n=20) a thermopulse (Ibramed, Amparo, Sao Paolo, Brazil) device set to continuous mode, 27.12MHz frequency and 150W input was used for 20 minutes, and the intensity was defined based on each participant reporting a warm sensation (one sensation, described as soft but pleasant heat). **Laser therapy** (n=20) Prior to the exercise protocol, participants in the exercise and photobiomodulation (PHOTO) group underwent photobiomodulation therapy using a laserpulse device (Ibramed, Amparo, SP, Brazil). The power of each infrared laser was as follows: wavelength of 904nm, frequency of 9500Hz, pulse duration of 60ns, peak power of 70W, average power of 0.04W, energy density of 6J/cm² applied on eight points, with a total dose of 48J/cm², each session.	N = 100 Definition: Unilateral knee OA according to American College of Rheumatology criteria, made through examination and the written opinion of a specialist in rheumatic disease. Severity (NRS pain score): Exercise group: 6.55 (1.09), exercise+placebo group: 6.50 (0.68), exercise+ICT group: 6.65 (0.98), exercise+SDT group: 6.40 (0.99), exercise+PHOTO group: 6.70 (0.86) Duration of symptoms: Not stated/unclear Presence of multi-morbidities: Not stated/unclear		

Study	Intervention and comparison	Population	Outcomes	Comments
	Sham electrotherapy (n=20) **No treatment** (n=20) Exercise therapy only (supervised strength exercises) **Concomitant therapy:** None of the participants undertook any form of physical therapy, in addition to the one stipulate. In addition they did not use intra-articular, anti-inflammatory or chondroprotective corticosteroids. The use of medications for concomitant diseases was not controlled.			
Fary 2011[79] Subsidiary paper: Fary 2008[80]	**Pulsed short-wave therapy** (n=34) Pulsed electrical stimulation delivering a pulsed asymmetrically biphasic, exponentially decreasing waveform with a frequency of 100Hz and a pulse width of 4ms. Delivered 7 hours daily, preferably overnight, for 26 weeks. **Sham electrotherapy** (n=36) Placebo device (identical, but set to switch off after 3 minutes of use)	**Knee osteoarthritis** Mean age (SD): 69.8 (10.3) years N = 70 Definition: Diagnosis in accordance with the American College of Rheumatology modified clinical classification system with plain radiographs being available for all participants Severity: Kellgren Lawrence grades 1-4, median grade 3	Quality of life at >3 months Pain at >3 months Physical function at >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Concomitant therapy: People were instructed to continue their usual treatment for osteoarthritis throughout the study (including prescribed medications, health professional interventions such as exercise programs, and complementary therapies). However, they were counselled against starting any new treatments	Duration of symptoms (mean [SD]): 12.0 (10.5) years Presence of multimorbidities: Not stated/Unclear		
Fukuda 2011[83]	**Pulsed short-wave therapy** (n=63) Low or high dose pulsed short-wave therapy (carrying frequency of 27.12 MHz, peak power of 250W, pulse duration of 400 microseconds, maximum power of 145Hz, resulting in a mean power of 14.5W. The low dose group was completed over 19 minutes per session delivering 17kJ of energy. The high dose group was completed over 38 minutes delivering 33kJ of energy. **Sham electrotherapy** (n=23) Sham electrotherapy (kept on standby mode during 19 minutes without the current delivered) **No treatment** (n=35)	**Knee osteoarthritis** Mean age (SD): 61.0 (9.3) years N = 121 Definition: Primary grade 2-3 knee osteoarthritis based on Gupta and colleagues' radiographic criteria and have had joint or anterior knee pain for at least 3 months Severity: Gupta and colleagues radiographic criteria: grade 2-3 Duration of symptoms: At least 3 months Presence of multimorbidities: Not stated/Unclear	Quality of life at ≤3 months and >3 months Pain at ≤3 months and >3 months Physical function at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	No treatment **Concomitant therapy:** No advice was given to participants in all groups in relation to physical activities, except to maintain their daily activities and to avoid using anti-inflammatory drugs			
Garland 2007[86]	**Pulsed short-wave therapy** (n=34) Pulsed electrical stimulation using a 100Hz, negative pulsed signal, turned up to a maximum of 12V over 12 weeks **Sham electrotherapy** (n=36) Placebo treatment (the devices were shut off when the dose was adjusted) **Concomitant therapy:** Stable NSAID and/or analgesic use was maintained 1 month prior to and throughout the study rather than being withdrawn to produce a disease flare	**Knee osteoarthritis** Mean age (SD): 66.1 (10.9) years N = 70 Definition: Moderate to severe osteoarthritis with persistence of pain on NSAID and/or analgesic therapy and the presence of Kellgren-Lawrence grade 3-4 changes on standing, weight bearing, and semiflexed x-ray views of the knees Severity: Kellgren Lawrence grade 3-4 Duration of symptoms (mean [range]): 8.4 (0.2-44) years Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months Physical function at ≤3 months Mild adverse events at ≤3 months	
Moffett 1996[155]	**Pulsed short-wave therapy** (n=30) Pulsed short wave therapy with 9 sessions of treatment over 3	**Knee osteoarthritis** Mean age (SD): 63.5 (9.9) years N = 90	Pain at ≤3 months Psychological distress at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	weeks, each application lasting 15 minutes **Sham electrotherapy** (n=30) Placebo treatment (same device, assigned random number settings on the machine that would produce a non-functioning result) **No treatment** (n=30) **Concomitant therapy:** No additional information	Definition: People with osteoarthritis of the hip or knee with radiological changes Severity: Not stated Duration of symptoms (mean [SD]): 92.1 (124.4) months Presence of multimorbidities: Not stated/Unclear		
Nelson 2013[160]	**Pulsed short-wave therapy** (n=15) Pulsed short wave therapy with a pulsed electromagnetic field consisting of a 7ms burst of 6.8mHz sinusoidal waves repeating at 1 burst/s delivering a peak induced electric field of 34+/-8V/m used twice daily for 15 minutes **Sham electrotherapy** (n=19) Sham devices **Concomitant therapy:** Standard care could include unrestricted NSAID use. Standard care was allowed throughout	**Knee osteoarthritis** Mean age (SD): 57.1 (2.9) years N = 34 Definition: People with knee pain and an imaging study confirming articular cartilage loss Severity: Kellgren Lawrence grade (mean [SD]): 2.8 (0.3) Duration of symptoms: At least 3 months Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
Ozguclu 2010[168]	**Pulsed short-wave therapy** (n=20) Pulsed electromagnetic therapy using 2 pairs of solenoid applicators. Applied at a frequency of 50Hz, 30-G intensity, 90s interval, 30 minute durations, 5 sessions weekly for 2 weeks. **Sham electrotherapy** (n=20) Sham devices **Concomitant therapy:** In each session 20 minutes hot pack and 5 minutes of therapeutic ultrasound were given. People were taught terminal isometric knee exercise to complete at home as required (three times a day, 30 repeats each). People were allowed to take paracetamol for knee pain if necessary. Other pain treatments (including NSAIDs) were not allowed	**Knee osteoarthritis** Mean age (SD): 61.3 (7.8) years N = 40 Definition: Diagnosis of knee osteoarthritis according to the American College of Rheumatology Severity: Kellgren Lawrence grade 2 and above Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months Physical function at ≤3 months	
Pipitone 2001[179]	**Pulsed short-wave therapy** (n=34) Pulsed short wave therapy using unipolar magnetic devices generating pulsed treatment. Pulses were selectable at three base frequencies (3Hz, 7.8Hz and 20Hz). Rise time of 1 microseconds, a decay time of	**Knee osteoarthritis** Mean age (range): 63.0 (40-84) years N = 69 Definition: Radiographic evidence and symptoms of osteoarthritis (incompletely relieved by conventional	Quality of life at ≤3 months Pain at ≤3 months Physical function at ≤3 months Mild adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	10 microseconds, a low magnetic ouput (<0.5 gauss), range of activity of up to 30cm around the unit. People were instructed to use the devices at 7.8Hz in the morning and afternoon, and 3Hz in the evening for 6 weeks **Sham electrotherapy** (n=19) Sham devices (with a 9V battery, which forced it to switch off automatically after a 10 minute period) **Concomitant therapy:** No additional information	treatments) as judged by the criteria of the American College of Rheumatology Severity: Not stated Duration of symptoms (mean [range]): 72 (5.5-372) months Presence of multimorbidities: Not stated/Unclear		
Thamsborg 2005[208]	**Pulsed short-wave therapy (**n=45) Pulsed short wave therapy using electromagnetic coils (a pulse generating using +/-50V in 50Hz pulses changing voltage in 3ms intervals) over 6 weeks **Sham electrotherapy** (n=45) Sham devices (same coil but used a DC current leading to a constant magnetic field rather than a pulsed one) **Concomitant therapy:** No additional information	**Knee osteoarthritis** Mean age (SD): 60.0 (8.7) years N = 90 Definition: Painful knee osteoarthritis of the femorotibial compartment fulfilling the combined clinical and radiological criteria of the American College of Rheumatology Severity: Not stated Duration of symptoms: Not stated	Pain at ≤3 months Physical function at ≤3 months Mild adverse events at ≤3 months Moderate/major adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
		Presence of multimorbidities: Not stated/Unclear		
Trock 1993[211]	**Pulsed short-wave therapy** (n=15) Pulsed electromagnetic field therapy using an extremely low frequency (less than 30Hz) varying, pulsed electromagnetic field averaging 10-20 gauss of energy at a coil current of up to 2A from a power source of 120V AC (pulse phase duration 67ms, pause duration 0.1s). Given for 30 minutes, 3-5 sessions per week for 18 treatments. **Sham electrotherapy** (n=12) Same device but switched off. **Concomitant therapy:** People were allowed to continue any treatment on a stable dose at the start of the trial	**Mixed osteoarthritis (knee, hand or ankle)** Age not stated N = 27 Definition: Diagnosis of osteoarthritis according to criteria by Altman, including radiographic evidence for all but one Severity: Not stated Duration of symptoms: At least one year duration Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months	
Wuschech 2015[220]	**Pulsed short-wave therapy** (n=44) Pulsed short wave therapy using pulsed electromagnetic field therapy. Disc area of 28cm2, disc rotation varied in 2Hz steps to produce frequencies between 4 and 12Hz, magnetic flux density of 420mT (peak-to-peak) on the device surface. Delivered for 18 days.	**Knee osteoarthritis** Mean age (SD): 61.1 (12.0) years N = 57 Definition: Osteoarthritis in their knee joint according to the American College of Rheumatology criteria	Pain at ≤3 months Physical function at ≤3 months Mild adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Sham electrotherapy (n=13) Sham devices (same device but no magnetic materials) **Concomitant therapy:** No additional information	Severity: American College of Rheumatology severity level (mean [SD]): 2.8 (0.8) Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear		
Zizic 1995[240]	**Pulsed short-wave therapy** (n=41) Pulsed short wave therapy using electrical impulses generated as low frequency (100Hz), low amplitude, monophasic spiked signal via a skin surface electrode. People were advised to use it for 6-10 hours/day during the 4 week treatment period. **Sham electrotherapy** (n=37) Sham devices (same device but switched off after reaching the subthreshold level) **Concomitant therapy:** Background, stable NSAID therapy was permitted as long as people remained symptomatic despite such therapy	**Knee osteoarthritis** Age: >20 years N = 78 Definition: Pain in the involved knee that was aggravated by activity and relieved by rest; morning stiffness upon rising or after disuse; at least one physical finding of joint crepitus, tenderness upon motion, swelling, or decreased range of motion; the presence of at least one of the following radiological findings in the involved knee: narrowing of the joint space of either the medial or lateral compartment on standing anteroposterior radiograph, subchondral bony sclerosis, or osteophyte formation. Severity: Not stated Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Mild adverse events at ≤3 months	

1.1.5.2 Pulsed short-wave therapy compared to no treatment

Table 3: Summary of studies included in the pulsed short-wave therapy compared to no treatment comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Akyol 2010[6]	**Pulsed short-wave therapy** (n=20) Short-wave diathermy and isokinetic exercise using a frequency of 27.12 MHz for 20 minutes per knee 3 times a week for 4 weeks **No treatment** (n=20) Isokinetic exercises only 3 times a week for 4 weeks **Concomitant therapy:** The use of NSAID, other analgesic drugs and antidepressant drugs was not permitted during the study period. Any pretreatment with these drugs had to be discontinued 7 days before the start of study. The use of other medication for comorbid diseases was permitted during study period.	**Knee osteoarthritis** Mean age (SD): 57.2 (9.5) years N = 40 Definition: Bilateral knee osteoarthritis according to the American College of Rheumatology criteria with confirmation in standing anteroposterior and lateral radiographs of both knees Severity: Kellgren Lawrence grades <4 Duration of symptoms (mean [SD]): 71.03 (60.98) months Presence of multimorbidities: Not stated/Unclear	Quality of life at ≤3 months and >3 months Pain at ≤3 months and >3 months Physical function at ≤3 months and >3 months Psychological distress at ≤3 months and >3 months	
Cetin 2008[44]	**Pulsed short-wave therapy** (n=20) Short-wave diathermy, hot packs and isokinetic exercise using a frequency of 27.12 MHz for 15 minutes per knee 3 times a week for 8 weeks	**Knee osteoarthritis** Mean age (SD): 59.8 (9.2) years N = 100 Definition: Defined by the American College of	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Transcutaneous electrical nerve stimulation (n=20) TENS, hot packs and isokinetic exercise. Unit set to 60-100Hz, pulse duration set to 60ms for 24 sessions, 3 times a week for 8 weeks. **Ultrasound** (n=20) Ultrasound, hot packs and isokinetic exercise. 1MHz ultrasound head, intensity of 1.5W/cm2, 3 times a week for 8 weeks **No treatment** (n=20) Hot pack and isokinetic exercise only A fifth group (n=20) was reported by not included as it did not fulfil the inclusion criteria **Concomitant therapy:** After application of physical agents, each person underwent individual warm up exercises on a stationary bike set for 20 cycles/min for 5 mins before undergoing muscle-strengthening exercises. People were instructed to continue taking any current medications and not to start any new	Rheumatology with radiographic confirmation Severity: Radiographic grade 1-4, median grade 3 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear		

Study	Intervention and comparison	Population	Outcomes	Comments
	therapies for knee osteoarthritis during the 8 week studies.			
De Paula Gomes 2020[66]	**Interferential therapy** (n=20) The sessions were held three times a week, over 8 weeks (24 sessions), on alternate days, lasting approximately 90 minutes each treatment session. Interferential therapy (n=20) ICT was performed using a premodulated tetrapolar method with a carrier frequency of 4KHz, 1/1s sweep mode, 75 Hz frequency modulation amplitude, 25Hz delta frequency modulation amplitude, and automatic vector mode for 40 minutes. **Short wave therapy** (n=20) a thermopulse (Ibramed, Amparo, Sao Paolo, Brazil) device set to continuous mode, 27.12MHz frequency and 150W input was used for 20 minutes, and the intensity was defined based on each participant reporting a warm sensation (one sensation, described as soft but pleasant heat). **Laser therapy** (n=20) Prior to the exercise protocol, participants in the exercise and photobiomodulation (PHOTO)	**Knee osteoarthritis** Mean age (SD): Exercise group: 67.85 (4.49) years, exercise+placebo group: 69.4 (4.45) years, exercise+ICT group: 71.85 (2.62) years, exercise+SDT group: 68.45 (4.62) years, exercise+PHOTO group: 65.75 (4.48) years N = 100 Definition: Unilateral knee OA according to American College of Rheumatology criteria, made through examination and the written opinion of a specialist in rheumatic disease. Severity (NRS pain score): Exercise group: 6.55 (1.09), exercise+placebo group: 6.50 (0.68), exercise+ICT group: 6.65 (0.98), exercise+SDT group: 6.40 (0.99), exercise+PHOTO group: 6.70 (0.86) Duration of symptoms: Not stated/unclear Presence of multi-morbidities: Not stated/unclear	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	group underwent photobiomodulation therapy using a laserpulse device (Ibramed, Amparo, SP, Brazil). The power of each infrared laser was as follows: wavelength of 904nm, frequency of 9500Hz, pulse duration of 60ns, peak power of 70W, average power of 0.04W, energy density of 6J/cm² applied on eight points, with a total dose of 48J/cm², each session. **Sham electrotherapy** (n=20) **No treatment** (n=20) Exercise therapy only (supervised strength exercises) **Concomitant therapy:** None of the participants undertook any form of physical therapy, in addition to the one stipulate. In addition they did not use intra-articular, anti-inflammatory or chondroprotective corticosteroids. The use of medications for concomitant diseases was not controlled.			
Fukuda 2011[83]	**Pulsed short-wave therapy** (n=63) Low or high dose pulsed short-wave therapy (carrying	**Knee osteoarthritis** Mean age (SD): 61.0 (9.3) years N = 121	Quality of life at ≤3 months and >3 months Pain at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	frequency of 27.12 MHz, peak power of 250W, pulse duration of 400 microseconds, maximum power of 145Hz, resulting in a mean power of 14.5W. The low dose group was completed over 19 minutes per session delivering 17kJ of energy. The high dose group was completed over 38 minutes delivering 33kJ of energy. **Sham electrotherapy** (n=23) Sham electrotherapy (kept on standby mode during 19 minutes without the current delivered) **No treatment** (n=35) No treatment **Concomitant therapy:** No advice was given to participants in all groups in relation to physical activities, except to maintain their daily activities and to avoid using anti-inflammatory drugs	Definition: Primary grade 2-3 knee osteoarthritis based on Gupta and colleagues' radiographic criteria and have had joint or anterior knee pain for at least 3 months Severity: Gupta and colleagues radiographic criteria: grade 2-3 Duration of symptoms: At least 3 months Presence of multimorbidities: Not stated/Unclear	Physical function at ≤3 months and >3 months	
Moffett 1996[155]	**Pulsed short-wave therapy** (n=30) Pulsed short wave therapy with 9 sessions of treatment over 3 weeks, each application lasting 15 minutes	**Knee osteoarthritis** Mean age (SD): 63.5 (9.9) years N = 90	Pain at ≤3 months Psychological distress at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Sham electrotherapy (n=30) Placebo treatment (same device, assigned random number settings on the machine that would produce a non-functioning result) **No treatment** (n=30) **Concomitant therapy:** No additional information	Definition: People with osteoarthritis of the hip or knee with radiological changes Severity: Not stated Duration of symptoms (mean [SD]): 92.1 (124.4) months Presence of multimorbidities: Not stated/Unclear		

1.1.5.3 Interferential therapy compared to pulsed short-wave therapy

Table 4: Summary of studies included in the interferential therapy compared to pulsed short-wave therapy comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Atamaz 2012[22]	**Transcutaneous electrical nerve stimulation** (n=37) TENS (frequency 80Hz, 10-30mA intensity) for 20 minutes three times a week for 3 weeks **Interferential therapy** (n=31) Interferential currents (frequency 100Hz generated by 4kHz sinusoidal waves) for 3 weeks **Pulsed short-wave therapy** (n=32) Pulsed short-wave diathermy (10cm diameter condenser plate, frequency 27.12mHz,	Knee osteoarthritis Mean age (SD): 61.5 (7.5) years N = 203 Definition: People with knee osteoarthritis according to the American College of Rheumatology criteria with radiologically confirmation with a Kellgren Lawrence grade of 2 or 3 Severity: Kellgren Lawrence grade 2-3 Duration of symptoms (mean [SD]): 43.7 (49.1) months.	Pain at ≤3 months and >3 months Physical function at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	input 300W, mean output 3.2W) for 3 weeks **Sham electrotherapy (TENS)** (n=37) Sham TENS **Sham electrotherapy (interferential therapy)** (n=35) Sham interferential therapy **Sham electrotherapy (pulsed short-wave therapy)** (n=31) Sham pulsed short-wave therapy **Concomitant therapy:** All people had an exercise program conducted in groups of 4-5 people three times a week for 3 weeks involving stretching, isometric quadriceps exercises and chair lift/minisquats. This was supplemented with additional instruction for home exercise. All people also attended an education program consisting of one 1 hour session discussing the functional anatomy of the knee, ergonomic principles, and understanding of osteoarthritis.	Presence of multimorbidities: Not stated/Unclear		
De Paula Gomes 2020[66]	**Interferential therapy** (n=20)	Knee osteoarthritis	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	The sessions were held three times a week, over 8 weeks (24 sessions), on alternate days, lasting approximately 90 minutes each treatment session. Interferential therapy (n=20) ICT was performed using a premodulated tetrapolar method with a carrier frequency of 4KHz, 1/1s sweep mode, 75 Hz frequency modulation amplitude, 25Hz delta frequency modulation amplitude, and automatic vector mode for 40 minutes. **Short wave therapy** (n=20) a thermopulse (Ibramed, Amparo, Sao Paolo, Brazil) device set to continuous mode, 27.12MHz frequency and 150W input was used for 20 minutes, and the intensity was defined based on each participant reporting a warm sensation (one sensation, described as soft but pleasant heat). **Laser therapy** (n=20) Prior to the exercise protocol, participants in the exercise and photobiomodulation (PHOTO) group underwent photobiomodulation therapy using a laserpulse device (Ibramed, Amparo, SP, Brazil).	Mean age (SD): Exercise group: 67.85 (4.49) years, exercise+placebo group: 69.4 (4.45) years, exercise+ICT group: 71.85 (2.62) years, exercise+SDT group: 68.45 (4.62) years, exercise+PHOTO group: 65.75 (4.48) years N = 100 Definition: Unilateral knee OA according to American College of Rheumatology criteria, made through examination and the written opinion of a specialist in rheumatic disease. Severity (NRS pain score): Exercise group: 6.55 (1.09), exercise+placebo group: 6.50 (0.68), exercise+ICT group: 6.65 (0.98), exercise+SDT group: 6.40 (0.99), exercise+PHOTO group: 6.70 (0.86) Duration of symptoms: Not stated/unclear Presence of multi-morbidities: Not stated/unclear	Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	The power of each infrared laser was as follows: wavelength of 904nm, frequency of 9500Hz, pulse duration of 60ns, peak power of 70W, average power of 0.04W, energy density of 6J/cm² applied on eight points, with a total dose of 48J/cm², each session. **Sham electrotherapy** (n=20) **No treatment** (n=20) Exercise therapy only (supervised strength exercises) **Concomitant therapy:** None of the participants undertook any form of physical therapy, in addition to the one stipulate. In addition they did not use intra-articular, anti-inflammatory or chondroprotective corticosteroids. The use of medications for concomitant diseases was not controlled.			

1.1.5.4 Interferential therapy compared to laser therapy

Table 5: Summary of studies included in the interferential therapy compared to laser therapy comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Alqualo-Costa 2020[15]	**Interferential therapy** (n=42)	**Knee osteoarthritis**	Pain at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Interferential current (IFC) three times a week for 4 week (12 sessions). Duration of each session ranged from 40 to 50 minutes. Parameters were used as follows: carrier current frequency of 4000Hz; amplitude-modulated frequency of 50Hz; sweep frequency of 50Hz; swing pattern of 1:1 second, and the current amplitude was increased until the patient reported strong but comfortable and non-painful stimulation paraesthesia. **Laser therapy** (n=42) Three times a week for 4 week (12 sessions). Duration of each session ranged from 40 to 50 minutes, and used a probe with a wavelength of 904nm, with a dose of 3J per point, totalling 9 points, total energy of 27J per session, peak power of 70W, pulse repetition frequency of 9500Hz, pulse duration of 60ns, average power of 40mW, application time of 75 seconds per point, and beam cross-sectional area of 0.5cm². **Combination therapy** (n=42) IFC plus PBM (interferential current plus photobiomodulation). Three	Mean age (SD): IFC group: 64.5 (7.8) years, PBM group: 61.3 (9.4) years, IFC+PBM group: 65.7 (10.1) years, placebo group: 65.3 (8.5) years N = 168 Definition: American College of Rheumatology criteria Severity (Kellgren-Lawrence): (Score 2): IFC group: 24, PBM group: 23, IFC+PBM group: 27, placebo group: 24 (Score 3): IFC group: 17, PBM group: 19, IFC+PBM group: 15, placebo group: 18 (Score 4): IFC group: 1, PBM group: 1, IFC+PBM group: 0, placebo group: 0 Duration of symptoms: not reported Presence of multi-morbidities: Not stated/unclear		

Study	Intervention and comparison	Population	Outcomes	Comments
	times a week for 4 weeks (12 sessions). **Sham electrotherapy** (n=42) Sham IFC and PBM. Three times a week for 4 week (12 sessions). **Concomitant therapy:** No analgesics 4 hours before the intervention.			
De Paula Gomes 2020[66]	**Interferential therapy** (n=20) The sessions were held three times a week, over 8 weeks (24 sessions), on alternate days, lasting approximately 90 minutes each treatment session. Interferential therapy (n=20) ICT was performed using a premodulated tetrapolar method with a carrier frequency of 4KHz, 1/1s sweep mode, 75 Hz frequency modulation amplitude, 25Hz delta frequency modulation amplitude, and automatic vector mode for 40 minutes. **Short wave therapy** (n=20) a thermopulse (Ibramed, Amparo, Sao Paolo, Brazil) device set to continuous mode, 27.12MHz frequency and 150W input was used for 20 minutes,	**Knee osteoarthritis** Mean age (SD): Exercise group: 67.85 (4.49) years, exercise+placebo group: 69.4 (4.45) years, exercise+ICT group: 71.85 (2.62) years, exercise+SDT group: 68.45 (4.62) years, exercise+PHOTO group: 65.75 (4.48) years N = 100 Definition: Unilateral knee OA according to American College of Rheumatology criteria, made through examination and the written opinion of a specialist in rheumatic disease. Severity (NRS pain score): Exercise group: 6.55 (1.09), exercise+placebo group: 6.50	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	and the intensity was defined based on each participant reporting a warm sensation (one sensation, described as soft but pleasant heat). **Laser therapy** (n=20) Prior to the exercise protocol, participants in the exercise and photobiomodulation (PHOTO) group underwent photobiomodulation therapy using a laserpulse device (Ibramed, Amparo, SP, Brazil). The power of each infrared laser was as follows: wavelength of 904nm, frequency of 9500Hz, pulse duration of 60ns, peak power of 70W, average power of 0.04W, energy density of 6J/cm² applied on eight points, with a total dose of 48J/cm², each session. **Sham electrotherapy** (n=20) **No treatment** (n=20) Exercise therapy only (supervised strength exercises) **Concomitant therapy:** None of the participants undertook any form of physical therapy, in addition to the one stipulate. In addition they did not	(0.68), exercise+ICT group: 6.65 (0.98), exercise+SDT group: 6.40 (0.99), exercise+PHOTO group: 6.70 (0.86) Duration of symptoms: Not stated/unclear Presence of multi-morbidities: Not stated/unclear		

Study	Intervention and comparison	Population	Outcomes	Comments
	use intra-articular, anti-inflammatory or chondroprotective corticosteroids. The use of medications for concomitant diseases was not controlled.			

1.1.5.5 Interferential therapy compared to sham electrotherapy

Table 6: Summary of studies included in the interferential therapy compared to sham electrotherapy comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Alqualo-Costa 2020[15]	**Interferential therapy** (n=42) Interferential current (IFC) three times a week for 4 week (12 sessions). Duration of each session ranged from 40 to 50 minutes. Parameters were used as follows: carrier current frequency of 4000Hz; amplitude-modulated frequency of 50Hz; sweep frequency of 50Hz; swing pattern of 1:1 second, and the current amplitude was increased until the patient reported strong but comfortable and non-painful stimulation paraesthesia. **Laser therapy** (n=42) Three times a week for 4 week (12 sessions). Duration of each session ranged from 40 to 50 minutes, and used a probe with a wavelength of 904nm, with a	**Knee osteoarthritis** Mean age (SD): IFC group: 64.5 (7.8) years, PBM group: 61.3 (9.4) years, IFC+PBM group: 65.7 (10.1) years, placebo group: 65.3 (8.5) years N = 168 Definition: American College of Rheumatology criteria Severity (Kellgren-Lawrence): (Score 2): IFC group: 24, PBM group: 23, IFC+PBM group: 27, placebo group: 24 (Score 3): IFC group: 17, PBM group: 19, IFC+PBM group: 15, placebo group: 18	Pain at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	dose of 3J per point, totalling 9 points, total energy of 27J per session, peak power of 70W, pulse repetition frequency of 9500Hz, pulse duration of 60ns, average power of 40mW, application time of 75 seconds per point, and beam cross-sectional area of 0.5cm². **Combination therapy** (n=42) IFC plus PBM (interferential current plus photobiomodulation). Three times a week for 4 weeks (12 sessions). **Sham electrotherapy** (n=42) Sham IFC and PBM. Three times a week for 4 week (12 sessions). **Concomitant therapy:** No analgesics 4 hours before the intervention.	(Score 4): IFC group: 1, PBM group: 1, IFC+PBM group: 0, placebo group: 0 Duration of symptoms: not reported Presence of multi-morbidities: Not stated/unclear		
Atamaz 2012[22]	**Transcutaneous electrical nerve stimulation** (n=37) TENS (frequency 80Hz, 10-30mA intensity) for 20 minutes three times a week for 3 weeks **Interferential therapy** (n=31)	**Knee osteoarthritis** Mean age (SD): 61.5 (7.5) years N = 203 Definition: People with knee osteoarthritis according to the American College of Rheumatology criteria with	Pain at ≤3 months and >3 months Physical function at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Interferential currents (frequency 100Hz generated by 4kHz sinusoidal waves) for 3 weeks **Pulsed short-wave therapy** (n=32) Pulsed short-wave diathermy (10cm diameter condenser plate, frequency 27.12mHz, input 300W, mean output 3.2W) for 3 weeks **Sham electrotherapy (TENS)** (n=37) Sham TENS **Sham electrotherapy (interferential therapy)** (n=35) Sham interferential therapy **Sham electrotherapy (pulsed short-wave therapy)** (n=31) Sham pulsed short-wave therapy **Concomitant therapy:** All people had an exercise program conducted in groups of 4-5 people three times a week for 3 weeks involving stretching, isometric quadriceps exercises and chair lift/minisquats. This was supplemented with additional instruction for home	radiologically confirmation with a Kellgren Lawrence grade of 2 or 3 Severity: Kellgren Lawrence grade 2-3 Duration of symptoms (mean [SD]): 43.7 (49.1) months. Presence of multimorbidities: Not stated/Unclear		

Study	Intervention and comparison	Population	Outcomes	Comments
	exercise. All people also attended an education program consisting of one 1 hour session discussing the functional anatomy of the knee, ergonomic principles, and understanding of osteoarthritis.			
De Paula Gomes 2020[66]	**Interferential therapy** (n=20) The sessions were held three times a week, over 8 weeks (24 sessions), on alternate days, lasting approximately 90 minutes each treatment session. Interferential therapy (n=20) ICT was performed using a premodulated tetrapolar method with a carrier frequency of 4KHz, 1/1s sweep mode, 75 Hz frequency modulation amplitude, 25Hz delta frequency modulation amplitude, and automatic vector mode for 40 minutes. **Short wave therapy** (n=20) a thermopulse (Ibramed, Amparo, Sao Paolo, Brazil) device set to continuous mode, 27.12MHz frequency and 150W input was used for 20 minutes, and the intensity was defined based on each participant reporting a warm sensation (one sensation, described as soft but pleasant heat).	**Knee osteoarthritis** Mean age (SD): Exercise group: 67.85 (4.49) years, exercise+placebo group: 69.4 (4.45) years, exercise+ICT group: 71.85 (2.62) years, exercise+SDT group: 68.45 (4.62) years, exercise+PHOTO group: 65.75 (4.48) years N = 100 Definition: Unilateral knee OA according to American College of Rheumatology criteria, made through examination and the written opinion of a specialist in rheumatic disease. Severity (NRS pain score): Exercise group: 6.55 (1.09), exercise+placebo group: 6.50 (0.68), exercise+ICT group: 6.65 (0.98), exercise+SDT group: 6.40 (0.99), exercise+PHOTO group: 6.70 (0.86)	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Laser therapy (n=20) Prior to the exercise protocol, participants in the exercise and photobiomodulation (PHOTO) group underwent photobiomodulation therapy using a laserpulse device (Ibramed, Amparo, SP, Brazil). The power of each infrared laser was as follows: wavelength of 904nm, frequency of 9500Hz, pulse duration of 60ns, peak power of 70W, average power of 0.04W, energy density of 6J/cm² applied on eight points, with a total dose of 48J/cm², each session. **Sham electrotherapy** (n=20) **No treatment** (n=20) Exercise therapy only (supervised strength exercises) **Concomitant therapy:** None of the participants undertook any form of physical therapy, in addition to the one stipulate. In addition they did not use intra-articular, anti-inflammatory or chondroprotective corticosteroids. The use of	Duration of symptoms: Not stated/unclear Presence of multi-morbidities: Not stated/unclear		

Study	Intervention and comparison	Population	Outcomes	Comments
	medications for concomitant diseases was not controlled.			
Gundog 2012[91]	**Interferential therapy** (n=45) Interferential therapy are different frequencies (40Hz, 100Hz or 180Hz) applied 5 times a week for 3 weeks (carrier frequency 4kHz) **Sham electrotherapy** (n=15) Sham treatment (no current delivered) **Concomitant therapy:** No additional information	**Knee osteoarthritis** Mean age (SD): 60.0 (9.1) years N = 60 Definition: Clinical (criteria of the American College of Rheumatology) and radiologic (a grade of 2 or 3 on the Kellgren Lawrence scale for severity of osteoarthritis) osteoarthritis of the knee for at least 6 months duration Severity: Not stated Duration of symptoms: At least 6 months Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months Physical function at ≤3 months	

1.1.5.6 Interferential therapy compared to no treatment

Table 7: Summary of studies included in the interferential therapy compared to no treatment comparison

Study	Intervention and comparison	Population	Outcomes	Comments
De Paula Gomes 2020[66]	**Interferential therapy** (n=20) The sessions were held three times a week, over 8 weeks (24 sessions), on alternate days, lasting approximately 90 minutes each treatment session. Interferential therapy (n=20)	**Knee osteoarthritis** Mean age (SD): Exercise group: 67.85 (4.49) years, exercise+placebo group: 69.4 (4.45) years, exercise+ICT group: 71.85 (2.62) years, exercise+SDT group: 68.45 (4.62) years,	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	ICT was performed using a premodulated tetrapolar method with a carrier frequency of 4KHz, 1/1s sweep mode, 75 Hz frequency modulation amplitude, 25Hz delta frequency modulation amplitude, and automatic vector mode for 40 minutes. **Short wave therapy** (n=20) a thermopulse (Ibramed, Amparo, Sao Paolo, Brazil) device set to continuous mode, 27.12MHz frequency and 150W input was used for 20 minutes, and the intensity was defined based on each participant reporting a warm sensation (one sensation, described as soft but pleasant heat). **Laser therapy** (n=20) Prior to the exercise protocol, participants in the exercise and photobiomodulation (PHOTO) group underwent photobiomodulation therapy using a laserpulse device (Ibramed, Amparo, SP, Brazil). The power of each infrared laser was as follows: wavelength of 904nm, frequency of 9500Hz, pulse duration of 60ns, peak power of 70W, average power of 0.04W, energy density of 6J/cm²	exercise+PHOTO group: 65.75 (4.48) years N = 100 Definition: Unilateral knee OA according to American College of Rheumatology criteria, made through examination and the written opinion of a specialist in rheumatic disease. Severity (NRS pain score): Exercise group: 6.55 (1.09), exercise+placebo group: 6.50 (0.68), exercise+ICT group: 6.65 (0.98), exercise+SDT group: 6.40 (0.99), exercise+PHOTO group: 6.70 (0.86) Duration of symptoms: Not stated/unclear Presence of multi-morbidities: Not stated/unclear		

Study	Intervention and comparison	Population	Outcomes	Comments
	applied on eight points, with a total dose of 48J/cm², each session. **Sham electrotherapy** (n=20) **No treatment** (n=20) Exercise therapy only (supervised strength exercises) **Concomitant therapy:** None of the participants undertook any form of physical therapy, in addition to the one stipulate. In addition they did not use intra-articular, anti-inflammatory or chondroprotective corticosteroids. The use of medications for concomitant diseases was not controlled.			

1.1.5.7 Neuromuscular electrical stimulation compared to no treatment

Table 8: Summary of studies included in the neuromuscular electrical stimulation compared to no treatment comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Arslan 2020[21]	**Neuromuscular electrical stimulation** (n=21) NMES and combined physiotherapy. Both groups received a combined physiotherapy programme, with 5 sessions per week. It included a hot pack, therapeutic	**Knee osteoarthritis** Mean age (SD): 71 (12) years N = 43 Definition: stage 2 or 3 on Kellgren Lawrence staging.	Quality of life at ≤3 months Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	ultrasound, TENS and exercise programme. **No treatment** (n=17) **Concomitant treatment:** Both groups received a combined physiotherapy programme, with 5 sessions per week. It included a hot pack, therapeutic ultrasound, TENS and exercise programme.	Severity: 48.43 (28.85) vs 52.29 (30.20) Duration of symptoms (years): not reported Presence of multi-morbidities: Not stated/unclear		
Bruce-brand 2012[36]	**Neuromuscular electrical stimulation** (n=14) Neuromuscular electrical stimulation (maximum root mean square output current 18mA, output frequency 50Hz, pulse width changes between 100-400 microseconds) for 20 minutes, 5 days a week for 6 weeks with exercise training after each treatment. **No treatment** (n=13) No treatment A third group (n=14) was reported but not included in the analysis as it did not fulfil the inclusion criteria. **Concomitant therapy:**	**Knee osteoarthritis** Mean age (SD): 64.0 (5.4) years N = 41 Definition: Symptomatic moderate to severe knee osteoarthritis confirmed radiographically as Kellgren Lawrence grade 3-4 Severity: Kellgren Lawrence grade 3-4 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Quality of life at ≤3 months Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Standard care was available to all including osteoarthritis education, weight loss, pharmacologic therapy and physical therapy			
Elboim-gabyzon 2013[76]	**Neuromuscular electrical stimulation** (n=33) Neuromuscular electrical stimulation to the rectus femoris proximal muscle belly and the vastus medialis muscle belly (150V, 100ms pulse duration, 1000mA intensity) for 12 bieweely treatments over 6 weeks **No treatment** (n=30) No electrotherapy treatment **Concomitant therapy:** All people participated in a group exercise programme, with 6-8 subjects in each group. The exercise sessions involved muscle strengthening exercises, functional activities and balance training. They took 45 minutes to complete. Patient education was incorporated into each session including information on self-management, which included activity and exercise planning, and a discussion of pain-coping strategies	**Knee osteoarthritis** Mean age (SD): 68.2 (8.0) years N = 63 Definition: Radiographic evidence of knee osteoarthritis at grade at least 2 according to the Kellgren Lawrence classification Severity: Kellgren Lawrence at least grade 2 Duration of symptoms (mean [SD]): 4.3 (5.6) years. Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
Laufer 2014[131]	**Neuromuscular electrical stimulation** (n=25) Neuromuscular electrical stimulation to the quadriceps femoris muscle giving 10 contractions at the maximal tolerated intensity for 12 sessions over 6 weeks **No treatment** (n=25) No electrotherapy treatment **Concomitant therapy:** An exercise program was completed with quadriceps muscle strengthening exercise.	**Knee osteoarthritis** Mean age (SD): 68.9 (7.7) years N = 50 Definition: Knee osteoarthritis at grade 2 or higher, according to the Kellgren and Lawrence classification Severity: Kellgren Lawrence radiographic grade 2 or higher Duration of symptoms (mean [SD]): 4.7 (6.1) years. Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months and >3 months	
Mizusaki imoto 2013[154]	**Neuromuscular electrical stimulation** (n=50) Neuromuscular electrical stimulation to the rectus femoris and vastus medialis muscle (pulsed current, biphasic, asymmetrical, rectangular waveform, frequency 50Hz, pulse duration 250microseconds, contraction time 10s, rest time 30s every 20 minutes, current intensity at the maximum tolerable) **No treatment** (n=50) No electrotherapy treatment **Concomitant therapy:**	**Knee osteoarthritis** Mean age (SD): 61.1 (6.8) years N = 100 Definition: Knee osteoarthritis based on the American College of Rheumatology criteria Severity: Kellgren Lawrence grade 2-4, median grade 2 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months Physical function at ≤3 months Mild adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Exercise including 10 minutes on a stationary bicycle, stretching of hamstring muscles (3 repetitions of 30 seconds) with the aid of an elastic band, and loaded quadriceps strengthening exercises combined with NMES. Performed in a sitting position with the knee and hip flexed to 90 degrees, people contracted their quadriceps at each NMES stimulus. Paracetamol was prescribed for pain, and diacerein and chloroquine for osteoarthritis control.			
Palmieri-smith 2010[170]	**Neuromuscular electrical stimulation** (n=16) Neuromuscular electrical stimulation 3 times per week over 4 weeks. Stimulating contractions to the quadriceps musculature (one limb only). Applied through a 2500Hz alternating current, modulated at 50 bursts per second, with a ramp up time of 2 seconds. The electrical current was set for a sequence of 10 seconds on (including the ramp up time) and 50 seconds off. **No treatment** (n=14) No electrotherapy treatment	**Knee osteoarthritis** Mean age (SD): 57.4 (2.9) years N = 30 Definition: Knee osteoarthritis with radiographic evidence, defined as a score of at least 2 on the Kellgren and Lawrence scale Severity: Kellgren Lawrence grade 2-3, majority grade 2 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months and >3 months Physical function at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Concomitant therapy: No additional information.			

1.1.5.8 Extracorporeal shockwave therapy compared to sham electrotherapy

Table 9: Summary of studies included in the extracorporeal shockwave therapy compared to sham electrotherapy comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Cho 2016[58]	**Extracorporeal shockwave therapy** (n=9) Extracorporeal shockwave therapy administered as 1000 impulses of shockwave at 0.05mL/mm2 on the proximal medial tibia of the affected knee over 2 weeks **Sham electrotherapy** (n=9) Sham therapy (same number of impulses, but shockwave of 0mJ/mm2) over 2 weeks **Concomitant therapy:** No additional information	**Knee osteoarthritis** Mean age (SD): 74.1 (7.0) years N = 18 Definition: Unilateral or bilateral knee osteoarthritis of at least Kellgren Lawrence grade 1 Severity: Kellgren Lawrence grade (mean [SD]): 1.9 (1.1) Duration of symptoms: Not stated Presence of multimorbidities: High morbidity score (At least everyone had previously had a stroke)	Pain at ≤3 months	Participants were people with knee osteoarthritis who had also had a chronic stroke.
Wang 2020[217]	**Extracorporeal shockwave therapy** (n=36) Extracorporeal shockwave therapy using a shockwave of 0.25 mJ/mm² for 4000 pulses in total at a frequency of 15 Hz/s. Therapy three times weekly for a total of 10 weeks.	**Knee osteoarthritis** Age (years): ≤75 years N = 72 Definition: Chronic knee pain (for more than 3 months) with a duration of morning knee	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Sham electrotherapy (n=36) Using a shockwave of 0 mJ/mm². The probe emitted the same noises as the therapy probe. Therapy three times weekly for a total of 10 weeks. **Concomitant therapy:** No additional information.	stiffness of less than 30 minutes Severity: Not stated/unclear Duration of symptoms (mean [SD]): 7.9 (3.7) years Presence of multi-morbidities: Not stated/unclear		
Zhang 2021[236]	**Extracorporeal shockwave therapy** (n=75) Radial extracorporeal shockwave therapy (rESWT) Participants received 4 sessions of rEWST, one week apart, with a shock frequency of 8Hs per session. The treatment protocols for the 4 rEWST groups were as follows: LD/2000, with a positive EFD of 0.12mJ/mm2 and 4000 impulses per session; HD/2000, with a positive EFD of 0.24mJ/mm2 and 2000 impulses per session; and HD/4000, with a positive EFD of 0.24mJ/mm2 and 4000 impulses per session. **Sham electrotherapy** (n=14)	**Knee osteoarthritis**Mean age (SD): LD/2000 group: 60.84 (8.36) years, LD/4000 group: 62.70 (7.50) years, HD/2000 group: 58.21 (9.47) years, HD/4000 group: 63.65 (6.94) years, control group: 61.5 (5.43) years N = 89 Definition: Diagnosed by 2 expert physicians according to American College of Rheumatology criteria. Severity: Not stated/unclear Duration of symptoms (months): LD/2000 group: 17.15 (5.36), LD/4000 group:	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	The placebo group also received 4 sessions of rEWST, one week apart, with a shock frequency of 8Hz per session, but was treated with the minimum positive EFD 0.02mJ/mm2 and 1000 impulses per session. **Concomitant treatment:** All participants were prevented from receiving any additional treatments, such as physical therapy, oral or parenteral steroid medications, anti-inflammatory drugs, stretching, acupuncture, orthotics etc., throughout the treatment sessions.	19.92(6.85), HD/2000 group: 18.56(7.48), HD/4000 group: 16.67 (4.72), control group: 15.73 (8.37) Presence of multi-morbidities: Not stated/unclear		
Zhao 2013[237]	**Extracorporeal shockwave therapy** (n=34) Extracorporeal shockwave therapy delivered at weekly intervals of 4 weeks. Delivered as 4000 pulses in total and applied at 0.25mJ/mm2 and a frequency of 6Hz. **Sham electrotherapy** (n=36) Sham therapy (same number of impulses, but shockwave of 0mJ/mm2) **Concomitant therapy:** No additional information	**Knee osteoarthritis** Mean age (SD): 60.9 (10.6) years N = 70 Definition: People with a diagnosis of primary symptomatic knee osteoarthritis according to the criteria of the American College of Rheumatology Severity: Kellgren Lawrence grade 2-3, median grade 2 Duration of symptoms: At least 3 months	Pain at ≤3 months Physical function at ≤3 months Mild adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
		Presence of multimorbidities: Not stated/unclear		
Zhong 2019[238]	**Extracorporeal shockwave therapy** (n=32) Once a week for 4 consecutive weeks (4 sessions in total). The parameters of therapy included a total of 2000 pulses of 8Hz frequency at 2.5 bars of pneumatic pressure. The first 1000 pulses were evenly distributed to pain points (the maximum number of pain points is 4). **Sham therapy** (n=31) Participants assigned to the placebo group were managed by the same physical therapist with the same ESWT protocol, but the air pressure was set at 0.2 bar. The stress value was set by the researcher responsible for randomisation. Participants and therapists could hear a sound similar to that of the regular ESWT, in order to enhance the sham design, but they were not able to see the dashboard. **Concomitant treatment:** All participants were educated on a simple home exercise programme for the first visit. the	**Knee osteoarthritis** Mean age (SD): 62.8 (7.9) years N = 63 Definition: Diagnosis by rehabilitation physicians in accordance with American College of Rheumatology criteria and radiographic criteria (Kellgren Lawrence grade) Severity (WOMAC pain at baseline): 6.6 (1.5) vs 7.0 (1.9) Duration of knee pain (months): 34.7 (15.4) vs 34.1 (14.2) Kellgren-Lawrence grade: II (n): ESWT group: 23, placebo group: 24 Kellgren-Lawrence grade: III (n): ESWT group: 9, placebo group: 7 Presence of multi-morbidities: Not stated/unclear	Pain at ≤3 months Physical function at ≤3 months Mild adverse events at ≤3 months Moderate/major adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	programme was comprised of a single knee extensor muscle strengthening. The patient sat in a chair, straightened his/ her knee as far as possible, kept it for 10 seconds, repeated 10 times, and did 3 groups per day. therapist- applied manual forces were not permitted in the exercise programme. The home exercise was supervised by a physiotherapist once every 3 days over the phone.			

1.1.5.9 Extracorporeal shockwave therapy compared to no treatment

Table 10: Summary of studies included in the extracorporeal shockwave therapy compared to no treatment comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Eftekharsadat 2019[74]	**Extracorporeal shockwave therapy** (n= 25) ESWT. Participants received 5 sessions of shock wave therapy through 3 weeks Then, radial ESWT was used with shockwaves of 2000 pulses/session with an energy flux density of 0.18mJ/mm², the energy level of 2-4, a frequency of 10-16Hz, and pulse rate of 160/ minute were generally applied each session. **Combination therapy** (n=25) Participants received 10 sessions (3 sessions, weekly) of	**Knee osteoarthritis** Mean age (SD): ESWT group: 58.00 (5.97) years, PT group: 55.76 (6.06) years, exercise group: 58.16 (7.20) years N = 75 Definition: American College of Rheumatology criteria Severity:(VAS score at baseline): ESWT group: 7.00 (1.63), combination group: 7.16 (1.37), exercise group: 6.32(1.44)	Pain at ≤3 months Physical function at ≤3 months	The combination therapy and extracorporeal shockwave therapy arms were not compared to each other as the combination therapy did not include the extracorporeal shockwave therapy as a component.

Study	Intervention and comparison	Population	Outcomes	Comments
	physical therapy including hot pack, TENS and ultrasound (US, HP: 74.5 degrees C, 20 minutes on the affected knee, TENS: pulse duration 20-100 microseconds, 50% duty cycle, current amplitude, maximum tolerated tingling, frequency <200pps, US: frequency of 1 MHz, the intensity of 2.5 W/cm², and duty cycle of 25%, and the probe of US was applied for 10 minutes. **No treatment** (n=25) The exercise programme was applied to all 3 groups. It consisted of the isometric strengthening of the quadriceps muscle in the form of 3 submaximal isometric contractions with gradually increasing intensity combined with weight- bearing water and land based exercises. Additionally, participants were advised to only use acetaminophen for pain relief in the event of severe pain and activities of daily living modifications (e.g. weight loss and the avoidance of heavy lifting, long-distance walking, and high-impact exercises) were taught as well.	Duration of symptoms: Not stated/unclear Presence of multi-morbidities: Not stated/unclear		

Study	Intervention and comparison	Population	Outcomes	Comments
	Concomitant therapy: None of the participants undertook any form of physical therapy, in addition to the ones stipulated. In addition, they did not use intra-articular, anti-inflammatory or chondroprotective corticosteroids. The use of medications for concomitant diseases was not controlled			
Gunaydin 2020[90]	**Extracorporeal shockwave therapy** (n=18) ESWT intervention was performed once a week for 6 weeks. During the treatment, participants were placed in supine position, and the affected knee was flexed at 90 degrees. Before starting, the intervention area on the tibiofemoral and patellofemoral joints was identified with a pen. The probe was then placed on the painted area after a gel application. An average of 2000 beats at a frequency of 6-8Hz was used per session. During the application, peroneal nerve and vein structures were avoided. **No treatment** (n=20) A third arm (n=22) was included in the study (receiving kinesio taping). This arm was not	**Knee osteoarthritis** Mean age (SD): 58.8 (6.2) years N = 60 Definition: Diagnosis made by an orthopaedic surgeon. Kellgren-Lawrence grade 1-3. Severity (baseline VAS during squats): ESWT group: 8.38 (3.42), exercise group: 7.84 (2.14) Duration of pain: not reported Presence of multi-morbidities: Not stated/unclear	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	included in the analysis as it did not fulfil the inclusion criteria in the protocol. **Concomitant treatment:** Home exercise, prescribed by a physiotherapist for 12 weeks (no further details).			

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2 **1.1.5.10 Laser therapy compared to pulsed short-wave therapy**

3 **Table 11: Summary of studies included in the pulsed short-wave therapy compared to laser therapy comparison**

Study	Intervention and comparison	Population	Outcomes	Comments
De Paula Gomes 2020[66]	**Interferential therapy** (n=20) The sessions were held three times a week, over 8 weeks (24 sessions), on alternate days, lasting approximately 90 minutes each treatment session. Interferential therapy (n=20) ICT was performed using a premodulated tetrapolar method with a carrier frequency of 4KHz, 1/1s sweep mode, 75 Hz frequency modulation amplitude, 25Hz delta frequency modulation amplitude, and automatic vector mode for 40 minutes. **Short wave therapy** (n=20)	**Knee osteoarthritis** Mean age (SD): Exercise group: 67.85 (4.49) years, exercise+placebo group: 69.4 (4.45) years, exercise+ICT group: 71.85 (2.62) years, exercise+SDT group: 68.45 (4.62) years, exercise+PHOTO group: 65.75 (4.48) years N = 100 Definition: Unilateral knee OA according to American College of Rheumatology criteria, made through examination and the written opinion of a specialist in rheumatic disease.	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	a thermopulse (Ibramed, Amparo, Sao Paolo, Brazil) device set to continuous mode, 27.12MHz frequency and 150W input was used for 20 minutes, and the intensity was defined based on each participant reporting a warm sensation (one sensation, described as soft but pleasant heat). **Laser therapy** (n=20) Prior to the exercise protocol, participants in the exercise and photobiomodulation (PHOTO) group underwent photobiomodulation therapy using a laserpulse device (Ibramed, Amparo, SP, Brazil). The power of each infrared laser was as follows: wavelength of 904nm, frequency of 9500Hz, pulse duration of 60ns, peak power of 70W, average power of 0.04W, energy density of 6J/cm² applied on eight points, with a total dose of 48J/cm², each session. **Sham electrotherapy** (n=20) **No treatment** (n=20) Exercise therapy only (supervised strength exercises)	Severity (NRS pain score): Exercise group: 6.55 (1.09), exercise+placebo group: 6.50 (0.68), exercise+ICT group: 6.65 (0.98), exercise+SDT group: 6.40 (0.99), exercise+PHOTO group: 6.70 (0.86) Duration of symptoms: Not stated/unclear Presence of multi-morbidities: Not stated/unclear		

Study	Intervention and comparison	Population	Outcomes	Comments
	Concomitant therapy: None of the participants undertook any form of physical therapy, in addition to the one stipulate. In addition they did not use intra-articular, anti-inflammatory or chondroprotective corticosteroids. The use of medications for concomitant diseases was not controlled.			

1.1.5.11 Laser therapy compared to neuromuscular electrical stimulation

Table 12: Summary of studies included in the laser therapy compared to neuromuscular electrical stimulation comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Melo mde 2015[152]	**Combination therapy** (n=15) Laser and neuromuscular electrical stimulation (combination of the same protocols for the other two) delivered over 8 weeks. **Laser therapy** (n=15) Low level laser therapy delivered as 30 seconds per point, 6J energy per point (36J in total) for 4 weeks, then a reduction of the dose by 30% for the remaining 4 weeks **Neuromuscular electrical stimulation** (n=15)	**Knee osteoarthritis** Mean age (SD): 68.8 (5.1) years N = 45 Definition: Grade 2 or 3 knee osteoarthritis diagnosed by a traumatology-orthopaedic physician according to the criteria proposed by Kellgren and Lawrence Severity: Kellgren-Lawrence grade 2-3 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Neuromuscular electrical stimulation sessions twice a week, at 48 hour intervals, over an 8 week period with a progressive increase in intensity and volume. **Concomitant therapy:** Kinesthetic exercise including stretching and isometric exercises for the entire lower limb conducted in supervised 20 minute sessions.			

1.1.5.12 Laser therapy compared to sham electrotherapy

Table 13: Summary of studies included in the laser therapy compared to sham electrotherapy comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Alfredo 2012[10] Subsidiary paper: Alfredo 2018[11]	**Laser therapy** (n=24) Low-intensity laser therapy (using gallium arsenide laser, wavelength 904nm, frequency 700Hz, average power 60mW, peak power 20W, pulse duration 4.3ms, 50 seconds per area, area 0.5cm2) followed by exercise. 3 times a week for 3 weeks (exercise for an additional 8 weeks after laser therapy ends) **Sham electrotherapy** (n=22) Placebo laser with exercise three times a week for 3 weeks	**Knee osteoarthritis** Mean age (SD): 61.7 (7.2) years N = 46 Definition: Knee osteoarthritis with levels 2-4 according to the Kellgren Lawrence grade Severity: Osteoarthritis grade 2-4, median grade 3 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months and >3 months Physical function at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	(exercise for an additional 8 weeks after laser therapy ends) **Concomitant therapy:** No additional information			
Alghadir 2014[13]	**Laser therapy** (n=20) Laser therapy (Ga-As laser, wavelength 850nm, power 100mW, spot size 1.0mm, total dose 48J/cm2) Eight points irradiated. Conducted over 4 weeks. **Sham electrotherapy** (n=20) Placebo laser therapy **Concomitant therapy:** Hot packs were wrapped in toweling and placed on the target knees for 20 minutes followed by laser therapy. All people were given an isometric knee extension and straight leg raising exercise program to complete at home for 10 times/set, for 3 sets. All people were advised to keep their activity level and medication unchanged (paracetamol 2g daily) throughout the study period.	**Knee osteoarthritis** Mean age (SD): 56.1 (8.0) years N = 40 Definition: Knee osteoarthritis according to the American College of Rheumatology criteria with knee osteoarthritis of grade 2-3 according to the Kellgren and Lawrence grade Severity: Kellgren Lawrence grade 2-3, median grade 2 Duration of symptoms (mean [SD]): 9.6 (4.0) months Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months Physical function at ≤3 months	
Alqualo-Costa, 2020[15]	**Interferential therapy** (n=42) Interferential current (IFC) three times a week for 4 week (12	**Knee osteoarthritis** Mean age (SD): IFC group: 64.5(7.8) years, PBM group:	Pain at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	sessions). Duration of each session ranged from 40 to 50 minutes. Parameters were used as follows: carrier current frequency of 4000Hz; amplitude-modulated frequency of 50Hz; sweep frequency of 50Hz; swing pattern of 1:1 second, and the current amplitude was increased until the patient reported strong but comfortable and non-painful stimulation paraesthesia. **Laser therapy** (n=42) Three times a week for 4 week (12 sessions). Duration of each session ranged from 40 to 50 minutes, and used a probe with a wavelength of 904nm, with a dose of 3J per point, totalling 9 points, total energy of 27J per session, peak power of 70W, pulse repetition frequency of 9500Hz, pulse duration of 60ns, average power of 40mW, application time of 75 seconds per point, and beam cross-sectional area of 0.5cm². **Combination therapy** (n=42) IFC plus PBM (interferential current plus photobiomodulation). Three times a week for 4 weeks (12 sessions).	61.3 (9.4) years, IFC+PBM group: 65.7 (10.1) years, placebo group: 65.3 (8.5) years N = 168 Definition: American College of Rheumatology criteria Severity (Kellgren-Lawrence): (Score 2): IFC group: 24, PBM group: 23, IFC+PBM group: 27, placebo group: 24 (Score 3): IFC group: 17, PBM group: 19, IFC+PBM group: 15, placebo group: 18 (Score 4): IFC group: 1, PBM group: 1, IFC+PBM group: 0, placebo group: 0 Duration of symptoms: not reported Presence of multi-morbidities: Not stated/unclear		

Study	Intervention and comparison	Population	Outcomes	Comments
	Sham electrotherapy (n=42) Sham IFC and PBM. Three times a week for 4 week (12 sessions). **Concomitant therapy:** No analgesics 4 hours before the intervention.			
Basford 1987[29]	**Laser therapy** (n=47) 0.9mW continuous wave Helium-Neon (632.8nm) laser 3 times a week for 3 weeks **Sham electrotherapy** (n=34) Sham laser therapy (a concealed switch is switched off to turn off the laser) **Concomitant therapy:** No additional information	**Thumb osteoarthritis** Mean age: 59.1 years N = 81 Definition: Symptomatic osteoarthritis of the thumb Severity: Not stated Duration of symptoms (mean): 9.1 years Presence of multimorbidities: Not stated/Unclear	Mild adverse events at ≤3 months	
Brosseau 2005[35]	**Laser therapy** (n=42) Low-intensity laser therapy (using gallium arsenide laser, wavelength 860nm, frequency 20Hz, average power 60mW, area 0.01cm2) for 20 minutes. 3 times a week for 6 weeks. **Sham electrotherapy** (n=46) Sham laser therapy **Concomitant therapy:** No additional information	**Knee osteoarthritis** Mean age (SD): 64.7 (10.1) years N = 88 Definition: Diagnosis made by rheumatologists and consistent with the clinical criteria as set out by the American College of Rheumatology classification of osteoarthritis of the hand, the radiologic criteria	Pain at ≤3 months and >3 months Physical function at ≤3 months and >3 months Mild adverse events at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
		according to Kallman and the disease activity criteria according to the Doyle Articular Index Severity: Not stated Duration of symptoms (mean [SD]): 8.0 (8.3) years Presence of multimorbidities: Not stated/Unclear		
Bulow 1994[37]	**Laser therapy** (n=13) Laser (Ga-Al-As, wavelength 830nm, mean effect 25mW, continuous beam, irradiation area 0.28cm2) 2-4 treatments per week for a total of 9 treatments over 3 weeks **Sham electrotherapy** (n=14) Placebo laser (laser was switched off) **Concomitant therapy:** Analgesics and NSAIDs were permitted including weak simple analgesics, NSAIDs and dextropropoxifen and opioids. These were noted for each participant.	**Knee osteoarthritis** Mean age (range): 74 (60-86) years N = 27 Definition: Clinically and x-ray verified uni- or bilateral osteoarthritis of the knee with exercise induced pain for at least 6 months Severity: Not stated Duration of symptoms: at least 6 months Presence of multimorbidities: Not stated/Unclear	Mild adverse events at ≤3 months	
Cantero-tellez 2020[42]	**Laser therapy** (n=22) Delivery parameters were established according to the acknowledged guidelines and were peak power 3.0W (duty	Thumb osteoarthritis Mean age (SD): 71 (12) years N = 43	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	cycle of 50%, mean power 1.5W), with intense super pulse mode, combined wavelength of 800 +970nM, pulse frequency 2Hz, energy dose 75J per session, spot size 5cm2, and treatment frequency three times per week. The phase time was 15 seconds, with a total treatment time of 45 seconds. **Sham therapy** (n=21) The same equipment was used with a pen emitting a red guide light and a warning sound, but without the emission of a laser beam. All conditions including indicator lights and sounds in the laser application were therefore identical in both groups, except the laser irradiation, which was not visible. **Concomitant therapy:** No therapeutic exercises, modalities, or other complementary treatments were provided in order to not interfere with assessment of the individual effectiveness of laser therapy.	Definition (intervention versus control): American College of Rheumatology diagnosis of thumb carpometacarpal osteoarthritis in dominant hand with a radiographic stage of 1-2. Severity: 6.3 (1.2) vs 5.9 (1.1) Duration of symptoms (years): not reported Presence of multi-morbidities: Not stated/unclear		
De Paula Gomes 2020[66]	**Interferential therapy** (n=20) The sessions were held three times a week, over 8 weeks (24	**Knee osteoarthritis** Mean age (SD): Exercise group: 67.85 (4.49) years,	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	sessions), on alternate days, lasting approximately 90 minutes each treatment session. Interferential therapy (n=20) ICT was performed using a premodulated tetrapolar method with a carrier frequency of 4KHz, 1/1s sweep mode, 75 Hz frequency modulation amplitude, 25Hz delta frequency modulation amplitude, and automatic vector mode for 40 minutes. **Short wave therapy** (n=20) a thermopulse (Ibramed, Amparo, Sao Paolo, Brazil) device set to continuous mode, 27.12MHz frequency and 150W input was used for 20 minutes, and the intensity was defined based on each participant reporting a warm sensation (one sensation, described as soft but pleasant heat). **Laser therapy** (n=20) Prior to the exercise protocol, participants in the exercise and photobiomodulation (PHOTO) group underwent photobiomodulation therapy using a laserpulse device (Ibramed, Amparo, SP, Brazil). The power of each infrared laser was as follows: wavelength of	exercise+placebo group: 69.4 (4.45) years, exercise+ICT group: 71.85 (2.62) years, exercise+SDT group: 68.45 (4.62) years, exercise+PHOTO group: 65.75 (4.48) years N = 100 Definition: Unilateral knee OA according to American College of Rheumatology criteria, made through examination and the written opinion of a specialist in rheumatic disease. Severity (NRS pain score): Exercise group: 6.55 (1.09), exercise+placebo group: 6.50 (0.68), exercise+ICT group: 6.65 (0.98), exercise+SDT group: 6.40 (0.99), exercise+PHOTO group: 6.70 (0.86) Duration of symptoms: Not stated/unclear Presence of multi-morbidities: Not stated/unclear		

Study	Intervention and comparison	Population	Outcomes	Comments
	904nm, frequency of 9500Hz, pulse duration of 60ns, peak power of 70W, average power of 0.04W, energy density of 6J/cm² applied on eight points, with a total dose of 48J/cm², each session. **Sham electrotherapy** (n=20) **No treatment** (n=20) Exercise therapy only (supervised strength exercises) **Concomitant therapy:** None of the participants undertook any form of physical therapy, in addition to the one stipulate. In addition they did not use intra-articular, anti-inflammatory or chondroprotective corticosteroids. The use of medications for concomitant diseases was not controlled.			
Fukuda 2011[84]	**Laser therapy** (n=13) Laser (AsGa laser, wavelength 904nm, frequency 700Hz, mean power of 60mW, peak power of 20W, 50 seconds per point, beam area of 0.5cm2) given over 3 weeks **Sham electrotherapy** (n=14)	**Knee osteoarthritis** Mean age (SD): 63.0 (8.6) years N = 47 Definition: People with knee pain and reduced functional ability over the preceding three months and a radiographic examination	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Placebo laser **Concomitant therapy:** People with knee pain and reduced functional ability over the preceding three months and a radiographic examination showing knee osteoarthritis of grade 2-4 according to the classification of Kellgren and Lawrence.	showing knee osteoarthritis of grade 2-4 according to the classification of Kellgren and Lawrence Severity: Kellgren Lawrence grade 2-4, median grade 2 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear		
Gur 2003[92]	**Laser therapy** (n=60) Laser (AsGa laser, wavelength 904nm, frequency 700Hz. Either 5 minutes of 3J total dose, or 3 minutes of 2J. Both were combined with exercise. Completed as 10 treatments over 14 weeks. **Sham electrotherapy** (n=30) Placebo laser **Concomitant therapy:** All people received exercise therapy that was continued for 14 weeks and involved isometric quadriceps exercise (straight leg raising).	**Knee osteoarthritis** Mean age (SD): 59.7 (7.0) years N = 90 Definition: Osteoarthritis according to the American College of Rheumatology criteria and radiographic evidence of knee osteoarthritis of Kelgren-Lawrence grade 2-4 Severity: Radiographic grade 2-4, median grade 3 Duration of symptoms (mean [SD]): 57.0 (45.0) months Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months	
Gworys 2012[93]	**Laser therapy** (n=94) Laser performed once a day, 5 days a week over 2 weeks. Group 1 received one-wave	**Knee osteoarthritis** Mean age (SD): 64.0 (11.3) years N = 125	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	laser irradiation (wave length 810nm, dose 8J/point, surface density of energy 12.7 J/cm², power 400mW, surface density of power 634.9 mW/cm²) in the continuous mode. Group 2 received MLS laser irradiation (power 1100mW, frequency 2000Hz, dose 12.4 J/point, energy density 6.21 J/cm²). Group 3, received MLS laser irradiation (power 1100mW, frequency 2000Hz, dose 6.6J/point, energy density 3.28J/cm²). **Sham electrotherapy** (n=31) Placebo laser **Concomitant therapy:** No additional information	Definition: Diagnosis of knee osteoarthritis according to the criteria established by the American College of Rheumatology Severity: 2nd degree joint injury according to Seyfried on the basis of clinical examination Duration of symptoms: Pain for at least 6 weeks Presence of multimorbidities: Not stated/Unclear		
Helianthi 2016[96]	**Laser therapy** (n=31) Laser acupuncture (output power 50mW, output power 25mW/cm2, wavelength 785nm, dose 4J for 80 seconds at each point) given twice a week for 10 sessions **Sham electrotherapy** (n=31) Placebo laser **Concomitant therapy:**	**Knee osteoarthritis** Mean age (SD): 69 (5) years N = 62 Definition: People with grade 2 and grade 3 knee osteoarthritis based on the Kellgren-Lawrence grading scale, either unilateral or bilateral and who also had average pain intensity of more than 40 on a 100mm visual analogue scale	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	People were allowed to take paracetamol as required for severe pain (with a maximum dose of 4g/day).	Severity: Grade 2-3 (median grade 3) Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear		
Hinman 2014[97]	**Laser therapy** (n=71) Laser acupuncture (measured output 10mW, energy output 0.2J/point) given over 12 weeks **Sham electrotherapy** (n=70) Placebo laser **No treatment** (n=71) A fourth group (n=70) was not included as it did not fulfil the inclusion criteria for this review. **Concomitant therapy:** No additional information	**Knee osteoarthritis** Mean age (SD): 63.6 (8.4) years N = 282 Definition: Knee pain of longer than 3 months duration, knee pain on most days with average severity of 4 or more out of 10 on a numeric rating scale, and had morning stiffness lasting less than 30 minutes (consistent with a clinical diagnosis of osteoarthritis) Severity: Not stated Duration of symptoms: Median 5-<10 years Presence of multimorbidities: Not stated/Unclear	Quality of life at ≤3 months and >3 months Pain at ≤3 months and >3 months Physical function at ≤3 months and >3 months	
Hsieh 2012[100]	**Laser therapy** (n=37) Short-term monochromatic infrared energy (radiant power at 6.24W, gallium-aluminium arsenide diodes, 890nm, 40 minutes of treatment) achieved 3 times a week for 2 weeks	**Knee osteoarthritis** Mean age (SD): 61.2 (10.7) years N = 72 Definition: Combined clinical and radiographic criteria of	Quality of life at ≤3 months Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Sham electrotherapy (n=35) Placebo laser **Concomitant therapy:** No additional information	knee osteoarthritis, as established by the American college of Rheumatology Severity: Kellgren Lawrence scores of 2 or greater in both knees Duration of symptoms: Not stated Presence of multimorbidities: High morbidity score		
Kheshie 2014[120]	**Laser therapy** (n=38) High or low intensity laser therapy. High intensity (using a Nd:YAG laser, 1250J through three treatment phases) and low intensity (using a gallium-arsenide diode laser, 830nm wavelength, 800mW output power, average energy density of 50J/cm2, frequency of 1kHz, duty cycle of 80%). **Sham electrotherapy** (n=15) Placebo laser **Concomitant therapy:** All groups received an exercise program consisting of active range of motion exercises, muscle strengthening, and flexibility exercises. These were completed in a supervised form and at home.	**Knee osteoarthritis** Mean age (SD): 54.6 (8.49) years N = 53 Definition: Painful knee osteoarthritis for at least 6 months with degenerative osteoarthritic knee of grade 2-3 or less based on radiographic diagnosis in the Kellgren and Lawrence grading of osteoarthritis Severity: Radiographic grade 2-3, median grade 2 Duration of symptoms: At least 3 months Presence of multimorbidities: Not stated/unclear	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
Madani 2014[146]	**Laser therapy** (n=10) Active laser treatment (810nm wavelength, 50mW average page, pulse repetition rate of 1500Hz, pulse length of 1 microsecond, 6J per point, 3.4J/cm2, spot size 1.76cm2, 2 minutes per point). 3 times a week for 4 weeks. **Sham electrotherapy** (n=10) Placebo laser **Concomitant therapy:** No additional information.	**Temporomandibular joint osteoarthritis** Age range: 35-60 years N = 20 Definition: People with limited mandibular movements, and suffered from arthralgia and crepitation, especially in the late afternoon or evening, based on the Research Diagnostic Criteria for Temporomandibular Disorders and confirmed through cone beam-computed tomography images taken from the TMJs Severity: Not stated Duration of symptoms: Not stated Presence of multimorbidities: Not stated/unclear	Pain at ≤3 months	
Mahler 2019[148]	**Laser therapy** (n=27) Laser therapy consisting of a total dose of 6 Gray, applied in 6 fractions of 1 Gray, delivered every other weekday over 2 weeks. **Sham electrotherapy** (n=28) Sham laser delivering 0 Gray **Concomitant therapy:**	**Knee osteoarthritis** Mean age (SD): 65 (10) years N = 55 Definition: American College of Rheumatology knee osteoarthritis criteria Severity: The majority had a Kellgren Lawrence score of at least 2	Quality of life at ≤3 months Pain at ≤3 months Physical function at ≤3 months Mild adverse events at ≤3 months Moderate/major adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	No additional information	Duration of symptoms: The majority had symptoms for less than or equal to 5 years Presence of multimorbidities: Low morbidity score		
Marquina 2012[150]	**Laser therapy** (n=27) Laser treatment (905nm, 50000mW peak power, up to 100mW average power, 200ns pulse width, up to 10000Hz frequency) and four 660nm visible red laser diodes (25 mW average power). Delivered as 3 treatments per week over 4 weeks **Sham electrotherapy** (n=28) Sham laser with no near-IR optical output and instead only using visible red laser diodes. **Concomitant therapy:** No additional information	**Knee osteoarthritis** Age (range): 25-80 years N = 126 Definition: People with chronic knee pain Severity: Not stated Duration of symptoms: Not stated Presence of multimorbidities: Not stated/unclear	Pain at ≤3 months	
Shen 2009[193]	**Laser therapy** (n=20) Laser acupuncture (two lasers, one 0.65-0.66 micrometer with an output power of 36mW, the other a 10.6 micrometer carbon dioxide laser with an output power of 200mW, pulse frequency of 20Hz, duty factor of 50%) given for 20 minutes three times a week for 4 weeks	**Knee osteoarthritis** Mean age (SD): 58.3 (7.4) years N = 40 Definition: Diagnosis of osteoarthritis, radiographic evidence of at least one osteophyte at the tibiofemoral joint, Kellgren-Lawrence grade at least 2, moderate or	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Sham electrotherapy (n=20) Placebo laser **Concomitant therapy:** No additional information	greater clinically significant knee pain on most days during the previous month Severity: Kellgren Lawrence grade of at least 2 Duration of symptoms (mean [SD]): 5.2 (6.6) years Presence of multimorbidities: Not stated/Unclear		
Yurtkuran 2007[229]	**Laser therapy** (n=28) Laser acupuncture (infrared 27 GaAs diode laser, output power 4mW, 10mW/cm2 power density, 0.4cm2 spot size, 120s treatment time, 0.48J dose per session). This was delivered in pulses (1 pulse per 200nanoseconds). Delivered 5 times per week over 2 weeks. **Sham electrotherapy** (n=27) Placebo laser **Concomitant therapy:** All people received exercise, consisting of 10 sets of isometric contraction to quadriceps muscle and active range of motion exercises (20 repetitions) for knee. They were instructed not to use any analgesic or non-steroidal anti-inflammatory drugs during the follow-up period	**Knee osteoarthritis** Mean age (SD): 52.6 (7.0) years N = 55 Definition: People with knee osteoarthritis diagnosed according to the American College of Rheumatology criteria, with Kellgren Lawrence grade 2-3 knee osteoarthritis and an average pain intensity of 40 or more on a 100mm visual analogue scale for the last month before baseline assessment Severity: Kellgren Lawrence grade 2-3 Duration of symptoms (mean [SD]): 64.0 (55.0) months Presence of multimorbidities: Not stated/Unclear	Quality of life at ≤3 months Pain at ≤3 months Physical function at ≤3 months	

1.1.5.13 Laser therapy compared to no treatment

Table 14: Summary of studies included in the laser therapy compared to no treatment comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Alayat 2017[8]	**Laser therapy** (n=25) High-intensity laser therapy using a pulsed Nd:YAG laser (wavelength 1064nm, average power 10.5W, fluency 510-1780mJ/cm2, pulsed duration <120μs, probe diameter of 0.5cm, spot size of 0.2cm2) with glucosamine sulfate, chondroitin sulfate and exercise. Laser given twice a week for 6 weeks. **No treatment** (n=25) Exercise, glucosamine sulfate and chondroitin sulfate only A third group (n=25) was reported but not included in the analysis as it did not fulfil the inclusion criteria. **Concomitant therapy:** Hot packs were allowed after exercise in cases of muscle soreness or pain.	**Knee osteoarthritis** Mean age (SD): 53.9 (4.5) years N = 75 Definition: People with a degenerative osteoarthritic knee of grade 3 or less based on the Kellgren and Lawrence classification Severity: Kellgren Lawrence grades 3 or less Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months Physical function at ≤3 months	
De matos brunelli braghin 2018[64]	**Laser therapy (no additional treatment)** (n=15) Low level laser therapy (wavelength 808nm, 0.028cm2 spot area, 100mW power output, fluence of 200J/cm2,	**Knee osteoarthritis** Mean age (SD): 60.5 (8.0) years N = 60	Pain at ≤3 months Physical function at ≤3 months	In the final analysis, the two laser therapy groups were pooled and the two no treatment groups were pooled.

Study	Intervention and comparison	Population	Outcomes	Comments
	energy per point of 5.6J) for 2 months. **Laser therapy (with additional treatment)** (n=15) Low level laser therapy (wavelength 808nm, 0.028cm2 spot area, 100mW power output, fluence of 200J/cm2, energy per point of 5.6J) for 2 months and exercise therapy. **No treatment (no additional treatment)** (n=15) No treatment **No treatment (with additional treatment)** (n=15) Exercise therapy only **Concomitant therapy:** No additional information	Definition: Knee osteoarthritis with a radiographic diagnosis (Kellgren Lawrence grade 1-3) Severity: Kellgren Lawrence grade 1-3 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear		
De Paula Gomes 2020[66]	**Interferential therapy** (n=20) The sessions were held three times a week, over 8 weeks (24 sessions), on alternate days, lasting approximately 90 minutes each treatment session. Interferential therapy (n=20) ICT was performed using a premodulated tetrapolar method with a carrier frequency of 4KHz, 1/1s sweep mode, 75 Hz frequency modulation amplitude,	**Knee osteoarthritis** Mean age (SD): Exercise group: 67.85 (4.49) years, exercise+placebo group: 69.4 (4.45) years, exercise+ICT group: 71.85 (2.62) years, exercise+SDT group: 68.45 (4.62) years, exercise+PHOTO group: 65.75 (4.48) years N = 100	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	25Hz delta frequency modulation amplitude, and automatic vector mode for 40 minutes. **Short wave therapy** (n=20) a thermopulse (Ibramed, Amparo, Sao Paolo, Brazil) device set to continuous mode, 27.12MHz frequency and 150W input was used for 20 minutes, and the intensity was defined based on each participant reporting a warm sensation (one sensation, described as soft but pleasant heat). **Laser therapy** (n=20) Prior to the exercise protocol, participants in the exercise and photobiomodulation (PHOTO) group underwent photobiomodulation therapy using a laserpulse device (Ibramed, Amparo, SP, Brazil). The power of each infrared laser was as follows: wavelength of 904nm, frequency of 9500Hz, pulse duration of 60ns, peak power of 70W, average power of 0.04W, energy density of 6J/cm² applied on eight points, with a total dose of 48J/cm², each session. **Sham electrotherapy** (n=20)	Definition: Unilateral knee OA according to American College of Rheumatology criteria, made through examination and the written opinion of a specialist in rheumatic disease. Severity (NRS pain score): Exercise group: 6.55 (1.09), exercise+placebo group: 6.50 (0.68), exercise+ICT group: 6.65 (0.98), exercise+SDT group: 6.40 (0.99), exercise+PHOTO group: 6.70 (0.86) Duration of symptoms: Not stated/unclear Presence of multi-morbidities: Not stated/unclear		

Study	Intervention and comparison	Population	Outcomes	Comments
	No treatment (n=20) Exercise therapy only (supervised strength exercises) **Concomitant therapy:** None of the participants undertook any form of physical therapy, in addition to the one stipulate. In addition they did not use intra-articular, anti-inflammatory or chondroprotective corticosteroids. The use of medications for concomitant diseases was not controlled.			
Hinman 2014[97]	**Laser therapy** (n=71) Laser acupuncture (measured output 10mW, energy output 0.2J/point) given over 12 weeks **Sham electrotherapy** (n=70) Placebo laser **No treatment** (n=71) A fourth group (n=70) was not included as it did not fulfil the inclusion criteria for this review. **Concomitant therapy:** No additional information	**Knee osteoarthritis** Mean age (SD): 63.6 (8.4) years N = 282 Definition: Knee pain of longer than 3 months duration, knee pain on most days with average severity of 4 or more out of 10 on a numeric rating scale, and had morning stiffness lasting less than 30 minutes (consistent with a clinical diagnosis of osteoarthritis) Severity: Not stated	Quality of life at ≤3 months and >3 months Pain at ≤3 months and >3 months Physical function at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
		Duration of symptoms: Median 5-<10 years Presence of multimorbidities: Not stated/Unclear		

1.1.5.14 Transcutaneous electrical nerve stimulation compared to pulsed short-wave therapy

Table 15: Summary of studies included in the transcutaneous electrical nerve stimulation compared to pulsed short-wave therapy comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Atamaz 2012[22]	**Transcutaneous electrical nerve stimulation** (n=37) TENS (frequency 80Hz, 10-30mA intensity) for 20 minutes three times a week for 3 weeks **Interferential therapy** (n=31) Interferential currents (frequency 100Hz generated by 4kHz sinusoidal waves) for 3 weeks **Pulsed short-wave therapy** (n=32) Pulsed short-wave diathermy (10cm diameter condenser plate, frequency 27.12mHz, input 300W, mean output 3.2W) for 3 weeks **Sham electrotherapy (TENS)** (n=37) Sham TENS	**Knee osteoarthritis** Mean age (SD): 61.5 (7.5) years N = 203 Definition: People with knee osteoarthritis according to the American College of Rheumatology criteria with radiologically confirmation with a Kellgren Lawrence grade of 2 or 3 Severity: Kellgren Lawrence grade 2-3 Duration of symptoms (mean [SD]): 43.7 (49.1) months. Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months and >3 months Physical function at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Sham electrotherapy (interferential therapy) (n=35) Sham interferential therapy **Sham electrotherapy (pulsed short-wave therapy)** (n=31) Sham pulsed short-wave therapy **Concomitant therapy:** All people had an exercise program conducted in groups of 4-5 people three times a week for 3 weeks involving stretching, isometric quadriceps exercises and chair lift/minisquats. This was supplemented with additional instruction for home exercise. All people also attended an education program consisting of one 1 hour session discussing the functional anatomy of the knee, ergonomic principles, and understanding of osteoarthritis.			
Cetin 2008[44]	**Pulsed short-wave therapy** (n=20) Short-wave diathermy, hot packs and isokinetic exercise using a frequency of 27.12 MHz for 15 minutes per knee 3 times a week for 8 weeks **Transcutaneous electrical nerve stimulation** (n=20)	**Knee osteoarthritis** Mean age (SD): 59.8 (9.2) years N = 100 Definition: Defined by the American College of Rheumatology with radiographic confirmation	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	TENS, hot packs and isokinetic exercise. Unit set to 60-100Hz, pulse duration set to 60ms for 24 sessions, 3 times a week for 8 weeks. **Ultrasound** (n=20) Ultrasound, hot packs and isokinetic exercise. 1MHz ultrasound head, intensity of 1.5W/cm2, 3 times a week for 8 weeks **No treatment** (n=20) Hot pack and isokinetic exercise only A fifth group (n=20) was reported by not included as it did not fulfil the inclusion criteria **Concomitant therapy:** After application of physical agents, each person underwent individual warm up exercises on a stationary bike set for 20 cycles/min for 5 mins before undergoing muscle-strengthening exercises. People were instructed to continue taking any current medications and not to start any new therapies for knee osteoarthritis during the 8 week studies.	Severity: Radiographic grade 1-4, median grade 3 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear		

1.1.5.15 Transcutaneous electrical nerve stimulation compared to interferential therapy

Table 16: Summary of studies included in the transcutaneous electrical nerve stimulation compared to interferential therapy comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Atamaz 2012[22]	**Transcutaneous electrical nerve stimulation** (n=37) TENS (frequency 80Hz, 10-30mA intensity) for 20 minutes three times a week for 3 weeks **Interferential therapy** (n=31) Interferential currents (frequency 100Hz generated by 4kHz sinusoidal waves) for 3 weeks **Pulsed short-wave therapy** (n=32) Pulsed short-wave diathermy (10cm diameter condenser plate, frequency 27.12mHz, input 300W, mean output 3.2W) for 3 weeks **Sham electrotherapy (TENS)** (n=37) Sham TENS **Sham electrotherapy (interferential therapy)** (n=35) Sham interferential therapy **Sham electrotherapy (pulsed short-wave therapy)** (n=31)	**Knee osteoarthritis** Mean age (SD): 61.5 (7.5) years N = 203 Definition: People with knee osteoarthritis according to the American College of Rheumatology criteria with radiologically confirmation with a Kellgren Lawrence grade of 2 or 3 Severity: Kellgren Lawrence grade 2-3 Duration of symptoms (mean [SD]): 43.7 (49.1) months. Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months and >3 months Physical function at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Sham pulsed short-wave therapy **Concomitant therapy:** All people had an exercise program conducted in groups of 4-5 people three times a week for 3 weeks involving stretching, isometric quadriceps exercises and chair lift/minisquats. This was supplemented with additional instruction for home exercise. All people also attended an education program consisting of one 1 hour session discussing the functional anatomy of the knee, ergonomic principles, and understanding of osteoarthritis.			
Burch 2008[38]	**Interferential therapy** (n=57) Interferential therapy with patterned stimulation (15 minutes, base frequency 500Hz, premodulated beat frequency sweeping between 1 and 150Hz, patterned muscle stimulation delivered as 50hz impulses for 200ms every 1500ms with a biphasic square waveform with a fixed amplitude of 50mA, stimulation intensity pulse width ranging from 3.39 to 102.2 microseconds) for 8 weeks	**Knee osteoarthritis** Mean age (SD): 61.7 (11.0) years N = 116 Definition: Evidence of osteoarthritis in more than one joint based on a physician's assessment of patient-reported symptoms and a differential diagnosis of radiographic evidence Severity: Not stated Duration of symptoms (mean [SD]): 8.3 (7.9) years	Pain at ≤3 months Physical function at ≤3 months Mild adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Transcutaneous electrical nerve stimulation (n=59) Low current TENS for 35 minutes (biphasic square wave, 0.2Hz frequency, fixed amplitude of 60mA, pulse width adjusted to provide a net output of 73nC, delivered across 300microseconds, peak output 0.5mA) for 1 session daily over 8 weeks **Concomitant therapy:** Stable doses of medications were permitted.	Presence of multimorbidities: Not stated/Unclear		

1.1.5.16 Transcutaneous electrical nerve stimulation compared to sham electrotherapy

Table 17: Summary of studies included in transcutaneous electrical nerve stimulation compared to sham electrotherapy comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Altay 2010[17]	**Transcutaneous electrical nerve stimulation** (n=20) TENS using two electrodes applied to painful areas on the knee (frequency 100Hz, pulse time 200, current strength 20-35mA) for 40 minutes a day for 3 weeks **Sham electrotherapy** (n=20) Sham TENS device (switched on but delivered no current) **Concomitant therapy:**	**Knee osteoarthritis** Mean age (SD): 59.5 (9.0) years N = 20 Definition: Primary knee osteoarthritis according to the American college of Rheumatology criteria confirmed with standing anteroposterior and lateral radiographs of both knees	Quality of life at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	All people received an exercise program for 30 minutes and hot packs for 15 minutes in a day for 3 weeks.	Severity: Kellgren Lawrence grade <4 Duration of symptoms (mean [SD]): 7.9 (5.9) years Presence of multimorbidities: Not stated/Unclear		
Atamaz 2012[22]	**Transcutaneous electrical nerve stimulation** (n=37) TENS (frequency 80Hz, 10-30mA intensity) for 20 minutes three times a week for 3 weeks **Interferential therapy** (n=31) Interferential currents (frequency 100Hz generated by 4kHz sinusoidal waves) for 3 weeks **Pulsed short-wave therapy** (n=32) Pulsed short-wave diathermy (10cm diameter condenser plate, frequency 27.12mHz, input 300W, mean output 3.2W) for 3 weeks **Sham electrotherapy (TENS)** (n=37) Sham TENS **Sham electrotherapy (interferential therapy)** (n=35) Sham interferential therapy	**Knee osteoarthritis** Mean age (SD): 61.5 (7.5) years N = 203 Definition: People with knee osteoarthritis according to the American College of Rheumatology criteria with radiologically confirmation with a Kellgren Lawrence grade of 2 or 3 Severity: Kellgren Lawrence grade 2-3 Duration of symptoms (mean [SD]): 43.7 (49.1) months. Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months and >3 months Physical function at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Sham electrotherapy (pulsed short-wave therapy) (n=31) Sham pulsed short-wave therapy **Concomitant therapy:** All people had an exercise program conducted in groups of 4-5 people three times a week for 3 weeks involving stretching, isometric quadriceps exercises and chair lift/minisquats. This was supplemented with additional instruction for home exercise. All people also attended an education program consisting of one 1 hour session discussing the functional anatomy of the knee, ergonomic principles, and understanding of osteoarthritis.			
Inal 2016[107]	**Transcutaneous electrical nerve stimulation** (n=60) TENS over 10 sessions (5 sessions per week). This was achieved in two doses, 4Hz and 100Hz. **Sham electrotherapy** (n=30) Sham TENS **Concomitant therapy:** All people had physical therapy in the inpatient clinic and were educated primarily about the	**Knee osteoarthritis** Mean age (SE): Placebo = 64.6 (1.88) years, 4Hz TENS = 64.4 (1.70) years, 100Hz TENS = 64.1 (0.99) years. N = 90 Definition: Symptomatic knee osteoarthritis according to the American College of Rheumatology criteria Severity: Radiographic grade 2-4, median grade 3	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	harmful movements and conditions for her knees. This included hot pack, therapeutic ultrasonography, TENS and exercise programs. Hot packs were applied during 20 minutes to both knees of the people. Therapeutic ultrasound was performed separately to both knees during 5 minutes with a stimulation of 1.5W/cm². Exercise programs consisted of three sessions of range of motion, quadriceps isometric and isotonic exercises in a day with 20 repetition of each exercise in each session. After ten sessions of physical therapy in the hospital the people were discharged with a home exercise program.	Duration of symptoms (median [range]): Placebo = 48 (24-120) months, 4Hz TENS = 48 (16.5-120), 100Hz TENS = 30 (12-75) Presence of multimorbidities: Not stated/Unclear		
Law 2004[132]	**Transcutaneous electrical nerve stimulation** (n=38) TENS for 40 minutes (frequency 2Hz, pulse width 200microseconds, alternating frequencies of 2Hz and 100Hz). The current was adjusted from 25mA to 35mA. Conducted over 2 weeks. **Sham electrotherapy** (n=10) Sham TENS **Concomitant therapy:**	**Knee osteoarthritis** Mean age (SD): 82.5 (6.3) years N = 48 Definition: Osteoarthritis of the knee with at least grade 2 changes on their x-rays Severity: Osteoarthritis grade 2 radiographic changes Duration of symptoms (mean [SD]): 8.7 (9.7) years	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	No additional information	Presence of multimorbidities: Not stated/Unclear		
Palmer 2014[169]	**Transcutaneous electrical nerve stimulation** (n=73) TENS delivered through a continuous mode (program A: 110Hz, 50 microseconds), delivered with asymmetric and biphasic pulses **Sham electrotherapy** (n=74) Sham TENS (same device type but released no current) A third group (n=77) was reported but not included as it did not fulfil the inclusion criteria. **Concomitant therapy:** All people received a knee exercise and education program. This was a 6 week program involving a group of up to 12 people attending for 1 hour (30 minutes of education and 30 minutes of group exercise) on 6 consecutive weeks. The education program aimed to enhance people's ability to self-manage their condition. The education program included information on setting personal objectives, pacing, managing flares, diet, medical management of osteoarthritis,	**Knee osteoarthritis** Mean age (SD): 61.4 (10.5) years N = 224 Definition: Knee osteoarthritis confirmed by the American College of Rheumatology clinical criteria (including knee pain accompanied by at least 3 out of 6 signs and symptoms [age >50 years, stiffness <30 minutes, crepitus, body tenderness, bony enlargement and no palpable warmth) Severity: Not stated Duration of symptoms (mean [SD]): 4.0 (8.7) years Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months and >3 months Physical function at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	local community exercise opportunities and long-term exercise adherence. The exercise component included a 5 minute warm up followed by a circuit of exercises aimed at improving lower extremity strength, proprioception and function. Each exercise had specific ideas for progression that people advanced as able to over the 6 weeks. All people were taught home exercises during the second session and advised to perform them daily. These included step ups, sit to stand, balancing on one leg, and heel to toe walking. This was supported by a booklet containing written advice on the topics covered in the education session, details of the home exercises and tools to aid goal setting			
Pietrosimone 2011[178] Subsidiary study: Pietrosimone 2010[176]	**Transcutaneous electrical nerve stimulation** (n=12) TENS as a 150Hz biphasic pulsatile current, with a phase duration of 150microseconds. People were allowed to increase or decrease the amplitude from 1 to 60mA. **Sham electrotherapy** (n=12) Sham TENS	**Knee osteoarthritis** Age not stated N = 36 Definition: People with a clinical diagnosis of tibiofemoral osteoarthritis with a quadriceps CAR of less than 0.90 and a Kellgren Lawrence score between 1-4	Pain at ≤3 months Physical function at ≤3 months Mild adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	No treatment (n=12) **Concomitant therapy:** Therapeutic exercise was available to all participants including quadriceps strengthening lower extremity exercises 3 times a week for 4 weeks, for a total of 12 sessions.	Severity: Kellgren Lawrence score 1-4, median grade 3 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear		
Pietrosimone 2020[175]	**Transcutaneous electrical nerve stimulation** (n=32) Participants were instructed to utilise the TENS or sham TENS units during all TE sessions and during activities of daily living. The stimulator units were set to deliver a continuous TENS biphasic pulsatile current at 150Hz, with a phase duration of 150µs. maintain an arbitrary intensity level of 4. **Sham electrotherapy** (n=29) The sham TENS units provided a low-level sensory stimulation for 30s and then were programmed to automatically decrease the electrical current over approx. 10s until no electricity was emitted. **No treatment** (n=29) **Concomitant therapy:**	**Knee osteoarthritis** Mean age (SD): TENS group: 60.8 (7.3) years, sham TENS group: 62.5 (7.7) years, exercise group: 63 (7.4) years N = 90 Definition: Radiographic and clinical diagnosis of knee osteoarthritis Severity: Kellgren-Lawrence grade 2: TENS group: 9, sham: 7, exercise: 9 Kellgren-Lawrence grade 3: TENS group: 18, sham: 17, exercise: 14 Kellgren-Lawrence grade 4: TENS group: 5, sham: 5, exercise: 6 Duration of symptoms (years): not reported	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	10 sessions of therapeutic exercise (TE) over a 28 day period	Presence of multi-morbidities: Not stated/unclear		

1.1.5.17 Transcutaneous electrical nerve stimulation compared to no treatment

Table 18: Summary of studies included in the transcutaneous electrical nerve stimulation compared to no treatment comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Cetin 2008[44]	**Pulsed short-wave therapy** (n=20) Short-wave diathermy, hot packs and isokinetic exercise using a frequency of 27.12 MHz for 15 minutes per knee 3 times a week for 8 weeks **Transcutaneous electrical nerve stimulation** (n=20) TENS, hot packs and isokinetic exercise. Unit set to 60-100Hz, pulse duration set to 60ms for 24 sessions, 3 times a week for 8 weeks. **Ultrasound** (n=20) Ultrasound, hot packs and isokinetic exercise. 1MHz ultrasound head, intensity of 1.5W/cm2, 3 times a week for 8 weeks **No treatment** (n=20)	**Knee osteoarthritis** Mean age (SD): 59.8 (9.2) years N = 100 Definition: Defined by the American College of Rheumatology with radiographic confirmation Severity: Radiographic grade 1-4, median grade 3 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Hot pack and isokinetic exercise only A fifth group (n=20) was reported by not included as it did not fulfil the inclusion criteria **Concomitant therapy:** After application of physical agents, each person underwent individual warm up exercises on a stationary bike set for 20 cycles/min for 5 mins before undergoing muscle-strengthening exercises. People were instructed to continue taking any current medications and not to start any new therapies for knee osteoarthritis during the 8 week studies.			
Mascarin 2012[151]	**Transcutaneous electrical nerve stimulation** (n=12) TENS (100Hz frequency, pulse width 50 microseconds, modulation up to 50% of variation frequency, quadratic biphasic symmetrical pulse and a length of application of 20 minutes). 24 sessions delivered over 12 weeks. **Ultrasound** (n=12) Ultrasound delivering continuous ultrasonic waves (1MHz frequency, 0.8W/cm	**Knee osteoarthritis** Mean age (SD): 62.1 (7.6) years N = 40 Definition: People with knee osteoarthritis according to the American College of Rheumatology criteria Severity: Not stated Duration of symptoms (mean [SD]): 5.2 (5.5) years	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	power, 5cm diameter applicator, each session lasted 3-4 minutes, depending on the knee size due to oedema) 24 sessions delivered over 12 weeks. **No treatment** (n=16) No electrotherapy **Concomitant therapy:** Kinesthetic exercise including stretching and isometric exercises for the entire lower limb conducted in supervised 20 minute sessions.	Presence of multimorbidities: Not stated/Unclear		
Pietrosimone 2011[178] Subsidiary study: Pietrosimone 2010[176]	**Transcutaneous electrical nerve stimulation** (n=12) TENS as a 150Hz biphasic pulsatile current, with a phase duration of 150microseconds. People were allowed to increase or decrease the amplitude from 1 to 60mA. **Sham electrotherapy** (n=12) Sham TENS **No treatment** (n=12) **Concomitant therapy:** Therapeutic exercise was available to all participants including quadriceps	**Knee osteoarthritis** Age not stated N = 36 Definition: People with a clinical diagnosis of tibiofemoral osteoarthritis with a quadriceps CAR of less than 0.90 and a Kellgren Lawrence score between 1-4 Severity: Kellgren Lawrence score 1-4, median grade 3 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months Physical function at ≤3 months Mild adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	strengthening lower extremity exercises 3 times a week for 4 weeks, for a total of 12 sessions.			
Pietrosimone 2020[175]	**Transcutaneous electrical nerve stimulation** (n=32) Participants were instructed to utilise the TENS or sham TENS units during all TE sessions and during activities of daily living. The stimulator units were set to deliver a continuous TENS biphasic pulsatile current at 150Hz, with a phase duration of 150µs. maintain an arbitrary intensity level of 4. **Sham electrotherapy** (n=29) The sham TENS units provided a low-level sensory stimulation for 30s and then were programmed to automatically decrease the electrical current over approx. 10s until no electricity was emitted. **No treatment** (n=29) **Concomitant therapy:** 10 sessions of therapeutic exercise (TE) over a 28 day period	**Knee osteoarthritis** Mean age (SD): TENS group: 60.8 (7.3) years, sham TENS group: 62.5 (7.7) years, exercise group: 63 (7.4) years N = 90 Definition: Radiographic and clinical diagnosis of knee osteoarthritis Severity: Kellgren-Lawrence grade 2: TENS group: 9, sham: 7, exercise: 9 Kellgren-Lawrence grade 3: TENS group: 18, sham: 17, exercise: 14 Kellgren-Lawrence grade 4: TENS group: 5, sham: 5, exercise: 6 Duration of symptoms (years): not reported Presence of multi-morbidities: Not stated/unclear	Pain at ≤3 months Physical function at ≤3 months	

1.1.5.18 Ultrasound compared to pulsed short-wave therapy

Table 19: Summary of studies included in the ultrasound compared to pulsed short-wave therapy comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Cetin 2008[44]	**Pulsed short-wave therapy** (n=20) Short-wave diathermy, hot packs and isokinetic exercise using a frequency of 27.12 MHz for 15 minutes per knee 3 times a week for 8 weeks **Transcutaneous electrical nerve stimulation** (n=20) TENS, hot packs and isokinetic exercise. Unit set to 60-100Hz, pulse duration set to 60ms for 24 sessions, 3 times a week for 8 weeks. **Ultrasound** (n=20) Ultrasound, hot packs and isokinetic exercise. 1MHz ultrasound head, intensity of 1.5W/cm2, 3 times a week for 8 weeks **No treatment** (n=20) Hot pack and isokinetic exercise only A fifth group (n=20) was reported by not included as it did not fulfil the inclusion criteria	**Knee osteoarthritis** Mean age (SD): 59.8 (9.2) years N = 100 Definition: Defined by the American College of Rheumatology with radiographic confirmation Severity: Radiographic grade 1-4, median grade 3 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Concomitant therapy: After application of physical agents, each person underwent individual warm up exercises on a stationary bike set for 20 cycles/min for 5 mins before undergoing muscle-strengthening exercises. People were instructed to continue taking any current medications and not to start any new therapies for knee osteoarthritis during the 8 week studies.			

1.1.5.19 Ultrasound compared to neuromuscular electrical stimulation

Table 20: Summary of studies included in the ultrasound compared to neuromuscular electrical stimulation

Study	Intervention and comparison	Population	Outcomes	Comments
Devrimsel 2019[69]	**Ultrasound** (n=20) Continuous ultrasound (1W/cm2, 1MHz, 5 minutes) applied with a 5cm diameter head bilaterally to each knee for 5 days a week for 3 weeks **Neuromuscular electrical stimulation** (n=30) Neuromuscular electrical stimulat applied to the vastus lateralis and quadriceps femoris muscles (50Hz freqeucny, pulse duration of 250micrseconds, 10s time on, 30s time off) for 20	**Knee osteoarthritis** Mean age (SD): 62.1 (7.8) years N = 50 Definition: American College of Rheumatology knee osteoarthritis with grade 2-3 Kellgren Lawrence changes Severity: Kellgren Lawrence (mean [SD]): 2.6 (0.5) Duration of symptoms (mean [SD]): 6.4 (3.5) years Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	minutes/session, once daily, 5 days a week for 3 weeks. **Concomitant therapy:** People received hot pack, exercise and analgesic treatment (paracetamol 1500mg/day).			

1.1.5.20 Ultrasound compared to transcutaneous electrical nerve stimulation

Table 21: Summary of studies included in the ultrasound compared to transcutaneous electrical nerve stimulation

Study	Intervention and comparison	Population	Outcomes	Comments
Cetin 2008[44]	**Pulsed short-wave therapy** (n=20) Short-wave diathermy, hot packs and isokinetic exercise using a frequency of 27.12 MHz for 15 minutes per knee 3 times a week for 8 weeks **Transcutaneous electrical nerve stimulation** (n=20) TENS, hot packs and isokinetic exercise. Unit set to 60-100Hz, pulse duration set to 60ms for 24 sessions, 3 times a week for 8 weeks. **Ultrasound** (n=20) Ultrasound, hot packs and isokinetic exercise. 1MHz ultrasound head, intensity of	**Knee osteoarthritis** Mean age (SD): 59.8 (9.2) years N = 100 Definition: Defined by the American College of Rheumatology with radiographic confirmation Severity: Radiographic grade 1-4, median grade 3 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	1.5W/cm2, 3 times a week for 8 weeks **No treatment** (n=20) Hot pack and isokinetic exercise only A fifth group (n=20) was reported by not included as it did not fulfil the inclusion criteria **Concomitant therapy:** After application of physical agents, each person underwent individual warm up exercises on a stationary bike set for 20 cycles/min for 5 mins before undergoing muscle-strengthening exercises. People were instructed to continue taking any current medications and not to start any new therapies for knee osteoarthritis during the 8 week studies.			
Mascarin 2012[151]	**Transcutaneous electrical nerve stimulation** (n=12) TENS (100Hz frequency, pulse width 50 microseconds, modulation up to 50% of variation frequency, quadratic biphasic symmetrical pulse and a length of application of 20 minutes). 24 sessions delivered over 12 weeks.	**Knee osteoarthritis** Mean age (SD): 62.1 (7.6) years N = 40 Definition: People with knee osteoarthritis according to the American College of Rheumatology criteria	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Ultrasound (n=12) Ultrasound delivering continuous ultrasonic waves (1MHz frequency, 0.8W/cm power, 5cm diameter applicator, each session lasted 3-4 minutes, depending on the knee size due to oedema) 24 sessions delivered over 12 weeks. **No treatment** (n=16) No electrotherapy **Concomitant therapy:** Kinesthetic exercise including stretching and isometric exercises for the entire lower limb conducted in supervised 20 minute sessions.	Severity: Not stated Duration of symptoms (mean [SD]): 5.2 (5.5) years Presence of multimorbidities: Not stated/Unclear		

1.1.5.21 Ultrasound compared to sham electrotherapy

Table 22: Summary of studies included in the ultrasound compared to sham electrotherapy comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Cakir 2014[40]	**Ultrasound** (n=40) Continuous or pulsed ultrasound using a 5cm2 head ultrasound device (Continuous ultrasound was administered at the frequency of 1MHz with an intensity of 1W/cm². Pulse ultrasound was used for same frequency and intensity on 1:4	**Knee osteoarthritis** Mean age (SD): 57.4 (8.9) years N = 60 Definition: Diagnosed knee osteoarthritis according to the American College of	Pain at ≤3 months and >3 months Physical function at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	pulse ratios) 5 times a week for 2 weeks **Sham electrotherapy** (n=20) Sham ultrasound (same device, but the power switch was off) **Concomitant therapy:** Paracetamol up to 2000mg/day was allowed. Other drugs for systemic diseases were not stopped	Rheumatology, confirmed with radiologically grade 2-3 Kellgren Lawrence changes Severity: Kellgren Lawrence grade 2-3 Duration of symptoms (mean [SD]): 4.5 (3.7) years Presence of multimorbidities: Not stated/Unclear		
Draper 2018[71]	**Ultrasound** (n=55) Low-intensity ultrasound treatment (3MHz continuous wave mode, 1.3W output power, 132mW/cm2 intensity, 18,720J total acoustic dose) for 6 weeks. Self-administered 4 hours per day, 7 days a week. **Sham electrotherapy** (n=35) Sham ultrasound (same device, but transducers deactivated) **Concomitant therapy:** People were permitted to continue use of pain medications as long as those medication were maintained at a stable dose throughout the trial. Co-interventions were not assessed in this study	**Knee osteoarthritis** Mean age (SD): 52.6 (9.0) years N = 90 Definition: Moderate to severe knee pain negatively affecting their life with radiographically-confirmed mild to moderate changes Severity: Kellgren Lawrence grade 1-2 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months Physical function at ≤3 months	
Jia 2016[115]	**Ultrasound** (n=53)	**Knee osteoarthritis**	Quality of life at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Ultrasound for 20 minutes once daily for a total treatment duration of 10 days in low intensity mode (ultrasonic transducer diameter of 25mm, a radius of curvature of 28mm, a frequency of 0.6MHz, a pulse repetition frequency of 300Hz, a spatial and temporal average intensity of 120mW/cm², and a duty cycle of 20%). **Sham electrotherapy** (n=53) Sham ultrasound **Concomitant therapy:** All people received diclofenac sodium (oral sustained release, 75mg) once daily for the 10 day period	Mean age (SD): 62.4 (10.1) years N = 106 Definition: Knee osteoarthritis fulfilling the American College of Rheumatology classification criteria, Kellgren and Lawrence grade 2-3 with knee pain and limitation on most days within the past 6 months Severity: Radiographic grade 2-3 Duration of symptoms (mean [SD]): 62.4 (10.1) months Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months	
Karakas 2020[118]	**Ultrasound** (n=48) The pulsed ultrasound group received a total of 24 sessions of pulsed ultrasound treatment (1 MHz, 1w/cm², 1:4 ratio, 10 minutes) 3 sessions a week for 8 weeks. **Sham electrotherapy** (n=48) Sham ultrasound (no further details) given as per the active treatment group. **Concomitant treatment:**	**Knee osteoarthritis** Mean age (SD): US group: 59.10 (7.45) years, sham group: 60.75 (7.46) years N = 96 Definition: American College of Rheumatology criteria and stage 1-3 Kellgren-Lawrence stage.	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Both groups were given a standard home exercise programme consisting of knee joint range of motion and isometric strengthening. The home exercise programme was given to each patient before starting the treatment. In addition, when they came to the treatment, whether they exercise or not was constantly checked. In both groups, patients were only allowed to take paracetamol for pain. The use of any other analgesics was avoided during the treatment and until the end of the 4 weeks following the completion of the US therapy.	Severity (WOMAC pain at baseline): 8.92 (3.64) vs 8.25 (3.12) Duration of pain: not reported Presence of multi-morbidities: Not stated/unclear		
Kiraly 2021[124]	**Combination therapy** (n=15) Participants received combined UST and TENS therapy for 10 minutes per day (continuous US: 0.5 W/cm2 intensity, 3MHs carrier frequency; TENS: 100 Hz frequency, 100μs impulse, constant frequency). **Ultrasound** (n=38) Combination of people receiving continuous and pulse ultrasound. Participants received continuous ultrasound therapy (UST) with moving head in three fields: 1) inguinal; 2) gluteal; and 3) trochanteric for 3	**Hip osteoarthritis** Mean age: 65 years N = 71 Definition: clinically and radiologically moderate hip osteoarthritis (Kellgren Lawrence II-III stage) as defined by American College of Rheumatology Severity (resting VAS pain at baseline): continuous US group: 64.38 (12.45), pulsed US group: 63.88 (14.47), combination	Quality of life at ≤3 months Pain at ≤3 months Mild adverse events at ≤3 months Moderate/major adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	minutes per field, altogether for 9 minutes every working day for 2 weeks, on a total of 10 occasions (calibrated BTL-4825S Premium device, head size: 5cm, 3 MHz frequency, 1.5 W/cm2 intensity). Participants received pulsed UST (1.5 W/cm2 intensity, 3 MHz frequency, 50% duty cycle). **Sham therapy** (n=18) Participants received sham UST (the device was switched off). **Concomitant treatment:** Participants in each group received conventional treatment (i.e. physical exercise, massage and balneotherapy) every working day for two weeks, on a total of 10 occasions. Exercises included standardised hip exercises. Swedish massage techniques were used during the massage therapy, and the balneotherapy was performed in thermal water at 34 degrees C. Participants were permitted to take analgesics or anti-rheumatic drugs during the study-these medications were recorded on their documents. They were not permitted to receive any additional therapy	group: 61.33 (17.78), placebo group: 62.94 (9.37) Duration of symptoms: at least 8 weeks prior to the start of the study Presence of multi-morbidities: continuous US group: 10/21, pulsed US group: 13/17, combination group: 6/15, placebo group: 12/18		

Study	Intervention and comparison	Population	Outcomes	Comments
	during the 3 months follow-up period.			
Koybasi 2010[126]	**Ultrasound** (n=15) Ultrasound and conventional physical therapy (frequency 1mHz, continuous mode, intensity 1W/cm2, head size 5cm2) applied for 5 minutes in each of the four fields. Given five times weekly for 2 weeks. **Sham electrotherapy** (n=15) Sham ultrasound **No treatment** (n=15) **Concomitant therapy:** Hot packs were applied on the hip joint for 20 minutes before the therapies. In all groups, the people performed strengthening exercises for the hip muscles and lengthening exercises for the ligaments around the hip joint, for a duration of 20 minutes, directed by an experienced physiotherapist. People were instructed to complete exercise three times a week, with ten repetitions for each exercise (strengthening exercises).	**Hip osteoarthritis** Mean age (SD): 65.3 (6.7) years N = 45 Definition: Hip pain for more than 3 months and having Kellgren Lawrence scores of 2-3 on radiologic evaluation. Diagnosis based on the American College of Rheumatology criteria, verified through history and physical examination. Severity: Kellgren Lawrence grade 2-3, median grade 2 Duration of symptoms (mean [SD]): 2.5 (1.7) years Presence of multimorbidities: Not stated/Unclear	Quality of life at ≤3 months Pain at ≤3 months	
Loyola-sanchez 2012[142]	**Ultrasound** (n=14) Ultrasound for 24 sessions with 3 session per week for 8 weeks	**Knee osteoarthritis** Mean age (SD): 61.9 (10.5) years	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	(1MHz ultrasound device, sound-head area of 5cm2, beam nonuniformity ratio of 5:1, therapeutic dose of approximately 112.5J/cm2. Pulsed therapy delivered for 9.5 minutes with a peak intensity of 1W/cm2 at 20% duty cycle, to achieve a spatial average temporal intensity of 0.2W/cm2). **Sham electrotherapy** (n=13) Sham ultrasound (identical device but no sound-head crystal) **Concomitant therapy:** No additional information	N = 27 Definition: People who fulfilled the American College of Rheumatology clinical and radiological diagnostic criteria for knee osteoarthritis and presented with OARSI atlas classification grades 1 or 2 tibiofemoral compartment joint space narrowing Severity: OARSI atlas grade 1-2, median grade 2 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Mild adverse events at ≤3 months	
Ozgonenel 2009[166]	**Ultrasound** (n=34) Ultrasound applied to a treatment area of 25cm2. Continuous ultrasonic waves with 1mHz frequency, 1W/cm2 power applied with a 3cm diameter applicator for 5 minutes each session, once a day for 10 days **Sham electrotherapy** (n=33) Sham ultrasound (applicator was disconnected) **Concomitant therapy:** No additional information	**Knee osteoarthritis** Mean age (SD): 54.9 (7.6) years N = 67 Definition: Clinical and radiological criteria defined by the American College of Rheumatology for knee osteoarthritis Severity: Kellgren Lawrence grade 2-3, median grade 3 Duration of symptoms: Not stated	Pain at ≤3 months Physical function at ≤3 months Mild adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
		Presence of multimorbidities: Not stated/Unclear		
Ozgonenel 2018[167]	**Ultrasound** (n=15) Ultrasound delivered as continuous ultrasonic waves with 1MHz frequency, 1W/cm2 power applied with a 4cm diameter applicator for 5 minutes over 2 weeks **Sham electrotherapy** (n=18) Sham ultrasound (applicator was disconnected) **Concomitant therapy:** No additional information	**Knee osteoarthritis** Mean age (SD): 54.8 (14.8) years N = 33 Definition: Clinical and radiological criteria defined by the American College of Rheumatology for knee osteoarthritis Severity: Kellgren Lawrence grade 3 Duration of symptoms: At least 6 months Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months	
Tascioglu 2010[205]	**Ultrasound** (n=60) Continuous or pulsed ultrasound. Continuous ultrasonic waves of 1MHz frequency, 2W/cm2, 5cm diameter applicator, 5 minutes per session. Pulsed ultrasound group used the same parameters, but with a pulsed mode duty cycle of 1:4. **Sham electrotherapy** (n=30) Sham ultrasound (applicator delivered no output)	**Knee osteoarthritis** Mean age (SD): 60.5 (3.2) years N = 90 Definition: People with idiopathic knee osteoarthritis according to the American College of Rheumatology criteria Severity: Kellgren Lawrence grade 2-3, median grade 2 Duration of symptoms (mean [SD]): 6.5 (1.8) years	Pain at ≤3 months Mild adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Concomitant therapy: No additional information	Presence of multimorbidities: Not stated/Unclear		
Ulus 2012[213]	**Ultrasound** (n=20) Therapeutic ultrasound delivered with continuous ultrasonic waves of 1MHz frequency and intensity of 1W/cm2 applied with a 5cm diameter applicator for 10 minutes per session. Treatment 5 times weekly for 3 weeks. **Sham electrotherapy** (n=20) Sham ultrasound (applicator disconnected from the back of the machine) **Concomitant therapy:** All people received 20 minutes of hot packs, 10 minutes of interferential current and 15 minutes of quadriceps isometric exercise of both knees. Non-steroid anti-inflammatory drugs and antidepressant drugs were not permitted throughout the physical therapy sessions; analgesics whenever needed and other medication for comorbid diseases were permitted during the study period.	**Knee osteoarthritis** Mean age (SD): 60.5 (9.5) years N = 40 Definition: People with bilateral knee osteoarthritis diagnosed in accordance with the American College of Rheumatology criteria Severity: Kellgren and Lawrence grade 2-3, median grade 3 Duration of symptoms (mean [SD]): 106.4 (105.1) months Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months Physical function at ≤3 months Psychological distress at ≤3 months	
Yegin 2017[224]	**Ultrasound** (n=32) Ultrasound applied to both knees for 10 sessions over 2	**Knee osteoarthritis** Age range: 40-70 years	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	weeks (continuous, 1W/cm2, 1MHz) **Sham electrotherapy** (n=33) Sham ultrasound (device switched off) **Concomitant therapy:** The use of analgesics except paracetamol was avoided during the treatment and until the end of the first month following completion of ultrasound treatment.	N = 62 Definition: Primary knee osteoarthritis according to the American Rheumatology Association with a minimum of stage 2 knee osteoarthritis on x-rays taken during the last 12 months according to the Kellgren Lawrence grading scale Severity: At least Kellgren Lawrence grade 2 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Psychological distress at ≤3 months	
Yildiz 2015[225]	**Ultrasound** (n=60) Continuous or pulsed ultrasound. Continuous (frequency 1Mhz, intensity 1.5W/cm2, duration 5 minutes) or pulsed (frequency 1MHz, intensity 1.5W/cm2, mode: 1/5, duration 5 minutes) given for 5 days a week for 2 weeks by the same 5cm2 head **Sham electrotherapy** (n=30) Sham ultrasound (device switched off) **Concomitant therapy:**	**Knee osteoarthritis** Mean (SD): 56.2 (6.9) years N = 90 Definition: Bilateral stage 2-3 primary knee osteoarthritis according to Kellgren-Lawrence criteria Severity: Kellgren Lawrence grade 2-3, median grade 3 Duration of symptoms (mean [SD]): 4.0 (3.2) years Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months Mild adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	All people were given a home exercise program and were instructed to perform exercises, including quadriceps isometric exercises and strengthening exercises, for 10 repetitions of the set, 3 times a day for 8 weeks from the beginning of the treatment. People were informed that they could take 500mg of paracetamol up to 3 times a day in case of pain during treatment.			

1.1.5.22 Ultrasound compared to no treatment

Table 23: Summary of studies included in the ultrasound compared to no treatment comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Alfredo 2020[12]	**Ultrasound** (n=80) Continuous/ pulsed ultrasound. The continuous ultrasound parameters were as follows: a frequency of 1 MHz, an intensity of 1.5 W/cm2 (spatial average, temporal average (SATA)), a duty cycle of 100% and an application time of 5 minutes on the medial side and 5 minutes on the lateral side of the knee. The pulsed ultrasound parameters were as follows: a frequency of 1 MHz, an intensity of 2.5 W/cm2 (SATA), a pulsed mode of 25% and an application time of 5 minutes on the medial	**Knee osteoarthritis** Age (range): 50-75 years N = 100 Definition: American College of Rheumatology criteria Severity (Kellgren-Lawrence): Grade 2-4 Duration of symptoms: not reported Presence of multi-morbidities: Not stated/unclear	Pain at ≤3 months Physical function at ≤3 months	Pulsed and continuous ultrasound groups combined (4 groups)

Study	Intervention and comparison	Population	Outcomes	Comments
	side and 5 minutes on the lateral side of the knee. **No treatment** (n=20) Exercise only. Three 45 minute sessions per week. **Concomitant therapy:** Participants were instructed not to use analgesic medications other than paracetamol (500mg/ day) or anti-inflammatory drugs during the study and not to perform any other type of physical exercise in addition to the treatment.			
Cetin 2008[44]	**Pulsed short-wave therapy** (n=20) Short-wave diathermy, hot packs and isokinetic exercise using a frequency of 27.12 MHz for 15 minutes per knee 3 times a week for 8 weeks **Transcutaneous electrical nerve stimulation** (n=20) TENS, hot packs and isokinetic exercise. Unit set to 60-100Hz, pulse duration set to 60ms for 24 sessions, 3 times a week for 8 weeks. **Ultrasound** (n=20)	**Knee osteoarthritis** Mean age (SD): 59.8 (9.2) years N = 100 Definition: Defined by the American College of Rheumatology with radiographic confirmation Severity: Radiographic grade 1-4, median grade 3 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Ultrasound, hot packs and isokinetic exercise. 1MHz ultrasound head, intensity of 1.5W/cm2, 3 times a week for 8 weeks **No treatment** (n=20) Hot pack and isokinetic exercise only A fifth group (n=20) was reported by not included as it did not fulfil the inclusion criteria **Concomitant therapy:** After application of physical agents, each person underwent individual warm up exercises on a stationary bike set for 20 cycles/min for 5 mins before undergoing muscle-strengthening exercises. People were instructed to continue taking any current medications and not to start any new therapies for knee osteoarthritis during the 8 week studies.			
Huang 2005[101]	**Ultrasound** (n=60) Continuous or pulsed ultrasound given 3 times weekly for 8 weeks. The continuous ultrasound included a duty cycle of 100%, with frequency of 1MHz and a spatial and temporal peak intensity of	**Knee osteoarthritis** Mean age (SD): 62.0 (8.4) years N = 120 Definition: Bilateral moderate knee osteoarthritis with	Pain at ≤3 months and >3 months	In Forest plots this study is referred to as Huang 2005B

Study	Intervention and comparison	Population	Outcomes	Comments
	1.5W/cm². The US probe was applied for 5 minutes to each treated region (a total treated area of approximately 25cm²). The pulsed sonication included a frequency of 1MHz and a spatial and temporal peak intensity of 2.5W/cm², and pulsed at a duty cycle of 25%. Given 3 times weekly over 8 weeks. **No treatment** (n=30) Isokinetic exercise only. A third group (n=30) was reported by not included as it did not fulfil the inclusion criteria. **Concomitant therapy:** All groups received 20 minutes of hot packs and 5 minutes of passive ROM exercise on an electric stationary bike (20 cycles/min) of both knees before undergoing muscle strengthening exercises.	periarticular soft tissue pain, as identified by painful sensations during palpation or passive stretching of the arthritic knee under orthopedic examination. The locations of soft tissue pain were confirmed by the findings of musculoskeletal ultrasound images. Severity: Altman grade 2 Duration of symptoms: 6 months - 11 years. Presence of multimorbidities: Not stated/Unclear		
Huang 2005[102]	**Ultrasound** (n=60) Isokinetic exercise with pulsed ultrasound. Ultrasound treatment given as a frequency of 1MHz and a spatial and temporal peak intensity of 2.5 W/cm², and pulsed at a duty cycle of 25%. Sonication was	**Knee osteoarthritis** Mean age (SD): 65.0 (6.4) years N = 140	Pain at ≤3 months and >3 months	In Forest plots this study is referred to as Huang 2005A

Study	Intervention and comparison	Population	Outcomes	Comments
	performed 3 times a week for 8 weeks **No treatment** (n=35) Isokinetic exercise only. A third group (n=35) and forth group (n=35) were reported by not included as it did not fulfil the inclusion criteria. **Concomitant therapy:** No additional information	Definition: People with bilateral moderate knee osteoarthritis Severity: Altman grade 2 Duration of symptoms: 5 months - 12 years Presence of multimorbidities: Not stated/Unclear		
Mascarin 2012[151]	**Transcutaneous electrical nerve stimulation** (n=12) TENS (100Hz frequency, pulse width 50 microseconds, modulation up to 50% of variation frequency, quadratic biphasic symmetrical pulse and a length of application of 20 minutes). 24 sessions delivered over 12 weeks. **Ultrasound** (n=12) Ultrasound delivering continuous ultrasonic waves (1MHz frequency, 0.8W/cm power, 5cm diameter applicator, each session lasted 3-4 minutes, depending on the knee size due to oedema) 24 sessions delivered over 12 weeks.	**Knee osteoarthritis** Mean age (SD): 62.1 (7.6) years N = 40 Definition: People with knee osteoarthritis according to the American College of Rheumatology criteria Severity: Not stated Duration of symptoms (mean [SD]): 5.2 (5.5) years Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months Physical function at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	No treatment (n=16) No electrotherapy **Concomitant therapy:** Kinesthetic exercise including stretching and isometric exercises for the entire lower limb conducted in supervised 20 minute sessions.			

1.1.5.23 Combination therapy compared to interferential therapy

Table 24: Summary of studies included in the combination therapy compared to interferential therapy comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Alqualo-Costa 2020[15]	**Interferential therapy** (n=42) Interferential current (IFC) three times a week for 4 week (12 sessions). Duration of each session ranged from 40 to 50 minutes. Parameters were used as follows: carrier current frequency of 4000Hz; amplitude-modulated frequency of 50Hz; sweep frequency of 50Hz; swing pattern of 1:1 second, and the current amplitude was increased until the patient reported strong but comfortable and non-painful stimulation paraesthesia. **Laser therapy** (n=42) Three times a week for 4 week (12 sessions). Duration of each	**Knee osteoarthritis** Mean age (SD): IFC group: 64.5 (7.8) years, PBM group: 61.3 (9.4) years, IFC+PBM group: 65.7 (10.1) years, placebo group: 65.3 (8.5) years N = 168 Definition: American College of Rheumatology criteria Severity (Kellgren-Lawrence): (Score 2): IFC group: 24, PBM group: 23, IFC+PBM group: 27, placebo group: 24	Pain at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	session ranged from 40 to 50 minutes, and used a probe with a wavelength of 904nm, with a dose of 3J per point, totalling 9 points, total energy of 27J per session, peak power of 70W, pulse repetition frequency of 9500Hz, pulse duration of 60ns, average power of 40mW, application time of 75 seconds per point, and beam cross-sectional area of 0.5cm². **Combination therapy** (n=42) IFC plus PBM (interferential current plus photobiomodulation). Three times a week for 4 weeks (12 sessions). **Sham electrotherapy** (n=42) Sham IFC and PBM. Three times a week for 4 week (12 sessions). **Concomitant therapy:** No analgesics 4 hours before the intervention.	(Score 3): IFC group: 17, PBM group: 19, IFC+PBM group: 15, placebo group: 18 (Score 4): IFC group: 1, PBM group: 1, IFC+PBM group: 0, placebo group: 0 Duration of symptoms: not reported Presence of multi-morbidities: Not stated/unclear		

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1.1.5.24 Combination therapy compared to neuromuscular electrical stimulation

Table 25: Summary of studies included in the combination therapy compared to neuromuscular electrical stimulation comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Melo mde 2015[152]	**Combination therapy** (n=15) Laser and neuromuscular electrical stimulation (combination of the same protocols for the other two) delivered over 8 weeks. **Laser therapy** (n=15) Low level laser therapy delivered as 30 seconds per point, 6J energy per point (36J in total) for 4 weeks, then a reduction of the dose by 30% for the remaining 4 weeks **Neuromuscular electrical stimulation** (n=15) Neuromuscular electrical stimulation sessions twice a week, at 48 hour intervals, over an 8 week period with a progressive increase in intensity and volume. **Concomitant therapy:** Kinesthetic exercise including stretching and isometric exercises for the entire lower limb conducted in supervised 20 minute sessions.	**Knee osteoarthritis** Mean age (SD): 68.8 (5.1) years N = 45 Definition: Grade 2 or 3 knee osteoarthritis diagnosed by a traumatology-orthopaedic physician according to the criteria proposed by Kellgren and Lawrence Severity: Kellgren-Lawrence grade 2-3 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months	

1.1.5.25 Combination therapy compared to laser therapy

Table 26: Summary of studies included in the combination therapy compared to laser therapy comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Alqualo-Costa 2020[15]	**Interferential therapy** (n=42) Interferential current (IFC) three times a week for 4 week (12 sessions). Duration of each session ranged from 40 to 50 minutes. Parameters were used as follows: carrier current frequency of 4000Hz; amplitude-modulated frequency of 50Hz; sweep frequency of 50Hz; swing pattern of 1:1 second, and the current amplitude was increased until the patient reported strong but comfortable and non-painful stimulation paraesthesia. **Laser therapy** (n=42) Three times a week for 4 week (12 sessions). Duration of each session ranged from 40 to 50 minutes, and used a probe with a wavelength of 904nm, with a dose of 3J per point, totalling 9 points, total energy of 27J per session, peak power of 70W, pulse repetition frequency of 9500Hz, pulse duration of 60ns, average power of 40mW, application time of 75 seconds per point, and beam cross-sectional area of 0.5cm².	**Knee osteoarthritis** Mean age (SD): IFC group: 64.5 (7.8) years, PBM group: 61.3 (9.4) years, IFC+PBM group: 65.7 (10.1) years, placebo group: 65.3 (8.5) years N = 168 Definition: American College of Rheumatology criteria Severity (Kellgren-Lawrence): (Score 2): IFC group: 24, PBM group: 23, IFC+PBM group: 27, placebo group: 24 (Score 3): IFC group: 17, PBM group: 19, IFC+PBM group: 15, placebo group: 18 (Score 4): IFC group: 1, PBM group: 1, IFC+PBM group: 0, placebo group: 0 Duration of symptoms: not reported Presence of multi-morbidities: Not stated/unclear	Pain at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Combination therapy (n=42) IFC plus PBM (interferential current plus photobiomodulation). Three times a week for 4 weeks (12 sessions). **Sham electrotherapy** (n=42) Sham IFC and PBM. Three times a week for 4 week (12 sessions). **Concomitant therapy:** No analgesics 4 hours before the intervention.			
Melo mde 2015[152]	**Combination therapy** (n=15) Laser and neuromuscular electrical stimulation (combination of the same protocols for the other two) delivered over 8 weeks. **Laser therapy** (n=15) Low level laser therapy delivered as 30 seconds per point, 6J energy per point (36J in total) for 4 weeks, then a reduction of the dose by 30% for the remaining 4 weeks **Neuromuscular electrical stimulation** (n=15) Neuromuscular electrical stimulation sessions twice a	**Knee osteoarthritis** Mean age (SD): 68.8 (5.1) years N = 45 Definition: Grade 2 or 3 knee osteoarthritis diagnosed by a traumatology-orthopaedic physician according to the criteria proposed by Kellgren and Lawrence Severity: Kellgren-Lawrence grade 2-3 Duration of symptoms: Not stated Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	week, at 48 hour intervals, over an 8 week period with a progressive increase in intensity and volume. **Concomitant therapy:** Kinesthetic exercise including stretching and isometric exercises for the entire lower limb conducted in supervised 20 minute sessions.			

1.1.5.26 Combination therapy compared to transcutaneous electrical nerve stimulation

Table 27: Summary of studies included in the combination therapy compared to transcutaneous electrical nerve stimulation comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Kim 2019[121]	**Combination therapy** (n=20) LIPUS combined with TENS therapy. Performed using CARESTAR (GENEMEDI CO, Ltd, South Korea). CARESTAR consisted of two 2.8 diameter applicators and gave LIPUS energy and TENS in 1s shifts. Therefore, 50%of the stimulation was offered by LIPUS and the remaining 50% was provided by TENS. The LIPUS signal is transmitted at a frequency of 1MHz, with an intensity of 0.1 W/cm². The effective radiating area was 3.3cm². The duty cycle of pulsed ultrasonic waves was 40%. The TENS setting was in a conventional mode, with a	**Knee osteoarthritis** Mean age (SD): 57.6 (8.26) years N = 40 Definition: Kellgren-Lawrence grade I to IV by standing posteroanterior X-ray in 15 degree knee flexion were eligible. Severity (WOMAC pain at baseline): 8.63 (3.09) vs 7.53 (3.67) Duration of symptoms (SD): 64.84 (62.70) vs 62.74 (65.58) months	Quality of life at ≤3 months Pain at ≤3 months Physical function at ≤3 months Mild adverse events at ≤3 months Moderate/major adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	frequency of 80Hz and a pulse duration of 50-100μs. **Transcutaneous electrical nerve stimulation** (n=20) TENS alone. A commercially available TENS machine (Chil-Sung, Co, Ltd, South Korea) was used for stimulation. The TENS setting was in a conventional mode, with a frequency of 100Hz and a pulse duration of 50-100μs. **Concomitant treatment:** Participants were only allowed to take their pain medication which was started at least 2 months before the screening. They were not allowed to change the dose or type of pain medication or start any other types of treatment for knee OA during the trial. In addition, participants were requested not to change their physical exercise level.	Presence of multimorbidities: Not stated/unclear		

1.1.5.27 Combination therapy compared to ultrasound

Table 28: Summary of studies included in the combination therapy compared to ultrasound comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Kiraly 2021[124]	**Combination therapy** (n=15)	**Hip osteoarthritis** Mean age: 65 years	Quality of life at ≤3 months Pain at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Participants received combined UST and TENS therapy for 10 minutes per day (continuous US: 0.5 W/cm2 intensity, 3MHs carrier frequency; TENS: 100 Hz frequency, 100μs impulse, constant frequency). **Ultrasound** (n=38) Combination of people receiving continuous and pulse ultrasound. Participants received continuous ultrasound therapy (UST) with moving head in three fields: 1) inguinal; 2) gluteal; and 3) trochanteric for 3 minutes per field, altogether for 9 minutes every working day for 2 weeks, on a total of 10 occasions (calibrated BTL-4825S Premium device, head size: 5cm, 3 MHz frequency, 1.5 W/cm2 intensity). Participants received pulsed UST (1.5 W/cm2 intensity, 3 MHz frequency, 50% duty cycle). **Sham ultrasound** (n=18) Participants received sham UST (the device was switched off). **Concomitant treatment:** Participants in each group received conventional treatment (i.e. physical exercise, massage	N = 71 Definition: clinically and radiologically moderate hip osteoarthritis (Kellgren-Lawrence II-III stage) as defined by American College of Rheumatology criteria Severity (resting VAS pain at baseline): continuous US group: 64.38 (12.45), pulsed US group: 63.88 (14.47), combination group: 61.33 (17.78), placebo group: 62.94 (9.37) Duration of symptoms: at least 8 weeks prior to the start of the study Presence of multi-morbidities: continuous US group: 10/21, pulsed US group: 13/17, combination group: 6/15, placebo group: 12/18	Mild adverse events at ≤3 months Moderate/major adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	and balneotherapy) every working day for two weeks, on a total of 10 occasions. Exercises included standardised hip exercises. Swedish massage techniques were used during the massage therapy, and the balneotherapy was performed in thermal water at 34 degrees C. Participants were permitted to take analgesics or anti-rheumatic drugs during the study-these medications were recorded on their documents. They were not permitted to receive any additional therapy during the 3 months follow-up period.			
Sangtong 2019[190]	**Combination therapy** (n=74) Ultrasound and TENS. Ultrasound (frequency 1MHz, power 1W/cm2) for 10 minutes during each weekday over a 2 week period. TENS (symmetrical biphasic waveform, frequency 32-50Hz, pulse width 80 microseconds) for the same amount of time and the same number of days. **Ultrasound** (n=74) Ultrasound only. Ultrasound (frequency 1MHz, power 1W/cm2) for 10 minutes during each weekday over a 2 week period.	**Knee osteoarthritis** Mean age (SD): 63.0 (7.8) years N = 148 Definition: People with symptomatic knee osteoarthritis fulfilling the American College of Rheumatology criteria Severity: Not stated Duration of symptoms (median [range]): 12-24 (1-240) Presence of multimorbidities: Not stated/Unclear	Pain at ≤3 months Mild adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Concomitant therapy: People were asked to not accept pain medication or physical therapy from other clinics or hospitals for the duration of the study. People in both groups received informational brochures specific to knee osteoarthritis, including risk factors for osteoarthritis and how to properly use the affected knee during activities of daily living. Examples of provided information included reducing body weight, avoidance of knee flexion position >90 degrees, avoidance of unnecessary stair use and emphasis of the importance of knee strengthening exercises. People who were taking NSAIDs were asked to discontinue them one week before entering the study. People with intolerable pain were prescribed ibuprofen 1200mg/day as rescue medication for pain.			

1.1.5.28 Combination therapy compared to sham treatment

Table 29: Summary of studies included in the combination therapy compared to sham treatment comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Alqualo-Costa 2020[15]	**Interferential therapy** (n=42)	**Knee osteoarthritis**	Pain at ≤3 months and >3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	Interferential current (IFC) three times a week for 4 week (12 sessions). Duration of each session ranged from 40 to 50 minutes. Parameters were used as follows: carrier current frequency of 4000Hz; amplitude-modulated frequency of 50Hz; sweep frequency of 50Hz; swing pattern of 1:1 second, and the current amplitude was increased until the patient reported strong but comfortable and non-painful stimulation paraesthesia. **Laser therapy** (n=42) Three times a week for 4 week (12 sessions). Duration of each session ranged from 40 to 50 minutes, and used a probe with a wavelength of 904nm, with a dose of 3J per point, totalling 9 points, total energy of 27J per session, peak power of 70W, pulse repetition frequency of 9500Hz, pulse duration of 60ns, average power of 40mW, application time of 75 seconds per point, and beam cross-sectional area of 0.5cm². **Combination therapy** (n=42) IFC plus PBM (interferential current plus photobiomodulation). Three	Mean age (SD): IFC group: 64.5 (7.8) years, PBM group: 61.3 (9.4) years, IFC+PBM group: 65.7 (10.1) years, placebo group: 65.3 (8.5) years N = 168 Definition: American College of Rheumatology criteria Severity (Kellgren-Lawrence): (Score 2): IFC group: 24, PBM group: 23, IFC+PBM group: 27, placebo group: 24 (Score 3): IFC group: 17, PBM group: 19, IFC+PBM group: 15, placebo group: 18 (Score 4): IFC group: 1, PBM group: 1, IFC+PBM group: 0, placebo group: 0 Duration of symptoms: not reported Presence of multi-morbidities: Not stated/unclear		

Study	Intervention and comparison	Population	Outcomes	Comments
	times a week for 4 weeks (12 sessions). **Sham electrotherapy** (n=42) Sham IFC and PBM. Three times a week for 4 week (12 sessions). **Concomitant therapy:** No analgesics 4 hours before the intervention.			
Kiraly 2021[124]	**Combination therapy** (n=15) Participants received combined UST and TENS therapy for 10 minutes per day (continuous US: 0.5 W/cm2 intensity, 3MHs carrier frequency; TENS: 100 Hz frequency, 100µs impulse, constant frequency). **Ultrasound** (n=38) Combination of people receiving continuous and pulse ultrasound. Participants received continuous ultrasound therapy (UST) with moving head in three fields: 1) inguinal; 2) gluteal; and 3) trochanteric for 3 minutes per field, altogether for 9 minutes every working day for 2 weeks, on a total of 10 occasions (calibrated BTL-4825S Premium device, head size: 5cm, 3 MHz frequency, 1.5 W/cm2 intensity). Participants	**Hip osteoarthritis** Mean age: 65 years N = 71 Definition: clinically and radiologically moderate hip osteoarthritis (Kellgren-Lawrence II-III stage) as defined by American College of Rheumatology criteria Severity (resting VAS pain at baseline): continuous US group: 64.38 (12.45), pulsed US group: 63.88 (14.47), combination group: 61.33 (17.78), placebo group: 62.94 (9.37) Duration of symptoms: at least 8 weeks prior to the start of the study	Quality of life at ≤3 months Pain at ≤3 months Mild adverse events at ≤3 months Moderate/major adverse events at ≤3 months	

Study	Intervention and comparison	Population	Outcomes	Comments
	received pulsed UST (1.5 W/cm2 intensity, 3 MHz frequency, 50% duty cycle). **Sham therapy** (n=18) Participants received sham UST (the device was switched off). **Concomitant treatment:** Participants in each group received conventional treatment (i.e. physical exercise, massage and balneotherapy) every working day for two weeks, on a total of 10 occasions. Exercises included standardised hip exercises. Swedish massage techniques were used during the massage therapy, and the balneotherapy was performed in thermal water at 34 degrees C. Participants were permitted to take analgesics or anti-rheumatic drugs during the study-these medications were recorded on their documents. They were not permitted to receive any additional therapy during the 3 months follow-up period.	Presence of multi-morbidities: continuous US group: 10/21, pulsed US group: 13/17, combination group: 6/15, placebo group: 12/18		

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2 **1.1.5.29 Combination therapy compared to no treatment**

3 **Table 30: Summary of studies included in the combination therapy compared to no treatment comparison**

Study	Intervention and comparison	Population	Outcomes	Comments
Altas 2020[16]	**Combination therapy plus exercise** (n=20) Ten therapy sessions using hot pack, TENS and US. Both groups received the same home-based exercise program as in 30 sessions with 10 reps a day for three times a week. **No treatment** (n=20) Home based exercise, as above. **Concomitant treatment:** All patients were allowed to use paracetamol at a dose ≤3000mg/day for pain during the assessment. However, they were instructed not to use any other analgesics except for paracetamol. In addition, all patients were allowed to use other medications for their concomitant systemic diseases.	**Knee osteoarthritis** Mean age (SD): 56.6 (8.9) years N=40 Definition (intervention versus control): Severity (K-L grade 2): combination therapy group: 10, exercise group: 13 Severity (K-L grade 3): combination therapy group: 10, exercise group: 7 Duration (years): 3.13 (1.3), range 1-5 years	Quality of life at ≤3 months Pain at ≤3 months Psychological distress at ≤3 months	
Eftekharsadat 2019[74]	**Extracorporeal shockwave therapy** (n= 25) ESWT. Participants received 5 sessions of shock wave therapy through 3 weeks Then, radial ESWT was used with shockwaves of 2000 pulses/session with an energy flux density of 0.18mJ/mm², the energy level of 2-4, a frequency of 10-16Hz, and pulse rate of	**Knee osteoarthritis** Mean age (SD): ESWT group: 58.00 (5.97) years, PT group: 55.76 (6.06) years, exercise group: 58.16 (7.20) years N = 75 Definition: American College of Rheumatology criteria	Pain at ≤3 months Physical function at ≤3 months	The combination therapy and extracorporeal shockwave therapy arms were not compared to each other as the combination therapy did not include the extracorporeal shockwave therapy as a component.

Study	Intervention and comparison	Population	Outcomes	Comments
	160/ minute were generally applied each session. **Combination therapy** (n=25) Participants received 10 sessions (3 sessions, weekly) of physical therapy including hot pack, TENS and ultrasound (US, HP: 74.5 degrees C, 20 minutes on the affected knee, TENS: pulse duration 20-100 microseconds, 50% duty cycle, current amplitude, maximum tolerated tingling, frequency <200pps, US: frequency of 1 MHz, the intensity of 2.5 W/cm², and duty cycle of 25%, and the probe of US was applied for 10 minutes. **No treatment** (n=25) The exercise programme was applied to all 3 groups. It consisted of the isometric strengthening of the quadriceps muscle in the form of 3 submaximal isometric contractions with gradually increasing intensity combined with weight- bearing water and land based exercises. Additionally, participants were advised to only use acetaminophen for pain relief in the event of severe pain and activities of daily living	Severity:(VAS score at baseline): ESWT group: 7.00 (1.63), combination group: 7.16 (1.37), exercise group: 6.32(1.44) Duration of symptoms: Not stated/unclear Presence of multi-morbidities: Not stated/unclear		

Study	Intervention and comparison	Population	Outcomes	Comments
	modifications (e.g. weight loss and the avoidance of heavy lifting, long-distance walking, and high-impact exercises) were taught as well. **Concomitant therapy:** None of the participants undertook any form of physical therapy, in addition to the ones stipulated. In addition, they did not use intra-articular, anti-inflammatory or chondroprotective corticosteroids. The use of medications for concomitant diseases was not controlled			

1.1.5.30 Matrices

Table 31: Summary matrix for all interventions at ≤3 months

Intervention	Control	Quality of life at ≤3 months	Pain at ≤3 months	Physical function at ≤3 months	Psychological distress at ≤3 months	Osteoarthritis flares at ≤3 months	Mild adverse events at ≤3 months	Moderate/major adverse events at ≤3 months
Pulsed short-wave therapy	Interferential therapy	No evidence identified	1 GRADE Outcome (2 studies) N = 103 Moderate	1 GRADE Outcome (2 studies) N = 103 Moderate	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Neuromuscular electrical stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified

Intervention	Control	Quality of life at ≤3 months	Pain at ≤3 months	Physical function at ≤3 months	Psychological distress at ≤3 months	Osteoarthritis flares at ≤3 months	Mild adverse events at ≤3 months	Moderate/major adverse events at ≤3 months
	Extracorporeal shockwave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Laser therapy	No evidence identified	1 GRADE Outcome (1 study) N = 40 Low	1 GRADE Outcome (1 study) N = 40 Moderate	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Transcutaneous electrical nerve stimulation	No evidence identified	1 GRADE Outcome (2 studies) N = 109 Low	1 GRADE Outcome (1 study) N = 69 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Ultrasound	No evidence identified	1 GRADE Outcome (1 study) N = 40 Very low	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Combination therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Sham electrotherapy	3 GRADE Outcomes (5 studies) N = 301 High-Low	2 GRADE Outcomes (13 studies) N = 691 Very low	2 GRADE Outcomes (9 studies) N = 548 Low-Very low	1 GRADE Outcome (1 study) N = 60 Low	No evidence identified	1 GRADE Outcome (5 studies) N = 339 Very low	1 GRADE Outcome (1 study) N = 83 Moderate

Intervention	Control	Quality of life at ≤3 months	Pain at ≤3 months	Physical function at ≤3 months	Psychological distress at ≤3 months	Osteoarthritis flares at ≤3 months	Mild adverse events at ≤3 months	Moderate/major adverse events at ≤3 months
	No treatment	6 GRADE Outcomes (2 studies) N = 131 Very low	3 GRADE Outcomes (5 studies) N = 302 Moderate-Very low	2 GRADE Outcomes (3 studies) N = 171 Low-Very low	2 GRADE Outcomes (2 studies) N = 100 Very Low	No evidence identified	No evidence identified	No evidence identified
Interferential therapy	Pulsed short-wave therapy	No evidence identified	1 GRADE Outcome (2 studies) N = 103 Moderate	1 GRADE Outcome (2 studies) N = 103 Moderate	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Neuromuscular electrical stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Extracorporeal shockwave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Laser therapy	No evidence identified	1 GRADE Outcome (2 studies) N = 124 Moderate	1 GRADE Outcome (1 study) N = 40 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Transcutaneous electrical nerve stimulation	No evidence identified	1 GRADE Outcome (1 study) N = 68 Low	1 GRADE Outcome (1 study) N = 68 Low	No evidence identified	No evidence identified	1 GRADE Outcome (1 study) N = 116 Low	No evidence identified

Intervention	Control	Quality of life at ≤3 months	Pain at ≤3 months	Physical function at ≤3 months	Psychological distress at ≤3 months	Osteoarthritis flares at ≤3 months	Mild adverse events at ≤3 months	Moderate/major adverse events at ≤3 months
	Ultrasound	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Combination therapy	No evidence identified	1 GRADE Outcome (1 study) N = 84 Moderate	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Sham electrotherapy	No evidence identified	2 GRADE Outcomes (4 studies) N = 250 Moderate-Very low	1 GRADE Outcome (2 studies) N = 126 Very low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	No treatment	No evidence identified	1 GRADE Outcome (1 study) N = 40 Moderate	1 GRADE Outcome (1 study) N = 40 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
Neuromuscular electrical stimulation	Pulsed short-wave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Interferential therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Extracorporeal shockwave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified

Intervention	Control	Quality of life at ≤3 months	Pain at ≤3 months	Physical function at ≤3 months	Psychological distress at ≤3 months	Osteoarthritis flares at ≤3 months	Mild adverse events at ≤3 months	Moderate/major adverse events at ≤3 months
	Laser therapy	No evidence identified	1 GRADE Outcome (1 study) N = 30 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Transcutaneous electrical nerve stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Ultrasound	No evidence identified	1 GRADE Outcome (1 study) N = 60 Low	1 GRADE Outcome (1 study) N = 60 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Combination therapy	No evidence identified	1 GRADE Outcome (1 study) N = 29 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Sham electrotherapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	No treatment	8 GRADE Outcomes (2 study) N = 54 Very low	2 GRADE Outcome (6 studies) N = 284 Moderate-Very low	2 GRADE Outcomes (4 studies) N = 184 Very low	No evidence identified	No evidence identified	1 GRADE Outcome (1 study) N = 100 Low	No evidence identified

Intervention	Control	Quality of life at ≤3 months	Pain at ≤3 months	Physical function at ≤3 months	Psychological distress at ≤3 months	Osteoarthritis flares at ≤3 months	Mild adverse events at ≤3 months	Moderate/major adverse events at ≤3 months
Extracorporeal shockwave therapy	Pulsed short-wave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Interferential therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Neuromuscular electrical stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Laser therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Transcutaneous electrical nerve stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Ultrasound	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Combination therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Sham electrotherapy	No evidence identified	2 GRADE Outcomes (5 studies) N = 307 High-Very low	1 GRADE Outcome (2 studies) N = 200 High	No evidence identified	No evidence identified	1 GRADE Outcome (1 study) N = 70 Moderate	1 GRADE Outcome (1 study) N = 63 Low
	No treatment	No evidence identified	1 GRADE Outcome (2 studies)	1 GRADE Outcome (1 study)	No evidence identified	No evidence identified	No evidence identified	No evidence identified

Intervention	Control	Quality of life at ≤3 months	Pain at ≤3 months	Physical function at ≤3 months	Psychological distress at ≤3 months	Osteoarthritis flares at ≤3 months	Mild adverse events at ≤3 months	Moderate/major adverse events at ≤3 months
			N = 73 Low	N = 45				
Laser therapy	Pulsed short-wave therapy	No evidence identified	1 GRADE Outcome (1 study) N = 40 Low	1 GRADE Outcome (1 study) N = 40 Moderate	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Interferential therapy	No evidence identified	1 GRADE Outcome (2 studies) N = 124 Moderate	1 GRADE Outcome (1 study) N = 40 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Neuromuscular electrical stimulation	No evidence identified	1 GRADE Outcome (1 study) N = 30 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Electrocorporeal shockwave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Transcutaneous electrical nerve stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Ultrasound	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified

Intervention	Control	Quality of life at ≤3 months	Pain at ≤3 months	Physical function at ≤3 months	Psychological distress at ≤3 months	Osteoarthritis flares at ≤3 months	Mild adverse events at ≤3 months	Moderate/major adverse events at ≤3 months
	Combination therapy	No evidence identified	1 GRADE Outcome (2 studies) N = 113 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Sham electrotherapy	5 GRADE Outcomes (4 studies) N = 305 High-Moderate	2 GRADE Outcomes (18 studies) N = 1150 Very low	2 GRADE Outcomes (10 studies) N = 591 High-Very low	No evidence identified	No evidence identified	1 GRADE Outcome (4 studies) N = 227 Very low	1 GRADE Outcome (1 study) N = 55 Moderate
	No treatment	2 GRADE Outcomes (1 study) N = 134 Low-Very low	1 GRADE Outcome (4 studies) N = 279 Very low	1 GRADE Outcome (4 studies) N = 279 Very low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
Transcutaneous electrical nerve stimulation	Pulsed short-wave therapy	No evidence identified	1 GRADE Outcome (2 studies) N = 109 Low	1 GRADE Outcome (1 study) N = 69 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Interferential therapy	No evidence identified	1 GRADE Outcome (2 studies) N = 173 Very low	1 GRADE Outcome (2 studies) N = 173 Very low	No evidence identified	No evidence identified	1 GRADE Outcome (1 study) N = 116 Low	No evidence identified

Intervention	Control	Quality of life at ≤3 months	Pain at ≤3 months	Physical function at ≤3 months	Psychological distress at ≤3 months	Osteoarthritis flares at ≤3 months	Mild adverse events at ≤3 months	Moderate/major adverse events at ≤3 months
	Neuromuscular electrical stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Electrocorporeal shockwave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Laser therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Ultrasound	No evidence identified	2 GRADE Outcomes (1 study) N = 64 Low-Very low	1 GRADE Outcome (1 study) N = 24 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Combination therapy	1 GRADE Outcome (1 study) N = 38 Very low	1 GRADE Outcome (1 study) N = 38 Moderate	1 GRADE Outcome (1 study) N = 38 Moderate	No evidence identified	No evidence identified	1 GRADE Outcome (1 study) N = 40 Low	1 GRADE Outcome (1 study) N = 40 Low
	Sham electrotherapy	5 GRADE Outcomes (1 study) N = 40 Low-Very low	2 GRADE Outcomes (6 studies) N = 435 Low-Very low	2 GRADE Outcomes (5 studies) N = 387 Low-Very low	No evidence identified	No evidence identified	1 GRADE Outcome (1 study) N = 24 Very low	No evidence identified

Intervention	Control	Quality of life at ≤3 months	Pain at ≤3 months	Physical function at ≤3 months	Psychological distress at ≤3 months	Osteoarthritis flares at ≤3 months	Mild adverse events at ≤3 months	Moderate/major adverse events at ≤3 months
	No treatment	No evidence identified	2 GRADE Outcomes (4 studies) N = 151 Very low	1 GRADE Outcome (3 studies) N = 111 Very low	No evidence identified	No evidence identified	1 GRADE Outcome (1 study) N = 24 Very low	No evidence identified
Ultrasound	Pulsed short-wave therapy	No evidence identified	1 GRADE Outcome (1 study) N = 40 Very low	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Interferential therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Neuromuscular electrical stimulation	No evidence identified	1 GRADE Outcome (1 study) N = 60 Very low	1 GRADE Outcome (1 study) N = 60 Very low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Electrocorporeal shockwave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Laser therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Transcutaneous electrical nerve stimulation	No evidence identified	2 GRADE Outcomes (2 studies) N = 64	1 GRADE Outcome (1 study) N = 24	No evidence identified	No evidence identified	No evidence identified	No evidence identified

Intervention	Control	Quality of life at ≤3 months	Pain at ≤3 months	Physical function at ≤3 months	Psychological distress at ≤3 months	Osteoarthritis flares at ≤3 months	Mild adverse events at ≤3 months	Moderate/major adverse events at ≤3 months
			Low-Very low	Low				
	Combination therapy	2 GRADE Outcomes (1 study) N = 53 Low	1 GRADE Outcome (2 studies) N = 201 Very low	No evidence identified	No evidence identified	No evidence identified	1 GRADE Outcome (2 studies) N = 185 Very low	1 GRADE Outcome (1 study) N = 53 Low
	Sham electrotherapy	10 GRADE Outcomes (4 studies) N = 245 High-Very low	2 GRADE Outcomes (13 studies) N = 799 Very low	2 GRADE Outcomes (7 studies) N = 411 Low	2 GRADE Outcomes (1 study) N = 40 Low	No evidence identified	1 GRADE Outcome (5 studies) N = 330 Very low	1 GRADE Outcome (1 study) N = 56 Low
	No treatment	2 GRADE Outcomes (1 study) N = 30 Very low	2 GRADE Outcomes (6 studies) N = 358 Very low	1 GRADE Outcome (2 study) N = 128 Very low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
Combination therapy	Pulsed short-wave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Interferential therapy	No evidence identified	1 GRADE Outcome (1 study) N = 84 Moderate	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified

Intervention	Control	Quality of life at ≤3 months	Pain at ≤3 months	Physical function at ≤3 months	Psychological distress at ≤3 months	Osteoarthritis flares at ≤3 months	Mild adverse events at ≤3 months	Moderate/major adverse events at ≤3 months
	Neuromuscular electrical stimulation	No evidence identified	1 GRADE Outcome (1 study) N = 29 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Electrocorporeal shockwave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Laser therapy	No evidence identified	1 GRADE Outcome (2 studies) N = 113 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Transcutaneous electrical nerve stimulation	1 GRADE Outcome (1 study) N = 38 Very low	1 GRADE Outcome (1 study) N = 38 Moderate	1 GRADE Outcome (1 study) N = 38 Moderate	No evidence identified	No evidence identified	1 GRADE Outcome (1 study) N = 40 Low	1 GRADE Outcome (1 study) N = 40 Low
	Ultrasound	2 GRADE Outcomes (1 study) N = 53 Low	1 GRADE Outcome (2 studies) N = 201 Very low	No evidence identified	No evidence identified	No evidence identified	1 GRADE Outcome (2 studies) N = 185 Very low	1 GRADE Outcome (1 study) N = 53 Low
	Sham electrotherapy	2 GRADE Outcomes (1 study) N = 33	1 GRADE Outcome (2 studies) N = 117	No evidence identified	No evidence identified	No evidence identified	1 GRADE Outcome (1 study)	1 GRADE Outcome (1 study) N = 33

Intervention	Control	Quality of life at ≤3 months	Pain at ≤3 months	Physical function at ≤3 months	Psychological distress at ≤3 months	Osteoarthritis flares at ≤3 months	Mild adverse events at ≤3 months	Moderate/major adverse events at ≤3 months
		Low	Moderate				N = 33 Low	Low
	No treatment	8 GRADE Outcomes (1 study) N = 40 Low-Very low	1 GRADE Outcome (2 studies) N = 84 Very low	1 GRADE Outcome (1 study) N = 44 Low	1 GRADE Outcome (1 study) N = 40 Very low	No evidence identified	No evidence identified	No evidence identified

Table 32: Summary matrix for all interventions at >3 months

Intervention	Control	Quality of life at >3 months	Pain at >3 months	Physical function at >3 months	Psychological distress at >3 months	Osteoarthritis flares at >3 months	Mild adverse events at >3 months	Moderate/major adverse events at >3 months
Pulsed short-wave therapy	Interferential therapy	No evidence identified	1 GRADE Outcome (1 study) N = 63 Low	1 GRADE Outcome (1 study) N = 63 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Neuromuscular electrical stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Extracorporeal shockwave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Laser therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified

Intervention	Control	Quality of life at >3 months	Pain at >3 months	Physical function at >3 months	Psychological distress at >3 months	Osteoarthritis flares at >3 months	Mild adverse events at >3 months	Moderate/major adverse events at >3 months
	Transcutaneous electrical nerve stimulation	No evidence identified	1 GRADE Outcome (2 studies) N = 69 Low	1 GRADE Outcome (1 study) N = 69 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Ultrasound	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Combination therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Sham electrotherapy	3 GRADE Outcomes (2 studies) N = 121 High-Very low	2 GRADE Outcomes (3 studies) N = 184 High-Low	2 GRADE Outcomes (3 studies) N = 184 High-Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	No treatment	5 GRADE Outcomes (1 study) N = 40 Very low	1 GRADE Outcome (1 study) N = 40 Very low	1 GRADE Outcome (1 study) N = 40 Very low	1 GRADE Outcome (1 study) N = 40 Very low	No evidence identified	No evidence identified	No evidence identified
Interferential therapy	Pulsed short-wave therapy	No evidence identified	1 GRADE Outcome (1 study) N = 63 Low	1 GRADE Outcome (1 study) N = 63 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified

Intervention	Control	Quality of life at >3 months	Pain at >3 months	Physical function at >3 months	Psychological distress at >3 months	Osteoarthritis flares at >3 months	Mild adverse events at >3 months	Moderate/major adverse events at >3 months
	Neuromuscular electrical stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Extracorporeal shockwave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Laser therapy	No evidence identified	1 GRADE Outcome (1 study) N = 84 Moderate	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Transcutaneous electrical nerve stimulation	No evidence identified	1 GRADE Outcome (1 study) N = 68 Low	1 GRADE Outcome (1 study) N = 68 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Ultrasound	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Combination therapy	No evidence identified	1 GRADE Outcome (1 study) N = 84 Moderate	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Sham electrotherapy	No evidence identified	2 GRADE Outcomes (2 studies) N = 150 Moderate-Low	1 GRADE Outcome (1 study) N = 66 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified

Intervention	Control	Quality of life at >3 months	Pain at >3 months	Physical function at >3 months	Psychological distress at >3 months	Osteoarthritis flares at >3 months	Mild adverse events at >3 months	Moderate/major adverse events at >3 months
	No treatment	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
Neuromuscular electrical stimulation	Pulsed short-wave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Interferential therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Extracorporeal shockwave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Laser therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Transcutaneous electrical nerve stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Ultrasound	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Combination therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Sham electrotherapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	No treatment	No evidence identified	2 GRADE Outcomes (2 studies)	1 GRADE Outcome (1 study)	No evidence identified	No evidence identified	No evidence identified	No evidence identified

Intervention	Control	Quality of life at >3 months	Pain at >3 months	Physical function at >3 months	Psychological distress at >3 months	Osteoarthritis flares at >3 months	Mild adverse events at >3 months	Moderate/major adverse events at >3 months
			N = 74 Very low	N = 30 Very low				
Extracorporeal shockwave therapy	Pulsed short-wave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Interferential therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Neuromuscular electrical stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Laser therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Transcutaneous electrical nerve stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Ultrasound	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Combination therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Sham electrotherapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	No treatment	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified

Intervention	Control	Quality of life at >3 months	Pain at >3 months	Physical function at >3 months	Psychological distress at >3 months	Osteoarthritis flares at >3 months	Mild adverse events at >3 months	Moderate/major adverse events at >3 months
Laser therapy	Pulsed short-wave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Interferential therapy	No evidence identified	1 GRADE Outcome (1 study) N = 84 Moderate	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Neuromuscular electrical stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Electrocorporeal shockwave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Transcutaneous electrical nerve stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Ultrasound	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Combination therapy	No evidence identified	1 GRADE Outcome (1 study) N = 84 Moderate	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Sham electrotherapy	2 GRADE Outcomes (1 study) N = 123 Moderate	2 GRADE Outcomes (4 studies) N = 319 High-Moderate	2 GRADE Outcomes (3 studies) N = 235	No evidence identified	No evidence identified	1 GRADE Outcome (1 study) N = 66 Very low	No evidence identified

Intervention	Control	Quality of life at >3 months	Pain at >3 months	Physical function at >3 months	Psychological distress at >3 months	Osteoarthritis flares at >3 months	Mild adverse events at >3 months	Moderate/major adverse events at >3 months
				High-Moderate				
	No treatment	2 GRADE Outcomes (1 study) N = 120 Low-Very low	1 GRADE Outcome (1 study) N = 120 Low	1 GRADE Outcome (1 study) N = 120 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
Transcutaneous electrical nerve stimulation	Pulsed short-wave therapy	No evidence identified	1 GRADE Outcome (2 studies) N = 69 Low	1 GRADE Outcome (1 study) N = 69 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Interferential therapy	No evidence identified	1 GRADE Outcome (1 study) N = 68 Low	1 GRADE Outcome (1 study) N = 68 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Neuromuscular electrical stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Electrocorporeal shockwave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Laser therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified

Intervention	Control	Quality of life at >3 months	Pain at >3 months	Physical function at >3 months	Psychological distress at >3 months	Osteoarthritis flares at >3 months	Mild adverse events at >3 months	Moderate/major adverse events at >3 months
	Ultrasound	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Combination therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Sham electrotherapy	No evidence identified	1 GRADE Outcome (2 studies) N = 221 Very low	1 GRADE Outcome (2 studies) N = 221 Moderate	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	No treatment	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
Ultrasound	Pulsed short-wave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Interferential therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Neuromuscular electrical stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Electrocorporeal shockwave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Laser therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified

Intervention	Control	Quality of life at >3 months	Pain at >3 months	Physical function at >3 months	Psychological distress at >3 months	Osteoarthritis flares at >3 months	Mild adverse events at >3 months	Moderate/major adverse events at >3 months
	Transcutaneous electrical nerve stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Combination therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Sham electrotherapy	No evidence identified	1 GRADE Outcome (1 study) N = 60 Low	1 GRADE Outcome (1 study) N = 60 Low	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	No treatment	No evidence identified	1 GRADE Outcome (2 studies) N = 160 Very low	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
Combination therapy	Pulsed short-wave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Interferential therapy	No evidence identified	1 GRADE Outcome (1 study) N = 84 Moderate	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Neuromuscular electrical stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Electrocorporeal shockwave therapy	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified

Intervention	Control	Quality of life at >3 months	Pain at >3 months	Physical function at >3 months	Psychological distress at >3 months	Osteoarthritis flares at >3 months	Mild adverse events at >3 months	Moderate/major adverse events at >3 months
	Laser therapy	No evidence identified	1 GRADE Outcome (1 study) N = 84 Moderate	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Transcutaneous electrical nerve stimulation	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Ultrasound	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	Sham electrotherapy	No evidence identified	1 GRADE Outcome (1 study) N = 84 High	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified
	No treatment	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified	No evidence identified

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1.1.6 Summary of the effectiveness evidence

1.1.6.1 Pulsed short-wave therapy compared to sham electrotherapy and no treatment

Table 33: Clinical evidence summary: pulsed short-wave therapy compared to sham electrotherapy

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with pulsed short-wave therapy	
Quality of life (EQ-5D, KOOS, AIMS, 0-100, high is good, change score and final values) at ≤3 months	178 (3 RCTs) follow up: mean 4 weeks	⊕⊕◯◯ LOW [a,b]	-	The mean quality of life was 27.0	MD **2.73 higher** (3.37 lower to 8.83 higher)	MID = 9 (0.5 x median baseline SD)
Quality of life (SF-36 physical component, 0-100, high is good, final value) at ≤3 months	63 (1 RCT) follow up: 4 weeks	⊕⊕⊕◯ MODERATE [c]	-	The mean quality of life was 53.1	MD **2.7 higher** (0.34 lower to 5.74 higher)	MID = 2 (established value)
Quality of life (SF-36 mental component, 0-100, high is good, final value) at ≤3 months	60 (1 RCT) follow up: 4 weeks	⊕⊕⊕⊕ HIGH	-	The mean quality of life was 43.6	MD **0.2 higher** (1.92 lower to 2.32 higher)	MID = 3 (established value)
Quality of life (KOOS, 0-100, high is good, final value) at >3 months	51 (1 RCT) follow up: 12 months	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 33	MD **3.4 higher** (5.26 lower to 12.06 higher)	MID = 0.5 SD (SMD)
Quality of life (SF-36 physical component, 0-100, high is good, change score) at >3 months	70 (1 RCT) follow up: 26 weeks	⊕⊕⊕◯ MODERATE [c]	-	The mean quality of life was 2.6	MD **1.6 lower** (4.64 lower to 1.44 higher)	MID = 2 (established value)
Quality of life (SF-36 mental component, 0-100, high is	70 (1 RCT)	⊕⊕⊕⊕ HIGH	-	The mean quality of life was 2.4	MD **1.2 lower** (5.3 lower to 2.9 higher)	MID = 3 (established value)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with pulsed short-wave therapy	
good, change score) at >3 months	follow up: 26 weeks					
Pain (WOMAC [different scale ranges], high is poor, change scores) at ≤3 months	247 (4 RCTs) follow up: mean 8 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	-	SMD **0.36 SD lower** (0.97 lower to 0.26 higher)	MID = 0.5 SD (SMD)
Pain (KOOS, WOMAC, VAS, NRS [different scale ranges], high is poor, final values) at ≤3 months	444 (9 RCTs) follow up: mean 6 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	-	SMD **0.67 SD lower** (1.12 lower to 0.21 lower)	MID = 0.5 SD (SMD)
Pain (WOMAC [different scale ranges], high is poor, change scores) at >3 months	133 (2 RCTs) follow up: mean 26 weeks	⊕⊕⊕⊕ HIGH	-	-	SMD **0.01 SD higher** (0.49 lower to 0.5 higher)	MID = 0.5 SD (SMD)
Pain (KOOS, 0-100, high is good, final value) at >3 months	51 (1 RCT) follow up: 52 weeks	⊕⊕◯◯ LOW [a]	-	The mean pain was 33	MD **24.6 higher** (16.63 higher to 32.57 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC [different scale ranges], high is poor, change scores) at ≤3 months	245 (4 RCTs) follow up: mean 8 weeks	⊕⊕◯◯ LOW [b,c]	-	-	SMD **0.51 SD lower** (0.89 lower to 0.12 lower)	MID = 0.5 SD (SMD)
Physical function (KOOS, WOMAC [different scale ranges], high is poor, final values) at ≤3 months	303 (5 RCTs) follow up: mean 6 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	-	SMD **0.52 SD lower** (0.97 lower to 0.06 lower)	MID = 0.5 SD (SMD)
Physical function (WOMAC [different scale ranges], high is	133 (2 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD **0.06 SD higher**	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with pulsed short-wave therapy	
poor, change scores) at >3 months	follow up: 26 weeks				(0.28 lower to 0.4 higher)	
Physical function (KOOS, 0-100, high is good, final value) at >3 months	51 (1 RCT) follow up: 12 months	⨁◯◯◯ VERY LOW [a,c]	-	The mean physical function was 41.6	MD **19 higher** (8.09 higher to 29.91 higher)	MID = 0.5 SD (SMD)
Psychological distress (GHQ, 0-90, high is poor, final value) at ≤3 months	60 (1 RCT) follow up: 12 weeks	⨁◯◯◯ VERY LOW [a,c]	-	The mean psychological distress was 26.79	MD **3.48 higher** (3.98 lower to 10.94 higher)	MID = 0.5 SD (SMD)
Mild adverse events at ≤3 months	339 (5 RCTs) follow up: mean 7 weeks	⨁◯◯◯ VERY LOW [a,d,e]	RD 0.03 (-0.05 to 0.11)	148 per 1,000	**30 fewer per 1,000** (110 fewer to 50 more)	Precision calculated through Optimal Information Size (OIS) due to zero events in some studies (0.8-0.9 = serious, <0.8 = very serious).
Moderate/major adverse events at ≤3 months	83 (1 RCT) follow up: 12 weeks	⨁⨁◯◯ MODERATE [a,e]	RD 0.00 (-0.05 to 0.05)	0 per 1,000	**0 fewer per 1,000** (50 fewer to 50 more)	Sample size used to determine precision: 75-150 = serious imprecision, <75 = very serious imprecision.

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

c. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

d. Downgraded for heterogeneity due to conflicting number of events in different studies (zero events in one or more studies)

e. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

1 **Table 34: Clinical evidence summary: pulsed short-wave therapy compared to no treatment**

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with pulsed short-wave therapy	
Quality of life (KOOS, 0-100, high is good, final value) at ≤3 months	91 (1 RCT) follow up: 3 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 26.4	MD **11.8 higher** (3.03 higher to 20.57 higher)	MID = 0.5 SD (SMD)
Quality of life (SF-36 physical function, 0-100, high is good, change score) at ≤3 months	40 (1 RCT) follow up: 4 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 19	MD **6.25 higher** (5.77 lower to 18.27 higher)	MID = 3 (established value)
Quality of life (SF-36 bodily pain, 0-100, high is good, change score) at ≤3 months	40 (1 RCT) follow up: 4 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 28.35	MD **2.5 lower** (16.2 lower to 11.2 higher)	MID = 3 (established value)
Quality of life (SF-36 vitality, 0-100, high is good, change score) at ≤3 months	40 (1 RCT) follow up: 4 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 7	MD **0.5 lower** (8.4 lower to 7.4 higher)	MID = 2 (established value)
Quality of life (SF-36 general health, 0-100, high is good, change score) at ≤3 months	40 (1 RCT) follow up: 4 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 6.5	MD **1 lower** (10.54 lower to 8.54 higher)	MID = 2 (established value)
Quality of life (SF-36 social function, 0-100, high is good, final value) at ≤3 months	40 (1 RCT) follow up: 4 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 59.4	MD **8.25 higher** (2.99 lower to 19.49 higher)	MID = 3 (established value)
Quality of life (SF-36 physical function, 0-100, high is good, change score) at >3 months	40 (1 RCT) follow up: 16 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 17	MD **7.25 higher** (5.07 lower to 19.57 higher)	MID = 3 (established value)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with pulsed short-wave therapy	
Quality of life (SF-36 bodily pain, 0-100, high is good, change score) at >3 months	40 (1 RCT) follow up: 16 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 28.45	MD **12.4 lower** (29.24 lower to 4.44 higher)	MID = 3 (established value)
Quality of life (SF-36 vitality, 0-100, high is good, change score) at >3 months	40 (1 RCT) follow up: 16 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was -0.75	MD **0.5 lower** (9.18 lower to 8.18 higher)	MID = 2 (established value)
Quality of life (SF-36 general health, 0-100, high is good, change score) at >3 months	40 (1 RCT) follow up: 16 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 5.75	MD **4.75 lower** (15.36 lower to 5.86 higher)	MID = 2 (established value)
Quality of life (SF-36 social function, 0-100, high is good, final value) at >3 months	40 (1 RCT) follow up: 16 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 59.95	MD **5.5 higher** (7.76 lower to 18.76 higher)	MID = 3 (established value)
Pain (WOMAC, VAS [different scale ranges], high is poor, change scores) at ≤3 months	80 (2 RCTs) follow up: mean 6 weeks	⊕⊕◯◯ LOW [a]	-	-	SMD **0.07 SD lower** (0.5 lower to 0.37 higher)	MID = 0.5 SD (SMD)
Pain (KOOS, WOMAC [different scale ranges], high is poor, final values) at ≤3 months	131 (2 RCTs) follow up: mean 6 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	-	SMD **0.28 SD higher** (2.28 lower to 2.84 higher)	MID = 0.5 SD (SMD)
Pain (WOMAC, 0-20, high is poor, change score) at >3 months	40 (1 RCT) follow up: 16 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean pain was -5	MD **0.5 lower** (3.04 lower to 2.04 higher)	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with pulsed short-wave therapy	
Physical function (WOMAC, 0-68, high is poor, change score and final value) at ≤3 months	80 (2 RCTs) follow up: mean 6 weeks	⊕⊕◯◯ LOW [a,b]	-	The mean physical function was 27	MD **2.2 lower** (4.05 lower to 0.35 lower)	MID = 3.4 (0.5 x median baseline SD)
Physical function (KOOS, 0-100, high is good, final value) at ≤3 months	91 (1 RCT) follow up: 3 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean physical function was 48.1	MD **14.2 higher** (6.45 higher to 21.95 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, change score) at >3 months	40 (1 RCT) follow up: 16 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean physical function was -15.35	MD **1.55 lower** (10 lower to 6.9 higher)	MID = 0.5 SD (SMD)
Psychological distress (Beck depression score, 0-63, high is poor, change score) at ≤3 months	40 (1 RCT) follow up: 4 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean psychological distress was -2.3	MD **0.15 lower** (2.33 lower to 2.03 higher)	MID = 0.5 SD (SMD)
Psychological distress (GHQ, 0-90, high is poor, final value) at ≤3 months	60 (1 RCT) follow up: 12 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean psychological distress was 32	MD **1.73 lower** (9.33 lower to 5.87 higher)	MID = 0.5 SD (SMD)
Psychological distress (Beck depression score, 0-63, high is poor, change score) at >3 months	40 (1 RCT) follow up: 16 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean psychological distress was -1.25	MD **0.1 higher** (2.61 lower to 2.81 higher)	MID = 0.5 SD (SMD)

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

c. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

1.1.6.2 Interferential therapy compared to pulsed short-wave therapy, laser therapy, sham electrotherapy and no treatment

Table 35: Clinical evidence summary: interferential therapy compared to pulsed short-wave therapy

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with pulsed short-wave therapy	Risk difference with interferential therapy	
Pain (WOMAC, 0-20, high is poor, final value) at ≤3 months	103 (2 RCTs) follow up: mean 10 weeks	⊕⊕⊕◯ MODERATE [a]	-	The mean pain was 8.1	**MD 0.52 lower** (1.25 lower to 0.21 higher)	MID = 1.4 (0.5 x median baseline SD)
Pain (WOMAC, 0-20, high is poor, final value) at >3 months	63 (1 RCT) follow up: 6 months	⊕⊕◯◯ LOW [a,b]	-	The mean pain was 4.5	**MD 1.1 lower** (2.93 lower to 0.73 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months	103 (2 RCTs) follow up: mean 10 weeks	⊕⊕⊕◯ MODERATE [a]	-	The mean physical function was 12.1	**MD 0.88 lower** (2.6 lower to 0.84 higher)	MID = 3.6 (0.5 x median baseline SD)
Physical function (WOMAC, 0-68, high is poor, final value) at >3 months	63 (1 RCT) follow up: 6 months	⊕⊕◯◯ LOW [a,b]	-	The mean physical function was 9.9	**MD 1.4 lower** (7.42 lower to 4.62 higher)	MID = 0.5 SD (SMD)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 36: Clinical evidence summary: interferential therapy compared to laser therapy

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with laser therapy	Risk difference with interferential therapy	
Pain (WOMAC, NRS [different scale ranges], high is poor, final values) at ≤3 months	124 (2 RCTs) follow-up: mean 10 weeks	⊕⊕⊕◯ MODERATE[a]	-	-	SMD **0.25 SD higher** (0.11 lower to 0.6 higher)	MID = 0.5 SD (SMD)
Pain (NRS, 0-10, high is poor, final value) at >3 months	84 (1 RCT) follow-up: 6 months	⊕⊕⊕◯ MODERATE[a]	-	The mean pain was 2.95	MD **0.7 higher** (0.46 lower to 1.86 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months	40 (1 RCT) follow-up: 8 weeks	⊕⊕◯◯ LOW[a,b]	-	The mean physical function was 39.2	MD **3 lower** (4.76 lower to 1.24 lower)	MID = 0.5 SD (SMD)

a. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

b. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Table 37: Clinical evidence summary: interferential therapy compared to sham electrotherapy

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with interferential therapy	
Pain (WOMAC, 0-20, high is poor, change score and final value) at ≤3 months	166 (3 RCTs) follow up: mean 11 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	The mean pain was 10.2	MD **2.84 lower** (9.07 lower to 3.39 higher)	MID = 1.1 (0.5 x median baseline SD)
Pain (NRS, 0-10, high is poor, final value) at ≤3 months	84 (1 RCT)	⊕⊕⊕◯ MODERATE [c]	-	The mean pain was 3.85	MD **0.3 lower**	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with interferential therapy	
	follow up: 12 weeks				(1.55 lower to 0.95 higher)	
Pain (WOMAC, 0-20, high is poor, change score) at >3 months	66 (1 RCT) follow up: 6 months	⊕⊕◯◯ LOW [a,c]	-	The mean pain was -3.2	MD **0.2 lower** (1.8 lower to 1.4 higher)	MID = 0.5 SD (SMD)
Pain (NRS, 0-10, high is poor, final value) at >3 months	84 (1 RCT) follow up: 6 months	⊕⊕⊕◯ MODERATE [c]	-	The mean pain was 4.1	MD **0.45 lower** (1.73 lower to 0.83 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, change score and final value) at ≤3 months	166 (3 RCTs) follow up: mean 11 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	The mean physical function was 36.7	MD **10.88 lower** (28.56 lower to 6.8 higher)	MID = 3.1 (0.5 x median baseline SD)
Physical function (WOMAC, 0-68, high is poor, change score) at >3 months	66 (1 RCT) follow up: 6 months	⊕⊕◯◯ LOW [a,c]	-	The mean physical function was -11.5	MD **3 higher** (1.94 lower to 7.94 higher)	MID = 0.5 SD (SMD)

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

c. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1

Table 38: Clinical evidence summary: interferential therapy compared to no treatment

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with interferential therapy	
Pain (WOMAC, 0-20, high is poor, final value) at ≤3 months	40 (1 RCT) follow-up: 8 weeks	⊕⊕⊕◯ MODERATE[a]	-	The mean pain was 9	MD **2 higher** (1.2 higher to 2.8 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months	40 (1 RCT) follow-up: 8 weeks	⊕⊕◯◯ LOW[a,b]	-	The mean physical function was 38.9	MD **2.7 lower** (4.91 lower to 0.49 lower)	MID = 0.5 SD (SMD)

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1.1.6.3 Neuromuscular electrical stimulation compared to no treatment

Table 39: Clinical evidence summary: neuromuscular electrical stimulation compared to no treatment

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with neuromuscular electrical stimulation	
Quality of life (SF-36 physical component, 0-100, high is good, final value) at ≤3 months	16 (1 RCT) follow up: 14 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 67.83	MD **20.23 lower** (38.83 lower to 1.63 lower)	MID = 2 (established value)
Quality of life (SF-36 mental component, 0-100, high is good, final value) at ≤3 months	16 (1 RCT) follow up: 14 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 70.5	MD **5.1 lower** (24.75 lower to 14.55 higher)	MID = 3 (established value)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with neuromuscular electrical stimulation	
Quality of life (NHP pain, scale range unclear, high is poor, final value) at ≤3 months	38 (1 RCT) follow up: 2 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 51.11	MD **13.35 lower** (31.41 lower to 4.71 higher)	MID = 0.5 SD (SMD)
Quality of life (NHP physical mobility, scale range unclear, high is poor, final value) at ≤3 months	38 (1 RCT) follow up: 2 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 33.53	MD **4.67 higher** (10.03 lower to 19.37 higher)	MID = 0.5 SD (SMD)
Quality of life (NHP energy level, scale range unclear, high is poor, final value) at ≤3 months	38 (1 RCT) follow up: 2 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 56.84	MD **20.23 lower** (45.51 lower to 5.05 higher)	MID = 0.5 SD (SMD)
Quality of life (NHP sleep, scale range unclear, high is poor, final value) at ≤3 months	38 (1 RCT) follow up: 2 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 34.23	MD **2.17 lower** (21.98 lower to 17.64 higher)	MID = 0.5 SD (SMD)
Quality of life (NHP social isolation, scale range unclear, high is poor, final value) at ≤3 months	38 (1 RCT) follow up: 2 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 10.38	MD **1.29 lower** (15.17 lower to 12.59 higher)	MID = 0.5 SD (SMD)
Quality of life (NHP total score, scale range unclear, high is poor, final value) at ≤3 months	38 (1 RCT) follow up: 2 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 213.07	MD **45.49 lower** (125.53 lower to 34.55 higher)	MID = 0.5 SD (SMD)
Pain (WOMAC, [different scale ranges], high is poor, change scores) at ≤3 months	130 (2 RCTs) follow up: 7 weeks	⊕⊕⊕◯ MODERATE [a]	-	-	SMD **0.12 SD higher** (0.22 lower to 0.47 higher)	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with neuromuscular electrical stimulation	
Pain (WOMAC, VAS [different scale ranges], high is poor, final values) at ≤3 months	154 (4 RCTs) follow up: mean 7 weeks	⊕◯◯◯ VERY LOW [a,b]	-	-	SMD **0.56 SD lower** (0.89 lower to 0.23 lower)	MID = 0.5 SD (SMD)
Pain (WOMAC, 5-25, high is poor, change score) at >3 months	30 (1 RCT) follow up: 16 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean pain was 1.4	MD **1.94 lower** (4.04 lower to 0.16 higher)	MID = 0.5 SD (SMD)
Pain (VAS, 0-10, high is poor, final value) at >3 months	44 (1 RCT) follow up: 18 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean pain was 5.3	MD **1.9 lower** (3.29 lower to 0.51 lower)	MID = 0.5 SD (SMD)
Physical function (WOMAC [different scale ranges], high is poor, change scores) at ≤3 months	130 (2 RCTs) follow up: 7 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	-	SMD **0.02 SD lower** (0.62 lower to 0.58 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, final values) at ≤3 months	54 (2 RCTs) follow up: mean 7 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean physical function was 20.5	MD **4.22 higher** (3.12 lower to 11.56 higher)	MID = 7.2 (0.5 x median baseline SD)
Physical function (WOMAC, 17-85, high is poor, change score) at >3 months	30 (1 RCT) follow up: 16 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean physical function was 5	MD **9.92 lower** (17.34 lower to 2.5 lower)	MID = 0.5 SD (SMD)
Mild adverse events at ≤3 months	100 (1 RCT) follow up: 8 weeks	⊕⊕◯◯ LOW [a,b]	Peto OR 7.39 (0.15 to 372.38)	0 per 1,000	**20 more per 1,000** (30 fewer to 70 more) [d]	MID (precision) = Peto OR 0.8-1.25.

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with neuromuscular electrical stimulation	
b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs c. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis d. Absolute effect calculated by risk difference due to zero events in at least one arm of one study						

1.1.6.4 Extracorporeal shockwave therapy compared to sham electrotherapy and no treatment

Table 40: Clinical evidence summary: extracorporeal shockwave therapy compared to sham electrotherapy

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with extracorporeal shockwave therapy	
Pain (WOMAC, 0-20, high is poor, change score and final values) at ≤3 months	200 (3 RCTs) follow up: mean 12 weeks	⊕⊕⊕◯ MODERATE a	-	The mean pain was -4.3	MD **2.99 lower** (3.57 lower to 2.42 lower)	MID = 1.1 (0.5 x median baseline SD)
Pain (VAS, 0-10, high is poor, change score and final value) at ≤3 months	107 (2 RCTs) follow up: mean 4 weeks	⊕◯◯◯ VERY LOW a.b,c	-	The mean pain was 2.4	MD **2.17 lower** (3.55 lower to 0.79 lower)	MID = 0.95 (0.5 x median baseline SD)
Physical function (WOMAC, 0-68, high is poor, change score and final values) at ≤3 months	200 (3 RCTs) follow up: mean 12 weeks	⊕⊕⊕◯ MODERATE a	-	The mean physical function was 14.2	MD **9.06 lower** (11.11 lower to 7.02 lower)	MID = 4.4 (0.5 x median baseline SD)
Mild adverse events at ≤3 months	70 (1 RCT)	⊕⊕⊕◯ MODERATE c	Peto OR 0.14	56 per 1,000	**60 fewer per 1,000** (150 fewer to 30 more) d	MID (precision) = Peto OR 0.8-1.25.

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with extracorporeal shockwave therapy	
	follow up: 12 weeks		(0.01 to 2.27)			
Moderate/major adverse events at ≤3 months	63 (1 RCT) follow up: 12 weeks	⨁⨁◯◯ LOW [e]	RD 0.00 (-0.06 to 0.06)	0 per 1,000	**0 fewer per 1,000** (60 fewer to 60 more)	Sample size used to determine precision: 75-150 = serious imprecision, <75 = very serious imprecision.

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis
[c] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[d] Absolute effect calculated by risk difference due to zero events in at least one arm of one study
[e] Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

1

2 **Table 41: Clinical evidence summary: extracorporeal shockwave therapy compared to no treatment**

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with extracorporeal shockwave therapy	
Pain (WOMAC, VAS [different scale ranges], high is poor, final values) at ≤3 months	73 (2 RCTs) follow-up: mean 10 weeks	⨁⨁◯◯ LOW[a,b]	-	-	SMD **0.43 SD higher** (0.05 lower to 0.91 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, final score) at ≤3 months	45 (1 RCT) follow-up: 7 weeks	⨁⨁◯◯ LOW[a,b]	-	The mean physical function was 20	MD **10.74 higher** (3.67 higher to 17.81 higher)	MID = 0.5 SD (SMD)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with extracorporeal shockwave therapy	
b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs						

1.1.6.5 Laser therapy compared to pulsed short-wave therapy, neuromuscular electrical stimulation, sham electrotherapy and no treatment

Table 42: Clinical evidence summary: laser therapy compared to pulsed short-wave therapy

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with pulsed short-wave therapy	Risk difference with laser therapy	
Pain (WOMAC, 0-20, high is poor, final value) at <3 months	40 (1 RCT) follow-up: 8 weeks	⊕⊕◯◯ LOW[a,b]	-	The mean pain was 11.3	MD **0.85 lower** (1.62 lower to 0.08 lower)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, final value) at <3 months	40 (1 RCT) follow-up: 8 weeks	⊕⊕⊕◯ MODERATE[a]	-	The mean physical function was 36	MD **3.2 higher** (1.84 higher to 4.56 higher)	MID = 0.5 SD (SMD)
a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs						

Table 43: Clinical evidence summary: laser therapy compared to neuromuscular electrical stimulation

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with neuromuscular electrical stimulation	Risk difference with laser therapy	
Pain (VAS, 0-10, high is poor, final value) at ≤3 months	30 (1 RCT) follow up: 12 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean pain was 0.9	MD **0.7 higher** (0.22 higher to 1.18 higher)	MID = 0.5 SD (SMD)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 44: Clinical evidence summary: laser therapy compared to sham electrotherapy

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with laser therapy	
Quality of life (KOOS, NHP [different scale ranges], high is good, final values) at ≤3 months	127 (2 RCTs) follow up: mean 8 weeks	⊕⊕⊕⊕ HIGH	-	-	SMD **0.08 SD higher** (0.27 lower to 0.43 higher)	MID = 0.5 SD (SMD)
Quality of life (SF-36 physical component, 0-50, high is good, change score) at ≤3 months	55 (1 RCT) follow up: 12 weeks	⊕⊕⊕◯ MODERATE [a]	-	The mean quality of life was 2.4	MD **2.3 lower** (5.97 lower to 1.37 higher)	MID = 0.5 SD (SMD)
Quality of life (SF-36 mental component, 0-50, high is good, change score) at ≤3 months	55 (1 RCT) follow up: 12 weeks	⊕⊕⊕◯ MODERATE [a]	-	The mean quality of life was -4.2	MD **5.1 higher** (0.03 lower to 10.23 higher)	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with laser therapy	
Quality of life (SF-12 physical component, 0-100, high is good, final value) at ≤3 months	123 (1 RCT) follow up: 12 weeks	⊕⊕⊕◯ MODERATE [c]	-	The mean quality of life was 40.2	MD **0.8 lower** (4.28 lower to 2.68 higher)	MID = 0.5 SD (SMD)
Quality of life (SF-12 mental component, 0-100, high is good, final value) at ≤3 months	123 (1 RCT) follow up: 12 weeks	⊕⊕⊕◯ MODERATE [c]	-	The mean quality of life was 53.2	MD **0.2 lower** (3.8 lower to 3.4 higher)	MID = 0.5 SD (SMD)
Quality of life (SF-12 physical component, 0-100, high is good, final value) at >3 months	123 (1 RCT) follow up: 12 months	⊕⊕⊕◯ MODERATE [c]	-	The mean quality of life was 38.2	MD **0.6 higher** (3.18 lower to 4.38 higher)	MID = 0.5 SD (SMD)
Quality of life (SF-12 mental component, 0-100, high is good, final value) at >3 months	123 (1 RCT) follow up: 12 months	⊕⊕⊕◯ MODERATE [c]	-	The mean quality of life was 52.8	MD **0.7 lower** (4.25 lower to 2.85 higher)	MID = 0.5 SD (SMD)
Pain (WOMAC, AUSCAN, VAS [different scale ranges], high is poor, change scores) at ≤3 months	328 (4 RCTs) follow up: mean 8 weeks	⊕◯◯◯ VERY LOW [b,c]	-	-	SMD **0.96 SD lower** (2.09 lower to 0.18 higher)	MID = 0.5 SD (SMD)
Pain (KOOS, WOMAC, VNPS, VAS [different scale ranges], high is poor, final values) at ≤3 months	822 (14 RCTs) follow up: mean 8 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	-	SMD **0.31 SD lower** (0.55 lower to 0.06 lower)	MID = 0.5 SD (SMD)
Pain (AUSCAN, 0-4, high is poor, change score) at >3 months	86 (1 RCT) follow up: 6 months	⊕⊕⊕⊕ HIGH	-	The mean pain was -0.35	MD **0.06 lower** (0.39 lower to 0.27 higher)	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with laser therapy	
Pain (WOMAC, NRS [different scale ranges], high is poor, final values) at >3 months	233 (3 RCTs) follow up: mean 8 months	⊕⊕⊕◯ MODERATE [b]	-	The mean pain was -5.5	SMD **0.12 SD higher** (0.38 lower to 0.14 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC, AUSCAN [different scale ranges], high is poor, change score) at ≤3 months	141 (2 RCTs) follow up: mean 12 weeks	⊕⊕⊕⊕ HIGH	-	-	SMD **0.15 SD lower** (0.48 lower to 0.19 higher)	MID = 0.5 SD (SMD)
Physical function (KOOS, WOMAC [different scale ranges], high is poor, final values) at ≤3 months	450 (8 RCTs) follow up: mean 8 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	-	SMD **0.37 SD lower** (0.89 lower to 0.16 higher)	MID = 0.5 SD (SMD)
Physical function (AUSCAN, 0-4, high is poor, change score) at >3 months	86 (1 RCT) follow up: 6 months	⊕⊕⊕◯ MODERATE [a]	-	The mean physical function was -0.31	MD **0.07 lower** (0.4 lower to 0.26 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, final value) at >3 months	149 (2 RCTs) follow up: mean 9 months	⊕⊕⊕◯ MODERATE [b]	-	The mean physical function was 22.2	MD **0.13 higher** (4.33 lower to 4.59 higher)	MID = 5.9 (0.5 x median baseline SD)
Mild adverse events at ≤3 months	227 (4 RCTs) follow up: mean 8 weeks	⊕◯◯◯ VERY LOW [c,d,e]	RD 0.04 (-0.03 to 0.10)	55 per 1,000	**40 more per 1,000** (30 fewer to 100 more)	Precision calculated through Optimal Information Size (OIS) due to zero events in some studies (0.8-0.9 = serious, <0.8 = very serious).

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with laser therapy	
Mild adverse event at >3 months	66 (1 RCT) follow up: 6 months	⨁◯◯◯ VERY LOW [a,e]	RD 0.00 (-0.06 to 0.06)	0 per 1,000	**0 fewer per 1,000** (60 fewer to 60 more)	Sample size used to determine precision: 75-150 = serious imprecision, <75 = very serious imprecision.
Moderate/major adverse events at ≤3 months	55 (1 RCT) follow up: 12 weeks	⨁⨁⨁◯ MODERATE [a]	Peto OR 0.14 (0.01 to 2.22)	71 per 1,000	**70 fewer per 1,000** (180 fewer to 40 more) [f]	MID (precision) = Peto OR 0.8-1.25.

a. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
b. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis
c. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
d. Downgraded for heterogeneity due to conflicting number of events in different studies (zero events in one or more studies)
e. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size
f. Absolute effect calculated by risk difference due to zero events in at least one arm of the study

Table 45: Clinical evidence summary: laser therapy compared to no treatment

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with laser therapy	
Quality of life (SF-12 physical component, 0-100, high is good, final value) at ≤3 months	134 (1 RCT) follow up: 12 weeks	⨁⨁◯◯ LOW [a]	-	The mean quality of life was 39.5	MD **0.1 lower** (3.52 lower to 3.32 higher)	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with laser therapy	
Quality of life (SF-12 mental component, 0-100, high is good, final value) at ≤3 months	134 (1 RCT) follow up: 12 weeks	⊕◯◯◯ VERY LOW [a,c]	-	The mean quality of life was 55.8	MD **2.8 lower** (6.03 lower to 0.43 higher)	MID = 0.5 SD (SMD)
Quality of life (SF-12 physical component, 0-100, high is good, final value) at >3 months	120 (1 RCT) follow up: 12 months	⊕⊕◯◯ LOW [a]	-	The mean quality of life was 38.9	MD **0.1 lower** (3.93 lower to 3.73 higher)	MID = 0.5 SD (SMD)
Quality of life (SF-12 mental component, 0-100, high is good, final value) at >3 months	120 (1 RCT) follow up: 12 months	⊕◯◯◯ VERY LOW [a,c]	-	The mean quality of life was 54.4	MD **2.3 lower** (5.88 lower to 1.28 higher)	MID = 0.5 SD (SMD)
Pain (WOMAC [different scale ranges], high is poor, final values) at ≤3 months	279 (4 RCTs) follow up: mean 10 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	-	SMD **0.39 SD higher** (0.2 lower to 0.98 higher)	MID = 0.5 SD (SMD)
Pain (WOMAC, 0-20, high is poor, final value) at >3 months	120 (1 RCT) follow up: 12 months	⊕⊕◯◯ LOW [a]	-	The mean pain was 7.4	MD **0.3 lower** (1.77 lower to 1.17 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC [different scale ranges], high is poor, final values) at ≤3 months	279 (4 RCTs) follow up: mean 10 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	-	SMD **1 SD lower** (2.23 lower to 0.23 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, final value) at >3 months	120 (1 RCT) follow up: 12 months	⊕⊕◯◯ LOW [a]	-	The mean physical function was 21.6	MD **1 lower** (3.78 lower to 5.78 higher)	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with laser therapy	

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

c. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1.1.6.6 Transcutaneous electrical nerve stimulation compared to pulsed short-wave therapy, interferential therapy, sham electrotherapy and no treatment

Table 46: Clinical evidence summary: transcutaneous electrical nerve stimulation compared to pulsed short-wave therapy

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with pulsed short-wave therapy	Risk difference with transcutaneous electrical nerve stimulation	
Pain (WOMAC, VAS [different scale ranges], high is poor, change score) at ≤3 months	109 (2 RCTs) follow up: mean 10 weeks	⊕⊕◯◯ LOW a,b	-	-	SMD **0.24 SD higher** (0.14 lower to 0.61 higher)	MID = 0.5 SD (SMD)
Pain (WOMAC, 0-20, high is poor, change score) at >3 months	69 (1 RCT) follow up: 6 months	⊕⊕◯◯ LOW a,b	-	The mean pain was 4.5	MD **1.5 higher** (0.21 lower to 3.21 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, change score) at ≤3 months	69 (1 RCT) follow up: 6 months	⊕⊕◯◯ LOW a,b	-	The mean physical function was 11.4	MD **2.7 higher** (2.99 lower to 8.39 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, change score) at >3 months	69 (1 RCT)	⊕⊕◯◯ LOW a,b	-	The mean physical function was 9.9	MD **0.4 higher** (5.49 lower to 6.29 higher)	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with pulsed short-wave therapy	Risk difference with transcutaneous electrical nerve stimulation	
	follow up: 6 months					

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 47: Clinical evidence summary: transcutaneous electrical nerve stimulation compared to interferential therapy

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with interferential therapy	Risk difference with transcutaneous electrical nerve stimulation	
Pain (WOMAC, 0-20, high is poor, change score) at ≤3 months	173 (2 RCTs) follow up: mean 10 weeks	⨁◯◯◯ VERY LOW [a,b,c]	-		MD **1.2 higher** (0.48 lower to 2.89 higher)	MID = 2.2 (0.5 x median baseline SD)
Pain (WOMAC, 0-20, high is poor, change score) at >3 months	68 (1 RCT) follow up: 6 months	⨁⨁◯◯ LOW [a,c]	-	The mean pain was 3.4	MD **0.3 higher** (1.39 lower to 1.99 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, change score) at ≤3 months	173 (2 RCTs) follow up: mean 10 weeks	⨁◯◯◯ VERY LOW [a,b,c]	-		MD **3.68 higher** (1.69 lower to 9.06 higher)	MID = 6.5 (0.5 x median baseline SD)
Physical function (WOMAC, 0-68, high is poor, change score) at >3 months	68 (1 RCT) follow up: 6 months	⨁⨁◯◯ LOW [a,c]	-	The mean physical function was 8.5	MD **1 higher** (4.39 lower to 6.39 higher)	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with interferential therapy	Risk difference with transcutaneous electrical nerve stimulation	
Mild adverse events at ≤3 months	116 (1 RCT) follow up: 8 weeks	⊕◯◯◯ VERY LOW [a,c]	RR 1.74 (0.62 to 4.88)	88 per 1,000	**65 more per 1,000** (33 fewer to 340 more)	MID (precision) = RR 0.8-1.25.

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis
[c] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 48: Clinical evidence summary: transcutaneous electrical nerve stimulation compared to sham electrotherapy

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with transcutaneous electrical nerve stimulation	
Quality of life (SF-36 physical function, 0-1, high is good, final value) at ≤3 months	40 (1 RCT) follow up: 3 weeks	⊕⊕◯◯ LOW [a]	-	The mean quality of life was 0.45	MD **0.16 higher** (0.07 higher to 0.25 higher)	MID = 0.5 SD (SMD)
Quality of life (SF-36 vitality, 0-1, high is good, final value) at ≤3 months	40 (1 RCT) follow up: 3 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 0.72	MD **0.02 lower** (0.12 lower to 0.08 higher)	MID = 0.5 SD (SMD)
Quality of life (SF-36 general health, 0-1, high is good, final value) at ≤3 months	40 (1 RCT) follow up: 3 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 0.67	MD **0.06 higher** (0.02 lower to 0.14 higher)	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with transcutaneous electrical nerve stimulation	
Quality of life (SF-36 mental health, 0-1, high is good, final value) at ≤3 months	40 (1 RCT) follow up: 3 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 0.02	MD **0.02 higher** (0.08 lower to 0.12 higher)	MID = 0.5 SD (SMD)
Quality of life (SF-36 social function, 0-1, high is good, final value) at ≤3 months	40 (1 RCT) follow up: 3 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 0.72	**MD 0.11 higher** (0.02 higher to 0.2 higher)	MID = 0.5 SD (SMD)
Pain (WOMAC, 0-20, high is poor, change score) at ≤3 months	74 (1 RCT) follow up: 12 weeks	⊕⊕◯◯ LOW [a,b]	-	The mean pain was 3.6	MD **0.8 lower** (2.26 lower to 0.66 higher)	MID = 0.5 SD (SMD)
Pain (WOMAC, VAS [different scale ranges], high is poor, final values) at ≤3 months	361 (5 RCTs) follow up: mean 6 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	-	SMD **0.32 SD lower** (0.76 lower to 0.13 higher)	MID = 0.5 SD (SMD)
Pain (WOMAC, 0-20, high is poor, change score and final value) at >3 months	221 (2 RCTs) follow up: mean 25 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean pain was 5	MD **0.49 higher** (0.81 lower to 1.8 higher)	MID = 2.4 (0.5 x median baseline SD)
Physical function (WOMAC, 0-68, high is poor, change score) at ≤3 months	74 (1 RCT) follow up: 12 weeks	⊕⊕◯◯ LOW [a,b]	-	The mean physical function was 9.4	MD **0.7 lower** (5.78 lower to 4.38 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC [different scale ranges], high is poor, final values) at ≤3 months	313 (4 RCTs) follow up: mean 7 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	-	SMD **0.17 SD lower** (0.52 lower to 0.18 higher)	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with transcutaneous electrical nerve stimulation	
Physical function (WOMAC, 0-68, high is poor, change score and final value) at >3 months	221 (2 RCTs) follow up: mean 25 weeks	⊕⊕⊕◯ MODERATE [a]	-	The mean physical function was 17.2	MD **0.45 higher** (2.97 lower to 3.88 higher)	MID = 6.5 (0.5 x median baseline SD)
Mild adverse events at ≤3 months	24 (1 RCT) follow up: 4 weeks	⊕◯◯◯ VERY LOW [a,d]	RD 0.00 (-0.15 to 0.15)	0 per 1,000	**0 fewer per 1,000** (150 fewer to 150 more) [e]	Sample size used to determine precision: 75-150 = serious imprecision, <75 = very serious imprecision.

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
c. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis
d. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size
e. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

Table 49: Clinical evidence summary: transcutaneous electrical nerve stimulation compared to no treatment

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with transcutaneous electrical nerve stimulation	
Pain (VAS, 0-10, high is poor, change score) at ≤3 months	40 (1 RCT) follow up: 8 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean pain was -2.27	MD **0.05 lower** (0.52 lower to 0.42 higher)	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with transcutaneous electrical nerve stimulation	
Pain (WOMAC [different scale ranges], high is poor, final values) at ≤3 months	111 (3 RCTs) follow up: mean 7 weeks	⨁◯◯◯ VERY LOW [a,b,c]	-	-	SMD **0 SD higher** (0.45 lower to 0.46 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC [different scale ranges], high is poor, final values) at ≤3 months	111 (3 RCTs) follow up: mean 7 weeks	⨁◯◯◯ VERY LOW [a,b,c]	-	-	SMD **0.08 SD higher** (0.53 lower to 0.68 higher)	MID = 0.5 SD (SMD)
Mild adverse events at ≤3 months	24 (1 RCT) follow up: 4 weeks	⨁◯◯◯ VERY LOW [a,d]	RD 0.00 (-0.15 to 0.15)	0 per 1,000	**0 fewer per 1,000** (150 fewer to 150 more) [e]	Sample size used to determine precision: 75-150 = serious imprecision, <75 = very serious imprecision.

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
c. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis
d. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size
e. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

1

1.1.6.7 Ultrasound compared to pulsed short-wave therapy, neuromuscular electrical stimulation, transcutaneous electrical nerve stimulation, sham ultrasound and no treatment

Table 50: Clinical evidence summary: ultrasound compared to pulsed short-wave therapy

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with pulsed short-wave therapy	Risk difference with ultrasound	
Pain (VAS, 0-10, high is poor, change score) at ≤3 months	40 (1 RCT) follow up: 8 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean pain was -2.33	MD **0.01 lower** (0.54 lower to 0.52 higher)	MID = 0.5 SD (SMD)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 51: Clinical evidence summary: ultrasound compared to neuromuscular electrical stimulation

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with neuromuscular electrical stimulation	Risk difference with ultrasound	
Pain (WOMAC, 0-20, high is poor, final value) at ≤3 months	60 (1 RCT) follow up: 3 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean pain was 5.1	MD **0.94 lower** (1.78 lower to 0.1 lower)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months	60 (1 RCT) follow up: 3 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean physical function was 13.26	MD **1.16 lower** (2.24 lower to 0.08 lower)	MID = 0.5 SD (SMD)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 52: Clinical evidence summary: ultrasound compared to transcutaneous electrical nerve stimulation

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with transcutaneous electrical nerve stimulation	Risk difference with ultrasound	
Pain (VAS, 0-10, high is poor, change score) at ≤3 months	40 (1 RCT) follow up: 8 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean pain was -2.32	MD **0.02 lower** (0.51 lower to 0.47 higher)	MID = 0.5 SD (SMD)
Pain (WOMAC, 0-20, high is poor, final value) at ≤3 months	24 (1 RCT) follow up: 8 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean pain was 3.2	MD **3 higher** (0.11 higher to 5.89 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months	24 (1 RCT) follow up: 8 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean physical function was 10.1	MD **10.5 higher** (3.23 higher to 17.77 higher)	MID = 0.5 SD (SMD)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 53: Clinical evidence summary: ultrasound compared to sham electrotherapy

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with ultrasound	
Quality of life (SF-36 physical function, 0-100, high is good, change score) at ≤3 months	97 (1 RCT)	⊕⊕⊕⊕ HIGH	-	The mean quality of life was 15.4	MD **11.5 higher**	MID = 3 (established value)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with ultrasound	
	follow up: 13 weeks				(6.4 higher to 16.6 higher)	
Quality of life (SF-36 bodily pain, 0-100, high is good, change score and final value) at ≤3 months	153 (2 RCTs) follow up: mean 13 weeks	⊕⊕◯◯ LOW [a]	-	The mean quality of life was 33.96	MD **8.67 higher** (8.02 lower to 25.36 higher)	MID = 3 (established value)
Quality of life (SF-36 role physical, 0-100, high is good, change score) at ≤3 months	97 (1 RCT) follow up: 13 weeks	⊕⊕◯◯ LOW [a]	-	The mean quality of life was 12.33	MD **0.67 higher** (6.09 lower to 7.43 higher)	MID = 3 (established value)
Quality of life (SF-36 vitality, 0-100, high is good, change score) at ≤3 months	97 (1 RCT) follow up: 13 weeks	⊕⊕⊕◯ MODERATE [a]	-	The mean quality of life was 15.9	MD **5.72 higher** (1.36 higher to 10.08 higher)	MID = 2 (established value)
Quality of life (SF-36 general health, 0-100, high is good, change score and final value) at ≤3 months	153 (2 RCTs) follow up: mean 13 weeks	⊕⊕◯◯ LOW [a]	-	The mean quality of life was 23.2	MD **7.30 higher** (7.57 lower to 22.17 higher)	MID = 2 (established value)
Quality of life (SF-36 mental health, 0-100, high is good, change score) at ≤3 months	97 (1 RCT) follow up: 13 weeks	⊕⊕⊕⊕ HIGH	-	The mean quality of life was 40.8	MD **0.6 higher** (1.78 lower to 2.98 higher)	MID = 3 (established value)
Quality of life (SF-36 role emotional, 0-100, high is good, change score) at ≤3 months	97 (1 RCT) follow up: 13 weeks	⊕⊕◯◯ LOW [a]	-	The mean quality of life was 14.88	MD **0.35 lower** (8.2 lower to 7.5 higher)	MID = 4 (established value)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with ultrasound	
Quality of life (SF-36 social function, 0-100, high is good, change score) at ≤3 months	97 (1 RCT) follow up: 13 weeks	⊕⊕⊕◯ MODERATE [a]	-	The mean quality of life was 19.5	MD **6.75 higher** (0.27 higher to 13.23 higher)	MID = 3 (established value)
Quality of life (SF-36 physical component, 0-100, high is good, change score and final value) at ≤3 months	92 (2 RCTs) follow up: mean 9 weeks	⊕⊕⊕◯ LOW [a,b]	-	The mean quality of life was 22.7	MD **1.75 higher** (1.57 lower to 5.06 higher)	MID = 2 (established value)
Quality of life (SF-36 mental component, 0-100, high is good, change score and final value) at ≤3 months	92 (2 RCTs) follow up: mean 9 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 20.5	MD **0.34 higher** (3.17 lower to 3.86 higher)	MID = 3 (established value)
Pain (WOMAC, VAS [different scale ranges], high is poor, change scores) at ≤3 months	341 (5 RCTs) follow up: mean 6 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	-	SMD **0.53 SD lower** (0.91 lower to 0.15 lower)	MID = 0.5 SD (SMD)
Pain (WOMAC, VAS [different scale ranges], high is poor, final values) at ≤3 months	458 (8 RCTs) follow up: mean 6 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	-	SMD **0.53 SD lower** (0.91 lower to 0.15 lower)	MID = 0.5 SD (SMD)
Pain (VAS, 0-100, high is poor, change score) at >3 months	60 (1 RCT) follow up: 6 months	⊕⊕◯◯ LOW [a,b]	-	The mean pain was -34.1	MD **1.4 lower** (8.54 lower to 5.74 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC [different scale ranges], high is poor, change scores) at ≤3 months	244 (4 RCTs) follow up: mean 5 weeks	⊕⊕◯◯ LOW [a,b]	-	-	SMD **0.41 SD lower** (0.67 lower to 0.15 lower)	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with ultrasound	
Physical function (WOMAC, 0-68, high is poor, final values) at ≤3 months	167 (3 RCTs) follow up: mean 5 weeks	⊕⊕◯◯ LOW [b]	-	The mean physical function was 23.0	MD 1.92 **lower** (5.67 lower to 1.83 higher)	MID = 5.7 (0.5 x median baseline SD)
Physical function (WOMAC, 0-68, high is poor, change score) at >3 months	60 (1 RCT) follow up: 6 months	⊕⊕◯◯ LOW [a,b]	-	The mean physical function was -17	MD **2.2 lower** (6.58 lower to 2.18 higher)	MID = 0.5 SD (SMD)
Psychological distress (HADS anxiety, 0-21, high is poor, change score) at ≤3 months	40 (1 RCT) follow up: 3 weeks	⊕⊕◯◯ LOW [a,b]	-	The mean psychological distress was -1.65	MD **0.45 lower** (1.93 lower to 1.03 higher)	MID = 0.5 SD (SMD)
Psychological distress (HADS depression, 0-21, high is poor, change score) at ≤3 months	40 (1 RCT) follow up: 3 weeks	⊕⊕◯◯ LOW [a,b]	-	The mean psychological distress was -1.35	MD **0.3 lower** (1.84 lower to 1.24 higher)	MID = 0.5 SD (SMD)
Mild adverse events at ≤3 months	330 (5 RCTs) follow up: mean 5 weeks	⊕◯◯◯ VERY LOW [b,d,e]	RD -0.01 (-0.05 to 0.03)	32 per 1,000	**10 fewer per 1,000** (50 fewer to 30 more) [f]	Precision calculated through Optimal Information Size (OIS) due to zero events in some studies (0.8-0.9 = serious, <0.8 = very serious).
Moderate/major adverse events at ≤3 months	56 (1 RCT) follow up: 14 weeks	⊕⊕◯◯ LOW [e]	RD 0.00 (-0.08 to 0.08)	0 per 1,000	**0 fewer per 1,000** (80 fewer to 80 more) [f]	Sample size used to determine precision: 75-150 = serious imprecision, <75 = very serious imprecision.

a. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

b. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

c. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with ultrasound	
d. Downgraded for heterogeneity due to conflicting number of events in different studies (zero events in one or more studies)						
e. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size						
f. Absolute effect calculated by risk difference due to zero events in at least one arm of one study						

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2 **Table 54: Clinical evidence summary: ultrasound compared to no treatment**

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with ultrasound	
Quality of life (SF-36 physical component, 0-100, high is poor, final value) at ≤3 months	30 (1 RCT) follow up: 12 weeks	⊕◯◯◯ VERY LOW a,b	-	The mean quality of life was 40.9	MD **0** (4.22 lower to 4.22 higher)	MID = 2 (established value)
Quality of life (SF-36 mental component, 0-100, high is poor, final value) at ≤3 months	30 (1 RCT) follow up: 12 weeks	⊕◯◯◯ VERY LOW a,b	-	The mean quality of life was 39.3	MD **2.1 higher** (1.13 lower to 5.33 higher)	MID = 3 (established value)
Pain (VAS, 0-10, high is poor, change scores) at ≤3 months	300 (4 RCTs) follow up: mean 8 weeks	⊕◯◯◯ VERY LOW a,b,c	-	-	SMD **0.38 SD lower** (1.16 lower to 0.4 higher)	MID = 0.5 SD (SMD)
Pain (WOMAC, VAS [different scale ranges], high is poor, final values) at ≤3 months	58 (2 RCTs) follow up: mean 10 weeks	⊕◯◯◯ VERY LOW a,b,c	-	-	SMD **0.18 SD lower** (2.99 lower to 2.64 higher)	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with ultrasound	
Pain (VAS, 0-10, high is poor, final values) at >3 months	160 (2 RCTs) follow up: 12 months	⊕◯◯◯ VERY LOW [a,b,c]	-	The mean pain was 3.1	MD **0.21 lower** (2.36 lower to 1.95 higher)	MID = 0.78 (0.5 x median baseline SD)
Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months	128 (2 RCTs) follow up: mean 8 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	The mean physical function was 3.5	MD **3.42 lower** (6.93 lower to 0.1 higher)	MID = 5.7 (0.5 x median baseline SD)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[c] Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

1.1.6.8 Combination therapy compared to interferential therapy, neuromuscular electrical stimulation, laser therapy, transcutaneous electrical nerve stimulation, ultrasound, sham electrotherapy and no treatment

Table 55: Clinical evidence summary: combination therapy compared to interferential therapy

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with interferential therapy	Risk difference with combination therapy	
Pain (VAS, 0-10, high is poor, final value) at ≤3 months	84 (1 RCT) follow up: 3 months	⊕⊕⊕◯ MODERATE[a]	-	The mean pain was 3.55	MD **1.1 lower** (2.33 lower to 0.13 higher)	MID = 0.5 SD (SMD)
Pain (VAS, 0-10, high is poor, final value) at >3 months	84 (1 RCT)	⊕⊕⊕◯ MODERATE[a]	-	The mean pain was 3.65	MD **1.15 lower** (2.25 lower to 0.05 lower)	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with interferential therapy	Risk difference with combination therapy	
	follow up: 6 months					

a. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 56: Clinical evidence summary: combination therapy compared to neuromuscular electrical stimulation

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with neuromuscular electrical stimulation	Risk difference with combination therapy	
Pain (VAS, 0-10, high is poor, final value) at ≤3 months	29 (1 RCT) follow up: 12 weeks	⨁◯◯◯ VERY LOW a,b	-	The mean pain was 0.9	MD **0.3 higher** (0.24 lower to 0.84 higher)	MID = 0.5 SD (SMD)

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 57: Clinical evidence summary: combination therapy compared to laser therapy

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with laser therapy	Risk difference with combination therapy	
Pain (VAS, NRS, 0-10, high is poor, final values) at ≤3 months	113 (2 RCTs) follow up: mean 12 weeks	⨁⨁◯◯ LOW a	-	The mean pain was 2.4	MD **0.46 lower** (1.02 lower to 0.09 higher)	MID = 1.2 (0.5 x median baseline SD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with laser therapy	Risk difference with combination therapy	
Pain (NRS, 0-10, high is poor, final value) at >3 months	84 (1 RCT) follow up: 6 months	⊕⊕⊕◯ MODERATE [b]	-	The mean pain was 2.95	MD **0.45 lower** (1.47 lower to 0.57 higher)	MID = 0.5 SD (SMD)

[a]. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b]. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 58: Clinical evidence summary: combination therapy compared to transcutaneous electrical nerve stimulation

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with transcutaneous electrical nerve stimulation	Risk difference with combination therapy	
Quality of life (SF-36, 0-100, high is good, final value) at ≤3 months	38 (1 RCT) follow-up: 3 weeks	⊕◯◯◯ VERY LOW[a,b]	-	The mean quality of life was 67.34	MD **0.46 higher** (9.12 lower to 10.04 higher)	MID = 0.5 SD (SMD)
Pain (WOMAC, 0-20, high is poor, final value) at ≤3 months	38 (1 RCT) follow-up: 3 weeks	⊕⊕⊕◯ MODERATE[b]	-	The mean pain was 4.26	MD **1.06 higher** (1.12 lower to 3.24 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months	38 (1 RCT) follow-up: 3 weeks	⊕⊕⊕◯ MODERATE[b]	-	The mean physical function was 10.79	MD **5.05 higher** (1.22 lower to 11.32 higher)	MID = 0.5 SD (SMD)
Mild adverse events at ≤3 months	40 (1 RCT)	⊕⊕◯◯ LOW[c]	RD 0.00 (-0.09 to 0.09)	0 per 1,000	**0 fewer per 1,000** (90 fewer to 90 more) [d]	Sample size used to determine precision: 75-150 = serious

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with transcutaneous electrical nerve stimulation	Risk difference with combination therapy	
	follow-up: 3 weeks					imprecision, <75 = very serious imprecision.
Moderate/major adverse events at ≤3 months	40 (1 RCT) follow-up: 3 weeks	⨁⨁◯◯ LOW[c]	RD 0.00 (-0.09 to 0.09)	0 per 1,000	**0 fewer per 1,000** (90 fewer to 90 more) [d]	Sample size used to determine precision: 75-150 = serious imprecision, <75 = very serious imprecision.

a. Downgraded by 1 increment due to outcome indirectness (reported the global score of SF-36 rather than subscales)
b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
c. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

Table 59: Clinical evidence summary: combination therapy compared to ultrasound

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with ultrasound	Risk difference with combination therapy	
Quality of life (SF-36 pain, 0-100, high is good, final value) at ≤3 months	53 (1 RCT) follow up: 14 weeks	⨁⨁◯◯ LOW [a]	-	The mean quality of life was 46.3	MD **1.75 higher** (12.59 lower to 16.09 higher)	MID = 3 (established value)
Quality of life (SF-36 general health, 0-100, high is good, final value) at ≤3 months	53 (1 RCT) follow up: 14 weeks	⨁⨁◯◯ LOW [a]	-	The mean quality of life was 42.75	MD **8.88 higher** (2.22 lower to 19.98 higher)	MID = 2 (established value)
Pain (VAS, 0-100, high is poor, change score and final value) at ≤3 months	201 (2 RCTs) follow up: mean 8 weeks	⨁◯◯◯ VERY LOW [a,b]	-	The mean pain was 34	MD **0.65 higher** (10.88 lower to 12.19 higher)	MID = 0.5 SD (SMD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with ultrasound	Risk difference with combination therapy	
Mild adverse events at ≤3 months	185 (2 RCTs) follow up: mean 8 weeks	⨁◯◯◯ VERY LOW [b,c,d]	RD 0.01 (-0.05 to 0.08)	28 per 1,000	**10 more per 1,000** (50 fewer to 80 more) [e]	Precision calculated through Optimal Information Size (OIS) due to zero events in some studies (0.8-0.9 = serious, <0.8 = very serious).
Moderate/major adverse events ≤3 months	53 (1 RCT) follow up: 14 weeks	⨁⨁◯◯ LOW [d]	RD 0.00 (-0.09 to 0.09)	0 per 1,000	**0 fewer per 1,000** (90 fewer to 90 more) [e]	Sample size used to determine precision: 75-150 = serious imprecision, <75 = very serious imprecision.

a. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
b. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
c. Downgraded for heterogeneity due to conflicting number of events in different studies (zero events in one or more studies)
d. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size
e. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

Table 60: Clinical evidence summary: combination therapy compared to sham electrotherapy

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with combination therapy	
Quality of life (SF-36 pain, 0-100, high is good, final values) at ≤3 months	33 (1 RCT) follow-up: 14 weeks	⨁⨁◯◯ LOW [a]	-	The mean quality of life was 47.15	MD **0.85 higher** (14.04 lower to 15.74 higher)	MID = 3 (established MID)
Quality of life (SF-36 general health, 0-100, high is good, final values) at ≤3 months	33 (1 RCT) follow-up: 14 weeks	⨁⨁◯◯ LOW [a]	-	The mean quality of life was 43.89	MD **7.74 higher** (4.55 lower to 20.03 higher)	MID = 2 (established MID)

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with sham electrotherapy	Risk difference with combination therapy	
Pain (VAS, 0-100, high is poor, final value) at ≤3 months	117 (2 RCTs) follow-up: mean 13 weeks	⊕⊕⊕◯ MODERATE [a]	-	The mean pain was 46.1	MD **16.04 lower** (24.97 lower to 7.11 lower)	MID = 15 (0.5 x median baseline SD)
Pain (VAS, 0-10, high is poor, final value) at >3 months	84 (1 RCT) follow-up: 6 months	⊕⊕⊕⊕ HIGH	-	The mean pain was 4.9	MD **3 lower** (4.03 lower to 1.97 lower)	MID = 0.5 SD (SMD)
Mild adverse events at ≤3 months	33 (1 RCT) follow-up: 14 weeks	⊕⊕◯◯ LOW [b]	RD 0.00 (-0.11 to 0.11)	0 per 1,000	**0 fewer per 1,000** (110 fewer to 110 more) [c]	Sample size used to determine precision: 75-150 = serious imprecision, <75 = very serious imprecision.
Moderate/major adverse events at ≤3 months	33 (1 RCT) follow-up: 14 weeks	⊕⊕◯◯ LOW [b]	RD 0.00 (-0.11 to 0.11)	0 per 1,000	**0 fewer per 1,000** (110 fewer to 110 more) [c]	Sample size used to determine precision: 75-150 = serious imprecision, <75 = very serious imprecision.

a. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
b. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size
c. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

1

1 **Table 61: Clinical evidence summary: combination therapy compared to no treatment**

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with combination therapy	
Quality of life (SF-36 physical function, 0-100, high is good, final value) at ≤3 months	40 (1 RCT) follow-up: 3 weeks	⊕⊕◯◯ LOW [a]	-	The mean quality of life was 59	MD **24 higher** (15.51 higher to 32.49 higher)	MID = 3 (established value)
Quality of life (SF-36 pain, 0-100, high is good, final value) at ≤3 months	40 (1 RCT) follow-up: 3 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 45.4	MD **10.2 higher** (1.58 higher to 18.82 higher)	MID = 3 (established value)
Quality of life (SF-36 role physical, 0-100, high is good, final value) at ≤3 months	40 (1 RCT) follow-up: 3 weeks	⊕⊕◯◯ LOW [a]	-	The mean quality of life was 28.75	MD **37.55 higher** (24.51 higher to 50.59 higher)	MID = 3 (established value)
Quality of life (SF-36 vitality, 0-100, high is good, final value) at ≤3 months	40 (1 RCT) follow-up: 3 weeks	⊕⊕◯◯ LOW [a]	-	The mean quality of life was 40	MD **22 higher** (13 higher to 31 higher)	MID = 2 (established value)
Quality of life (SF-36 general health, 0-100, high is good, final value) at ≤3 months	40 (1 RCT) follow-up: 3 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean quality of life was 40.9	MD **2.9 higher** (5.46 lower to 11.26 higher)	MID = 2 (established value)
Quality of life (SF-36 role emotion, 0-100, high is good, final value) at ≤3 months	40 (1 RCT) follow-up: 3 weeks	⊕⊕◯◯ LOW [a]	-	The mean quality of life was 47.9	MD **31.8 higher** (17.64 higher to 45.96 higher)	MID = 4 (established value)
Quality of life (SF-36 mental health, 0-100, high is good, final value) at ≤3 months	40 (1 RCT) follow-up: 3 weeks	⊕⊕◯◯ LOW [a]	-	The mean quality of life was 56	MD **13 higher** (4.56 higher to 21.44 higher)	MID = 3 (established value)

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with no treatment	Risk difference with combination therapy	
Quality of life (SF-36 social function, 0-100, high is good, final value) at ≤3 months	40 (1 RCT) follow-up: 3 weeks	⊕⊕◯◯ LOW [a]	-	The mean quality of life was 50	MD **26.2 higher** (14.16 higher to 38.24 higher)	MID = 3 (established value)
Pain (WOMAC, NRS [different scale ranges], high is poor, final values) at ≤3 months	84 (2 RCTs) follow-up: mean 5 weeks	⊕◯◯◯ VERY LOW [a,b,c]	-	-	SMD **0.59 SD lower** (2.69 lower to 1.52 higher)	MID = 0.5 SD (SMD)
Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months	44 (1 RCT) follow-up: 7 weeks	⊕⊕◯◯ LOW [a,b]	-	The mean physical function was 20	MD **4.18 higher** (2.27 lower to 10.63 higher)	MID = 0.5 SD (SMD)
Psychological distress (BDI, 0-51, high is poor, final value) at ≤3 months	40 (1 RCT) follow-up: 3 weeks	⊕◯◯◯ VERY LOW [a,b]	-	The mean psychological distress was 8.4	MD **1.6 lower** (3.2 lower to 0)	MID = 0.5 SD (SMD)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[c] Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

See Appendix F for full GRADE tables.

1.1.7 Economic evidence

1.1.7.1 Included studies

One health economic study with the relevant comparison was included in this review.[145] This is summarised in the health economic evidence profile below (**62**) and the health economic evidence table in Appendix H.

1.1.7.2 Excluded studies

No relevant health economic studies were excluded due to limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix G.

1.1.8 Summary of included economic evidence

Table 62: Health economic evidence profile: Electrotherapy versus usual care

Study	Applicability	Limitations	Other comments	Incremental cost[(d)]	Incremental effects	Cost effectiveness	Uncertainty
MacPherson 2017[145] (UK)	Partially applicable	Potentially serious limitations[(a)]	• Probabilistic model based on three separate network meta-analyses of RCTs[(b)] • Cost-utility analysis (QALYs) • Population: Patients reporting pain resulting from OA of the knee. • Comparators:[(c)] 1. Usual care 2. TENS 3. PES 4. NMES 5. Laser light therapy 6. Interferential therapy 7. PEMF Time horizon was 8 weeks	All trials 2-1: £31 3-1: £396 4-1: £481 5-1: £503 6-1: £770 7-1: £1,453 Trials with adequate allocation concealment and endpoint at 3-13 weeks 2-1: £30 3-1: £410 4-1: NR 5-1: £288 6-1: £1,179 7-1: £577	**Inc. QALYs** All trials 2-1: 0.011 3-1: 0.011 4-1: 0.005 5-1: 0.007 6-1: 0.033 7-1: 0.007 Trials with adequate allocation concealment and endpoint at 3-13 weeks 2-1: 0.006 3-1: 0.010 4-1: NR 5-1: 0.003 6-1: 0.017 7-1: 0.007	**Cost per QALY gained[(e)]** All trials 2-1: £2,690 3-1: £36,000 4-1: £96,200 5-1: £71,857 6-1: £23,333 7-1: £207,571 Trials with adequate allocation concealment and endpoint at 3-13 weeks 2-1: £6,142 3-1: £41,000 4-1: NR 5-1: £96,000 6-1: £69,353 7-1: £82,429	This study analysed a variety of different intervention classes and so all reports of uncertainty were based on an analysis of all interventions and not any intervention(s) in isolation. For a summary of the analysis of uncertainty involving all interventions, see Appendix H.

Abbreviations: ICER = incremental cost-effectiveness ratio; Inc.= incremental; NMES= neuromuscular electrical stimulation; NR = not reported; OA = Osteoarthritis; PEMF= pulsed electromagnetic field; PES= pulsed electrical stimulation; QALYs = quality-adjusted life years; RCT= randomised controlled trial; TENS= transcutaneous electrical nerve stimulation

(a) Unit costs taken from 2011/12 may not reflect current UK NHS practice. The time horizon was only 8 weeks. Adverse events and their downstream consequences were not considered.

(b) Only model results from 2 of the 3 network meta analyses presented in this evidence profile. See Appendix H for all model results.

(c) The original report listed 13 interventions in total. Only those interventions that fit the protocol for electrotherapy were included here. Please note intervention numbers in this profile do not match to intervention numbers in evidence table (Appendix H).

(d) 2011/12 UK pounds. Cost components incorporated: Physiotherapist's time to conduct sessions. Changes in non-treatment-related visits to GPs and specialists arising from changes to EQ-5D score

(e) In a full incremental analysis of all interventions, TENS was the most cost-effective option in the network meta-analysis all trials with a cost per QALY of £2,690. In the other two network meta-analyses (1. only those trials with adequate allocation concealment and 2. only those trials with adequate allocation concealment and an endpoint between 3-13 weeks), acupuncture was the most cost-effective option with costs per QALYs of £13,502 and £14,275, respectively.

1.1.9 Economic model

This area was not prioritised for new cost-effectiveness analysis.

1.1.10 Unit costs

Relevant unit costs are provided below to aid consideration of cost effectiveness.

Resource	Average unit cost	Source
Community physiotherapist (band 5/6/7)	£38/£50/£60(a)	PSSRU 2020[61]

(a) Per hour, including qualification costs

1.1.11 Economic evidence statements

- One cost-utility analysis compared usual care to a multitude of electrotherapy options; interferential therapy, laser light therapy, neuromuscular electrical stimulation (NMES), pulsed electromagnetic field (PEMF), pulsed electrical stimulation (PES) and transcutaneous electrical nerve stimulation (TENS) as well as non-electrotherapy options; acupuncture, braces, heat treatment insoles and static magnets. TENS was the only electrotherapy option that was cost effective compared with usual care with a cost per QALY gained of £2,690. This analysis was assessed as directly applicable with potentially serious limitations.

1.1.12 The committee's discussion and interpretation of the evidence

1.1.12.1. The outcomes that matter most

The critical outcomes were quality of life, pain and physical function. These were considered critical due to their importance to people with osteoarthritis. The Osteoarthritis Research Society International (OARSI) consider that pain and physical function were the most important outcomes for evaluating interventions. Quality of life gives a broader perspective on the person's wellbeing, allowing for examination of the biopsychosocial impact of interventions. Psychological distress, osteoarthritis flare, mild adverse events and moderate/major adverse events were included as important outcomes.

The committee considered osteoarthritis flares to be important in the lived experience and management of osteoarthritis. However, these were also considered difficult to measure with no clear consensus on their definition. The Flares in OA OMERACT working group have proposed an initial definition and domains of OA flares through a consensus exercise; "it is a transient state, different from the usual state of the condition, with a duration of a few days, characterized by onset, worsening of pain, swelling, stiffness, impact on sleep, activity, functioning, and psychological aspects that can resolve spontaneously or lead to a need to adjust therapy.". However, this has been considered to have limitations and has not been widely adopted. Therefore, the committee included the outcome accepting any reasonable definition provided by any studies discussing the event.

Mortality was included as a treatment adverse event rather than as a discreet outcome and categorised as an important outcome. Osteoarthritis as a disease process is not considered to cause mortality by itself and mortality is an uncommon outcome from osteoarthritis interventions.

There was evidence available for all outcomes apart from osteoarthritis flares. However, there was only limited evidence available regarding psychological distress and adverse events.

1.1.12.2 The quality of the evidence

Sixty-six randomised controlled trial studies were included in the review. The comparisons where evidence was present included:

- Pulsed short-wave therapy compared to sham electrotherapy

- Pulsed short-wave therapy compared to no treatment
- Interferential therapy compared to pulsed short-wave therapy
- Interferential therapy compared to laser therapy
- Interferential therapy compared to sham electrotherapy
- Interferential therapy compared to no treatment
- Neuromuscular electrical stimulation compared to no treatment
- Extracorporeal shockwave therapy compared to sham electrotherapy
- Extracorporeal shockwave therapy compared to no treatment
- Laser therapy compared to pulsed short-wave therapy
- Laser therapy compared to neuromuscular electrical stimulation
- Laser therapy compared to sham electrotherapy
- Laser therapy compared to no treatment
- Transcutaneous electrical nerve stimulation compared to pulsed short-wave therapy
- Transcutaneous electrical nerve stimulation compared to interferential therapy
- Transcutaneous electrical nerve stimulation compared to sham electrotherapy
- Transcutaneous electrical nerve stimulation compared to no treatment
- Ultrasound compared to pulsed short-wave therapy
- Ultrasound compared to neuromuscular electrical stimulation
- Ultrasound compared to transcutaneous electrical nerve stimulation
- Ultrasound compared to sham electrotherapy
- Ultrasound compared to no treatment
- Combination therapy compared to interferential therapy
- Combination therapy compared to neuromuscular electrical stimulation
- Combination therapy compared to laser therapy
- Combination therapy compared to transcutaneous electrical nerve stimulation
- Combination therapy compared to ultrasound
- Combination therapy compared to sham electrotherapy
- Combination therapy compared to no treatment

The evidence varied from high to very low quality, with the majority being of low quality. Outcomes were commonly downgraded for risk of bias, in particular for selection bias and performance bias (apart from where the comparator was sham therapy), and imprecision. Some outcomes were downgraded for inconsistency. When present, inconsistent results were not explained by subgroup analysis. The majority of comparisons consisted of studies with a small number of participants (less than 50) with a few studies that included a larger number of participants.

The committee agreed that there was some evidence comparing the majority of different forms of electrotherapy to sham or no treatment (with the exception of neuromuscular electrical stimulation that was not compared to sham electrotherapy). However, findings were often mixed and there is insufficient evidence to compare different types of electrotherapy to each other.

Pulsed short-wave therapy

Pulsed short-wave therapy was compared to interferential therapy, laser therapy, transcutaneous electrical nerve stimulation, ultrasound, sham electrotherapy and no treatment. Comparisons were available at less than and greater than 3 months.

- When compared to interferential therapy, the evidence was based on 2 studies and was of moderate to low quality due to risk of bias and imprecision.
- When compared to laser therapy, the evidence was based on 1 small study (N=40 for this comparison) reporting 2 outcomes that were of moderate and low quality respectively due to risk of bias and imprecision.
- When compared to transcutaneous electrical nerve stimulation, the evidence was based on 2 studies and was of low quality due to risk of bias and imprecision.
- When compared to ultrasound, the evidence was based on 1 small study (N=40) reporting 1 outcome that was of very low quality, due to risk of bias and imprecision.
- When compared to sham electrotherapy, the evidence was based on 15 studies and the quality of the outcomes was between high and very low quality, with the majority of evidence being of moderate-low quality. Outcomes were often downgraded due to risk of bias and imprecision. However, some outcomes were downgraded due to inconsistency (including some pain and physical function outcomes).
- When compared to no treatment, the evidence was based on 5 studies. Most outcomes included only 1 small study and were of moderate-very low quality, with the majority being of very low quality. Outcomes were often downgraded due to risk of bias and imprecision.

Interferential therapy

Interferential therapy was compared to pulsed short-wave therapy, laser therapy, transcutaneous electrical nerve stimulation, combination therapy, sham electrotherapy and no treatment. Comparisons were available at less than and greater than 3 months.

- When compared to interferential therapy, the evidence was based on 2 studies and the outcomes were of moderate to low quality due to risk of bias and imprecision.
- When compared to laser therapy, the evidence was based on 2 studies and the quality of the outcomes was between moderate and low quality. Outcomes were often downgraded for risk of bias and imprecision.
- When compared to transcutaneous electrical nerve stimulation, the evidence was based on 2 studies with only 1 study reporting each outcome and was of low quality due to risk of bias and imprecision.
- When compared to combination therapy (interferential therapy and laser therapy), the evidence was based on 1 small study (N=84 for this comparison) with the outcomes being of moderate quality due to imprecision.
- When compared to sham electrotherapy, the evidence was based on 4 studies where outcomes ranged from moderate to very low quality. Outcomes were often downgraded for risk of bias and imprecision. However, some outcomes were downgraded for inconsistency, with heterogeneity that could not be resolved by subgroup analysis.
- When compared to no treatment, the evidence was based on 1 small study (N=40) with outcomes ranging from moderate to low quality, due to concerns risk of bias and both risk of bias and imprecision respectively.

Neuromuscular electrical stimulation

Neuromuscular electrical stimulation was compared to laser therapy, ultrasound, combination therapy and no treatment. The majority of comparisons only had data reported at less than 3 months. The comparison to no treatment had data available at less than and more than 3 months.

- When compared to laser therapy, 1 outcome was reported in 1 small study (N=30) that was of low quality due to risk of bias and imprecision.
- When compared to ultrasound, outcomes were reported in 1 small study (N=60) that was of low quality due to risk of bias and imprecision.

- When compared to combination therapy (laser therapy and neuromuscular electrical stimulation), 1 outcome was reported in 1 small study (N=29) that was of low quality due to risk of bias and imprecision.
- When compared to no treatment, the evidence was based on 6 studies. The quality ranged from moderate to very low quality, with the majority being of very low quality. Studies were commonly downgraded due to risk of bias and imprecision. 1 outcome was downgraded due to inconsistency.

Extracorporeal shockwave therapy

Extracorporeal shockwave therapy was compared to sham electrotherapy and no treatment at ≤3 months only.

- When compared to sham electrotherapy, the evidence was based on 5 studies. The outcomes ranged from moderate to very low quality due to risk of bias, imprecision and in some cases, inconsistency with heterogeneity that could not be resolved by subgroup analysis.
- When compared to no treatment, the evidence was based on 2 studies. The outcomes were of low quality due to risk of bias and imprecision.

Laser therapy

Laser therapy was compared to pulsed short-wave therapy, interferential therapy, neuromuscular electrical stimulation, combination therapy, sham electrotherapy and no treatment. Sham electrotherapy and no treatment comparisons were available before and after 3 months.

- When compared to pulsed short-wave therapy, the evidence was based on 1 small study (N=40 for this comparison) reporting 2 outcomes that were of moderate and low quality respectively due to risk of bias and imprecision.
- When compared to interferential therapy, the evidence was based on 2 studies and the quality of the outcomes was between moderate and low quality. Outcomes were often downgraded for risk of bias and imprecision.
- When compared to neuromuscular electrical stimulation, 1 outcome was reported in 1 small study (N=30) that was of low quality due to risk of bias and imprecision.
- When compared to combination therapy (laser therapy and interferential therapy or laser therapy and neuromuscular electrical stimulation), 2 outcomes was reported in 2 studies that were of moderate and low quality due to risk of bias and imprecision respectively.
- When compared to sham electrotherapy, the evidence was based on 20 studies. The quality ranged between high and very low quality, with the majority being of moderate to low quality. Studies were often downgraded due to risk of bias, inconsistency or imprecision. 6 outcomes were downgraded due to inconsistency.
- When compared to no treatment, the evidence was based on 3 studies. The quality was of low or very low quality. Studies were often downgraded due to risk of bias and imprecision. 3 outcomes were downgraded due to inconsistency.

Transcutaneous electrical nerve stimulation

Transcutaneous electrical nerve stimulation was compared to pulsed short-wave therapy, interferential therapy, ultrasound, combination therapy, sham electrotherapy and no treatment. Evidence was available for most comparisons at both before and after 3 months.

- When compared to pulsed short-wave therapy, the evidence was based on 2 studies and was of low quality due to risk of bias and imprecision.
- When compared to interferential therapy, the evidence was based on 2 studies with only 1 study reporting each outcome and was of low quality due to risk of bias and imprecision.

- When compared to ultrasound, the evidence was based on 2 small studies with only 1 study reporting each outcome and was of very low quality due to risk of bias and imprecision.
- When compared to combination therapy (transcutaneous electrical nerve stimulation and ultrasound), the evidence was based on 1 small study (N=40 for this comparison) with outcomes ranging between moderate and very low quality due to indirectness (using the global score of SF-36 for quality of life rather than the relevant subscales) and imprecision.
- When compared to sham electrotherapy, the evidence was based on 6 studies. The quality of evidence ranged from moderate to very low quality, with the majority being of very low quality. Studies were often downgraded due to risk of bias and imprecision. 2 outcomes were downgraded due to inconsistency.
- When compared to no treatment, the evidence was based on 4 studies. The evidence ranged between low and very low quality. Studies were often downgraded for risk of bias, inconsistency and imprecision. 2 outcomes were downgraded due to inconsistency.

Ultrasound

Ultrasound was compared to pulsed short-wave therapy, neuromuscular electrical stimulation, transcutaneous electrical nerve stimulation, combination therapy, sham electrotherapy and no treatment. Evidence was available for all comparisons at ≤3 months but only limited evidence was available at >3 months when compared to sham electrotherapy and no treatment.

- When compared to pulsed short-wave therapy, the evidence was based on 1 small study (N=40) reporting 1 outcome that was of very low quality, due to risk of bias and imprecision.
- When compared to neuromuscular electrical stimulation, outcomes were reported in 1 small study (N=60) that was of low quality due to risk of bias and imprecision.
- When compared to transcutaneous electrical nerve stimulation, the evidence was based on 2 small studies with only 1 study reporting each outcome and was of very low quality due to risk of bias and imprecision.
- When compared to combination therapy (transcutaneous electrical nerve stimulation and ultrasound), the evidence was based on 2 studies with the outcomes being of low to very low quality due to risk of bias, imprecision and inconsistency, due to some studies reporting mild adverse events including zero events while others report events in all study arms.
- When compared to sham electrotherapy, the evidence was based on 11 studies. The quality of evidence ranged from high to very low quality, with the majority being of moderate to low quality. Studies were often downgraded for risk of bias and imprecision. 2 outcomes were downgraded due to inconsistency.
- When compared to no treatment, the evidence was based on 4 studies. The quality of evidence ranged from low to very low quality, with the majority being of very low quality. Studies were often downgraded for risk of bias and imprecision. 3 outcomes were downgraded due to inconsistency.

Combination therapy

Combination therapy was compared to interferential therapy, neuromuscular electrical stimulation, laser therapy, transcutaneous electrical nerve stimulation, ultrasound, sham electrotherapy and no treatment.

- When compared to interferential therapy, the evidence was based on 1 small study (N=84 for this comparison) with the outcomes being of moderate quality due to imprecision.
- When compared to neuromuscular electrical stimulation, 1 outcome was reported in 1 small study (N=29) that was of low quality due to risk of bias and imprecision.

- When compared to laser therapy, 2 outcomes was reported in 2 studies that were of moderate and low quality due to risk of bias and imprecision respectively.
- When compared to transcutaneous electrical nerve stimulation, the evidence was based on 1 small study (N=40 for this comparison) with outcomes ranging between moderate and very low quality due to indirectness (using the global score of SF-36 for quality of life rather than the relevant subscales) and imprecision.
- When compared to ultrasound, the evidence was based on 2 studies with the outcomes being of low to very low quality due to risk of bias, imprecision and inconsistency, due to some studies reporting mild adverse events including zero events while others report events in all study arms.
- When compared to sham electrotherapy, the evidence was based on 2 studies and ranged from high to low quality due to imprecision.
- When compared to no treatment, the evidence was based on 2 studies and ranged from low to very low quality due to risk of bias, imprecision and inconsistency with heterogeneity that could be not resolved by subgroup analysis.

1.1.12.3 Benefits and harms

Key uncertainties

The committee discussed that generally the adverse events data for these trials was limited as this was generally found in small studies with a short follow up time and so it is unclear whether this is representative of the events expected to be seen in real life practice. Given this, the committee considered the evidence for mild, moderate and severe adverse events to be unclear throughout the review reflecting this in their weighting of findings while making recommendations. The committee noted throughout the evidence that the number of adverse events was often low and where events were reported they were transient in nature (such as increased pain). Given this, while the committee acknowledged where clinically important differences were highlighted in the evidence, but also considered the nature and true number of these events.

On examining the evidence, the committee agreed that there was significant heterogeneity in the interventions being offered between studies investigating the same class, which made it difficult to draw conclusions regarding the interventions. This variation was also present in the use of sham comparisons, where the techniques used to achieve this varied from using the device but having no power entering the machine, to using devices made to simulate the effect. In some cases, these shams seemed like they may not effectively blind the participant due to the vigorous nature of the intervention (such as for extracorporeal shockwave therapy). The committee acknowledge the challenges in examining these interventions using these methods and considered this when making recommendations.

Pulsed short-wave therapy

Pulsed short-wave therapy was compared to interferential therapy, laser therapy, transcutaneous electrical nerve stimulation, ultrasound, sham electrotherapy and no treatment. When compared to sham electrotherapy, unclear effects were seen in quality of life and pain at ≤3 months, where 1 outcome including 1 and9 studies respectively showed a clinically important benefit, while 2 outcomes including 4 studies for quality of life and 1 outcome including 4 studies for pain showed no clinically important difference. The clinically important benefit for pain was seen in an analysis where the result was inconsistent, with some studies showing clinically important benefits while others showed no difference. These unclear effects for pain were also seen at >3 months. Clinically important benefits were seen in physical function (based on low to very low quality evidence). No clinically important differences were seen in psychological distress, mild and moderate/major adverse events. When compared to no treatment, unclear effects were seen for quality of life (present at less than and more than 3 months), pain and physical function where some outcomes showed

clinically important benefits while others showed no clinically important differences. When compared to other interventions, pulsed short-wave therapy had an unclear effect when compared to laser therapy (where laser therapy led to clinically important benefits in pain, while pulsed short-wave therapy led to clinically important benefits in physical function). Otherwise, there did not appear to be a clinically important difference between pulsed-short wave therapy and the other therapies mentioned above.

Interferential therapy

Interferential therapy was compared to pulsed short-wave therapy, laser therapy, transcutaneous electrical nerve stimulation, combination therapy, sham electrotherapy and no treatment. When compared to sham electrotherapy at ≤3 months, an unclear effect was seen for pain, with 1 outcome including 3 studies indicating a clinically important benefit based on very low quality evidence, while 1 outcome including 1 study indicated no clinically important difference based on moderate quality evidence. Clinically important benefits were seen for physical function based on two studies. When compared to other interventions, interferential therapy appeared to cause a clinically important benefit in mild adverse events when compared to transcutaneous electrical nerve stimulation. A clinically important difference in physical function was seen when compared to laser therapy based on evidence from 1 small study (N=40). No effects were sustained at >3 months.

Neuromuscular electrical stimulation

Neuromuscular electrical stimulation was compared to laser therapy, ultrasound, combination therapy and no treatment. When compared to no treatment at ≤3 months, unclear effects were seen in pain where 1 outcome showed a clinically important benefit with 1 outcome showed no clinically important difference. An unclear effect was seen in quality of life. However, in this case 6 outcomes indicated no clinically important difference while 2 outcomes indicated a clinically important harm. Otherwise, there was no clinically important difference seen in physical function and mild adverse events. However, at >3 months clinically important benefits were seen in pain and physical function. When compared to other interventions neuromuscular electrical stimulation appeared inferior. When compared to laser therapy there was a clinically important harm in pain based on 1 small study (N=30), and when compared to ultrasound there were clinically important harms in pain and physical function based on 1 small study (N=60). When compared to combination therapy there was no clinically important difference in pain based on 1 small study (N=29).

Extracorporeal shockwave therapy

Extracorporeal shockwave therapy was compared to sham electrotherapy and no treatment at ≤3 months only. When compared to sham electrotherapy clinically important benefits were seen in pain, physical function and mild adverse events, while no clinically important difference was seen in moderate/major adverse events. However, when compared to no treatment no clinically important difference was seen in pain while a clinically important harm was seen in physical function. The committee considered the studies and agreed that, while a sham comparison was used, it was unlikely to be sufficiently blinded due to the sensation that a person receiving extracorporeal shockwave therapy being of a likely greater amplitude to that received with sham. This meant that people may have known if they received the real or sham treatment, creating uncertainty in the effect. They also agreed that, while the overall number of participants in the meta-analysis was larger (N=307 and N=200 for pain and physical function respectively) the individual studies were still small. Given these factors and the uncertainty seen between the sham and no treatment comparisons, the committee agreed that there was currently insufficient evidence to support the use of extracorporeal shockwave therapy.

Laser therapy

Laser therapy was compared to pulsed short-wave therapy, interferential therapy, neuromuscular electrical stimulation, combination therapy, sham electrotherapy and no treatment. When compared to sham electrotherapy, a clinically important benefit was seen in moderate/major adverse events based on 1 small study (N=55). Unclear effects were seen in quality of life and pain with some outcomes showing a clinically important benefit while others showed no difference. For pain, 4 studies were included in the outcome showing a clinically important benefit while 14 were included in the outcome showing no clinically important difference. However, the outcomes showing a benefit were affected by inconsistency. No clinically important difference was seen in physical function and mild adverse events. When compared to no treatment, there was a clinically important benefit in physical function but no clinically important difference in quality of life and pain. For both comparisons, no effects were retained at >3 months.

When compared to other interventions, laser therapy had an unclear effect when compared to pulsed short-wave therapy (where laser therapy led to clinically important benefits in pain, while pulsed short-wave therapy led to clinically important benefits in physical function). Interferential therapy had a clinically important benefit in physical function when compared to laser therapy. Laser therapy had a clinically important benefit on pain when compared to neuromuscular electrical stimulation based on 1 small study (N=30). However, when compared to combination therapy, there was no clinically important difference in pain.

Transcutaneous electrical nerve stimulation

Transcutaneous electrical nerve stimulation was compared to pulsed short-wave therapy, interferential therapy, ultrasound, combination therapy, sham electrotherapy and no treatment. When compared to sham electrotherapy, there was an unclear effect on quality of life with 2 outcomes showing a clinically important benefit while 3 showed no clinically important difference. There was no clinically important difference in pain, physical function and mild adverse events. The effects on pain and physical function were both seen at less than and more than 3 months. When compared to no treatment there was no clinically important difference in pain, physical function and mild adverse events. When compared to other treatments, there was no clinically important difference in pain and physical function seen when compared to pulsed short-wave therapy and interferential therapy though there appeared to be a clinically important harm in mild adverse events when compared to interferential therapy. When compared to ultrasound, there was a mixed effect with 1 outcome including 1 small study (N=24) showing a clinically important benefit while 1 outcome including another 1 small study (N=40) showed no clinically important difference.

Ultrasound

Ultrasound was compared to pulsed short-wave therapy, neuromuscular electrical stimulation, transcutaneous electrical nerve stimulation, combination therapy, sham electrotherapy and no treatment. When compared to sham electrotherapy there was a clinically important benefit in pain (seen in 2 outcomes including 13 studies). This effect was not seen at greater than 3 months. However, these outcomes were affected by inconsistency. There was an unclear effect on quality of life with 5 outcomes showing a clinically important benefit and 5 outcomes showing no clinically important difference. There was no clinically important difference seen in physical function, psychological distress and mild adverse event. When compared to no treatment, there was no clinically important difference in quality of life and pain, but a clinically important harm seen in physical function based on 2 studies. When compared to other treatments, there were clinically important benefits in pain and physical function seen compared to neuromuscular electrical stimulation

based on 1 small study (N=60). There was no clinically important difference in pain seen when compared to pulsed short-wave therapy, and no difference in pain and mild adverse events when compared to combination therapy. There was an unclear effect with no clinically important difference in pain in 1 outcome including 1 small study (N=40), and a clinically important harm in 1 outcome including 1 small study (N=24).

Combination therapy

Combination therapy was compared to interferential therapy, neuromuscular electrical stimulation, laser therapy, transcutaneous electrical nerve stimulation, ultrasound, sham electrotherapy and no treatment. When compared to sham electrotherapy, clinically important benefits were seen in pain at less than and equal to 3 months. An unclear effect was seen for quality of life, with 1 outcome indicating a clinically important benefit while another indicated no clinically important difference. Otherwise, there was no clinically important difference seen in mild and moderate/major adverse events. When compared to no treatment, clinically important benefits were seen in quality of life, pain and psychological distress, with no clinically important difference in physical function. The outcomes were of low-very low quality and based on small studies. For each comparison to other interventions the majority of outcomes indicated no clinically important difference. However, a clinically important harm was seen in physical function when compared to transcutaneous electrical nerve stimulation based on 1 small study (N=38). An unclear effect was seen in quality of life when compared to ultrasound, with 1 outcome indicating a clinically important benefit while another indicated no clinically important difference based on 1 small study (N=53).

The committee took these results into consideration when evaluating the individual therapies. As they concluded that there was insufficient evidence of consistent benefit with any individual treatments, they agreed that while there was some evidence of benefit for the combination the effect was at times unclear and based on low quality evidence. Overall, they concluded that there was no indication from the available evidence that a combination of electrotherapy procedures would have more benefit than the individual therapies.

Weighing up the clinical benefits and harms

The committee noted that despite there being a large number of trials, the vast majority had very small sample sizes (with <50 participants in each study arm) and there was inconsistency in the findings which reduced their confidence in the evidence. This taken into consideration led them to conclude that there was insufficient evidence of high quality to form recommendations for this topic. Due to this being present throughout the evidence in this review, they recommended not routinely using electrotherapy and advised that more high quality research (including larger sample sizes, studies with sufficient blinding, adequate randomisation methods and with transparent reporting of the interventions and methods used) was required in this area through research recommendation. On weighing up the effects seen from the treatments investigated in this review, the committee agreed that extracorporeal shockwave therapy showed potential evidence of benefit. However, the quality of the evidence was insufficient to conclude that this was evidence was accurate. Therefore, the committee agreed the research recommendation should investigate the effect of this treatment specifically.

1.1.12.4 Cost effectiveness and resource use

One economic evaluation was identified for inclusion in this review. This was based on a network meta-analysis of randomised controlled trials (RCTs) and took a UK perspective. QALYs were calculated by mapping various measures to the EQ-5D, which were then pooled

to give an overall estimate. The study was deemed to be directly applicable to the review question.

The time horizon of the model was relatively short at 8 weeks. Unit costs were also taken from 2011/12 and were therefore unlikely to be representative of current NHS practice. The analysis was therefore graded as having potentially serious limitations.

There were three different meta-analyses used in the study, differentiating trials according to their level of grading and time frame within which outcomes were reported:

1. All trials
2. Subset of trials that were graded as having a low risk of bias for allocation concealment
3. Same as point 2 but further restricting trials to those that reported outcomes between 3 and 13 weeks.

The analysis compared usual care to a multitude of electrotherapy options; interferential therapy, laser light therapy, neuromuscular electrical stimulation (NMES), pulsed electromagnetic field (PEMF), pulsed electrical stimulation (PES) and transcutaneous electrical nerve stimulation (TENS) as well as non-electrotherapy options; acupuncture, braces, heat treatment insoles and static magnets. TENS was the only electrotherapy option that was cost effective compared with usual care with a cost per QALY gained of £2,690.

It should be noted that interventions such as laser therapy and ultrasound are commonly a shared resource across the NHS and would not be limited to osteoarthritis as they could feasibly be used for a range of conditions. They would be found in most physiotherapy departments and therefore the physiotherapists time is likely the main cost associated with these treatments. The cost of physiotherapist time was presented to the committee as the main cost associated with these treatments.

Due to the lack of quality evidence in the clinical review, the committee decided that a research recommendation evaluating the clinical and cost-effectiveness of electrotherapy in patients with osteoarthritis was warranted.

The previous osteoarthritis guideline recommended that healthcare professionals consider TENS as an adjunct to core treatments for pain relief. TENS machines can be loaned to an individual for a short period, and if effective, the person is advised to purchase their own. The committee's decision to not routinely offer electrotherapy to people with osteoarthritis may result in a cost saving, since if TENS machines were purchased directly by a person, the cost will not be incurred by the NHS.

1.1.12.5 Other factors the committee took into account

The committee reflected that electrotherapy is not commonly provided by healthcare professionals in the NHS (when provided it would be more commonly administered by physiotherapists). Laser therapy is the more common modality used, though some people are using extracorporeal shockwave therapy.

The committee noted that electrotherapy was more commonly used by people with osteoarthritis outside of formal medical care. Devices can be purchased and used by patients independent of health care professional involvement. These devices can be expensive for the individual. A lay committee member reported that the advertisement for these devices can be confusing, as there are lots of devices that advertise themselves as better than others, but it is difficult to know which to use and whether using them will lead to any improvements.

The committee noted that the research identified does not appear to represent the diverse population of people with osteoarthritis. They agreed that any further research should be representative of the population, including people from different family backgrounds, and socioeconomic backgrounds, disabled people, and people of different ages and genders. Future work should be done to consider the different experiences of people from diverse communities to ensure that the approach taken can be made equitable for everyone. With this in mind the committee subgrouped their research recommendation by these protected characteristics where appropriate while suggesting that people from each group should be included in the research to ensure that it is applicable to the entire population

1.1.13 Recommendations supported by this evidence review

This evidence review supports recommendation 1.3.9 and the research recommendation on electrotherapy. Other evidence supporting these recommendations can be found in evidence review G.

1.1.14 References

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Appendices

Appendix A – Review protocols

Review protocol for clinical and cost-effectiveness of electrotherapy in the management of osteoarthritis

ID	Field	Content
0.	PROSPERO registration number	N/A
1.	Review title	What is the clinical and cost-effectiveness of electrotherapy for the management of osteoarthritis?
2.	Review question	3.5 What is the clinical and cost-effectiveness of electrotherapy for the management of osteoarthritis?
3.	Objective	To evaluate the clinical and cost-effectiveness of electrotherapeutic interventions (including pulsed short-wave therapy, interferential therapy, laser, transcutaneous electrical nerve stimulation, and ultrasound) in the management of osteoarthritis in adults.
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE Searches will be restricted by: • English language • Human studies • Letters and comments are excluded

		Other searches: • Inclusion lists of relevant systematic reviews will be checked by the reviewer. The searches may be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion if relevant. The full search strategies for MEDLINE database will be published in the final review.
5.	Condition or domain being studied	Osteoarthritis in adults (defined as a clinical diagnosis of osteoarthritis with or without imaging)
6.	Population	Inclusion: • Adults (age ≥16 years) with osteoarthritis affecting any joint To note that where evidence for other rare forms of osteoarthritis is identified the committee will stratify into the most appropriate group. Exclusion: • Children (age ≤16 years) • People with conditions that may make them susceptible to osteoarthritis or often occur alongside osteoarthritis (including: crystal arthritis, inflammatory arthritis, septic arthritis, diseases of childhood that may predispose to osteoarthritis, medical conditions presenting with joint inflammation and malignancy). • Studies in people with meniscal injury without osteoarthritis • Studies with an unclear population (e,g, type of arthritis, proportion of participants with osteoarthritis) • Spinal osteoarthritis
7.	Intervention/Exposure/Test	Non-invasive electrotherapy interventions (minimum intervention duration 1 week), including: • Pulsed short-wave therapy

		• Interferential therapy • Neuromuscular electrical stimulation • Extracorporeal shockwave therapy • Laser therapy • Transcutaneous electrical nerve stimulation (TENS) • Ultrasound • Combination therapy (ultrasound and interferential therapy)

8.	Comparator/Reference standard/Confounding factors	• Compared to each other
		• Sham electrotherapy
		• No intervention (including either):
		  ○ Electrotherapy versus no treatment*
		  ○ Electrotherapy plus additional treatment versus additional treatment alone**
		
		**No treatment defined as either (1) doing nothing or (2) very low intensity intervention such as advice*
		***Inclusion of studies where additional treatment is the same in each arm will be assessed on a case by case basis. Studies including high intensity additional treatment may not be included due to the risk that treatment could have an interaction with the intervention of interest and mask the true treatment effect.*

9.	Types of study to be included	• Systematic reviews of RCTs • Parallel RCTs
10.	Other exclusion criteria	• Non-English language studies • Non-randomised/observational studies • Crossover RCTs

		Abstracts will be excluded as it is expected there will be sufficient full text published studies available.
11.	Context	N/A
12.	Primary outcomes (critical outcomes)	Stratify by ≤/>3 months (longest time-point in each): • Health-related quality of life [validated patient-reported outcomes, continuous data prioritised] • Pain [validated patient-reported outcomes, continuous data prioritised] • Physical function [validated patient-reported outcomes, continuous data prioritised] *The COMET database was searched and several core outcome sets were identified for specific sites of osteoarthritis (including hand, knee and hip). The committee took these into account when defining outcomes:* https://onlinelibrary.wiley.com/doi/full/10.1002/acr.22868 https://www.ncbi.nlm.nih.gov/pubmed/26136489 https://www.ncbi.nlm.nih.gov/pubmed/30647185 The committee did not include stiffness or global scores as Delphi discussions by the OMERACT group have found these to not be as important to people with osteoarthritis or clinicians. The outcomes included were universal for all groups allowing for broader comparisons.
13.	Secondary outcomes (important outcomes)	• Psychological distress [validated patient-reported outcomes, continuous data prioritised] • Osteoarthritis flares [validated patient-reported outcomes, continuous data prioritised] • Mild adverse events • Moderate/major adverse events
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above.

		EviBASE will be used for data extraction. Study investigators may be contacted for missing data where time and resources allow.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual For intervention reviews the following checklists will be used according to the study design being assessed: • Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) • Randomised Controlled Trial: Cochrane RoB (2.0) 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.
16.	Strategy for data synthesis	• Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). • GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome. Publication bias is tested for when there are more than 5 studies for an outcome. The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ • Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome. • WinBUGS will be used for network meta-analysis, if possible given the data identified.

		Heterogeneity between studies in the effect measures will be assessed using the I^2 statistic and visual inspection. We will consider an I^2 value great than 50% as indicative of substantial heterogeneity. If significant heterogeneity is identified during meta-analysis then subgroup analysis, using subgroups predefined by the GC, will take place. If this does not explain the heterogeneity, the results will be presented using a random-effects model.	
17.	Analysis of sub-groups	Subgroup analysis to be conducted if heterogeneity in the meta-analysis is present: • Diagnosis with or without imaging (indicative of severity) • Multimorbidity (high versus low morbidity score; as defined by study, measured by validated instruments e.g. Charlson Comorbidity Index) • Age (≤/> 75 years) • Site of osteoarthritis	
18.	Type and method of review	☒	Intervention
		☐	Diagnostic
		☐	Prognostic
		☐	Qualitative
		☐	Epidemiologic
		☐	Service Delivery
		☐	Other (please specify)
19.	Language	English	
20.	Country	England	

21.	Anticipated or actual start date	23/08/2019		
22.	Anticipated completion date	25/08/2021		
23.	Stage of review at time of this submission	Review stage	Started	Completed
		Preliminary searches	☑	☐
		Piloting of the study selection process	☐	☐
		Formal screening of search results against eligibility criteria	☐	☐
		Data extraction	☐	☐
		Risk of bias (quality) assessment	☐	☐
		Data analysis	☐	☐
24.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail [Guideline email]@nice.org.uk [Developer to check with Guideline Coordinator for email address] 5e Organisational affiliation of the review		

		National Institute for Health and Care Excellence (NICE) and the National Guideline Centre
25.	Review team members	From the National Guideline Centre: Carlos Sharpin [Guideline lead] Julie Neilson [Senior systematic reviewer] George Wood [Systematic reviewer] Emma Cowles [Senior health economist] Joseph Runicles [Information specialist] Amber Hernaman [Project manager]
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10127
29.	Other registration details	
30.	Reference/URL for published protocol	

31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
32.	Keywords	Adults; Electrotherapy; Inferential therapy; Intervention; Laser; Osteoarthritis; Pulsed short-wave therapy; TENS; Ultrasound	
33.	Details of existing review of same topic by same authors		
34.	Current review status	☒	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
35..	Additional information	N/A	
36.	Details of final publication	www.nice.org.uk	

1

2 **Table 63: Health economic review protocol**

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.

Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken for all years using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2005, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Studies published in 2005 or later, that were included in the previous guidelines, will be reassessed for inclusion and may be included or selectively excluded based on their relevance to the questions covered in this update and whether more applicable evidence is also identified. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[157] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for

	decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2005 or later (including any such studies included in the previous guidelines) but that depend on unit costs and resource data entirely or predominantly from before 2005 will be rated as 'Not applicable'. • Studies published before 2005 (including any such studies included in the previous guidelines) will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

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Appendix B – Literature search strategies

- What is the clinical and cost-effectiveness of electrotherapy for the management of osteoarthritis?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[157]

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

Searches were constructed using an Osteoarthritis population. All results were then sifted for each question. Search filters were applied to the search where appropriate.

Table 64: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 17 November 2021	Randomised controlled trials Systematic review studies Exclusions (animals studies, letters, comments)
Embase (OVID)	1974 – 17 November 2021	Randomised controlled trials Systematic review studies Exclusions (animals studies, letters, comments)
The Cochrane Library (Wiley)	Cochrane Reviews to 2021 Issue 11 of 12 CENTRAL to 2021 Issue 11 of 12	None

Medline (Ovid) search terms

1.	exp osteoarthritis/
2.	(osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*).ti,ab.
3.	(degenerative adj2 arthritis).ti,ab.
4.	coxarthrosis.ti,ab.
5.	gonarthrosis.ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14

16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/17-23
25.	6 not 24
26.	limit 25 to English language
27.	randomized controlled trial.pt.
28.	controlled clinical trial.pt.
29.	randomi#ed.ti,ab.
30.	placebo.ab.
31.	randomly.ti,ab.
32.	Clinical Trials as topic.sh.
33.	trial.ti.
34.	or/27-33
35.	Meta-Analysis/
36.	exp Meta-Analysis as Topic/
37.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
38.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
39.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
40.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
41.	(search* adj4 literature).ab.
42.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
43.	cochrane.jw.
44.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
45.	or/35-44
46.	26 and (34 or 45)

Embase (Ovid) search terms

1.	exp osteoarthritis/
2.	(osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*).ti,ab.
3.	(degenerative adj2 arthritis).ti,ab.
4.	coxarthrosis.ti,ab.
5.	gonarthrosis.ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.

12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice or rodent*).ti.
22.	or/14-21
23.	6 not 22
24.	Limit 23 not English language
25.	random*.ti,ab.
26.	factorial*.ti,ab.
27.	(crossover* or cross over*).ti,ab.
28.	((doubl* or singl*) adj blind*).ti,ab.
29.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
30.	crossover procedure/
31.	single blind procedure/
32.	randomized controlled trial/
33.	double blind procedure/
34.	or/25-33
35.	systematic review/
36.	meta-analysis/
37.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
38.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
39.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
40.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
41.	(search* adj4 literature).ab.
42.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
43.	cochrane.jw.
44.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
45.	or/35-44
46.	24 and (34 or 45)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Osteoarthritis] explode all trees
#2.	(osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*):ti,ab
#3.	(degenerative near/2 arthritis):ti,ab
#4.	coxarthrosis:ti,ab
#5.	gonarthrosis:ti,ab

#6.	(or #1-#5)

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to a Gout population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA – this ceased to be updates after March 2018). NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics studies and quality of life studies. Searches for quality of life studies were run for general information.

Table 65: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	1 January 2014 – 17 November 2021	Health economics studies Quality of life studies Exclusions (animals studies, letters, comments)
Embase	1 January 2014 – 17 November 2021	Health economics studies Quality of life studies Exclusions (animals studies, letters, comments)
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to 31 March 2015	None

Medline (Ovid) search terms

1.	exp osteoarthritis/
2.	(osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*).ti,ab.
3.	(degenerative adj2 arthritis).ti,ab.
4.	coxarthrosis.ti,ab.
5.	gonarthrosis.ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16

18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/17-23
25.	6 not 24
26.	limit 25 to English language
27.	Economics/
28.	Value of life/
29.	exp "Costs and Cost Analysis"/
30.	exp Economics, Hospital/
31.	exp Economics, Medical/
32.	Economics, Nursing/
33.	Economics, Pharmaceutical/
34.	exp "Fees and Charges"/
35.	exp Budgets/
36.	budget*.ti,ab.
37.	cost*.ti.
38.	(economic* or pharmaco?economic*).ti.
39.	(price* or pricing*).ti,ab.
40.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
41.	(financ* or fee or fees).ti,ab.
42.	(value adj2 (money or monetary)).ti,ab.
43.	or/27-42
44.	quality-adjusted life years/
45.	sickness impact profile/
46.	(quality adj2 (wellbeing or well being)).ti,ab.
47.	sickness impact profile.ti,ab.
48.	disability adjusted life.ti,ab.
49.	(qal* or qtime* or qwb* or daly*).ti,ab.
50.	(euroqol* or eq5d* or eq 5*).ti,ab.
51.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
52.	(hui or hui1 or hui2 or hui3).ti,ab.
53.	(health* year* equivalent* or hye or hyes).ti,ab.
54.	discrete choice*.ti,ab.
55.	rosser.ti,ab.
56.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.

57.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
58.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
59.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
60.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
61.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
62.	or/44-61
63.	26 and (43 or 62)

Embase (Ovid) search terms

1.	exp osteoarthritis/
2.	(osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*).ti,ab.
3.	(degenerative adj2 arthritis).ti,ab.
4.	coxarthrosis.ti,ab.
5.	gonarthrosis.ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice or rodent*).ti.
22.	or/14-21
23.	6 not 22
24.	Limit 23 to English language
25.	health economics/
26.	exp economic evaluation/
27.	exp health care cost/
28.	exp fee/
29.	budget/
30.	funding/
31.	budget*.ti,ab.

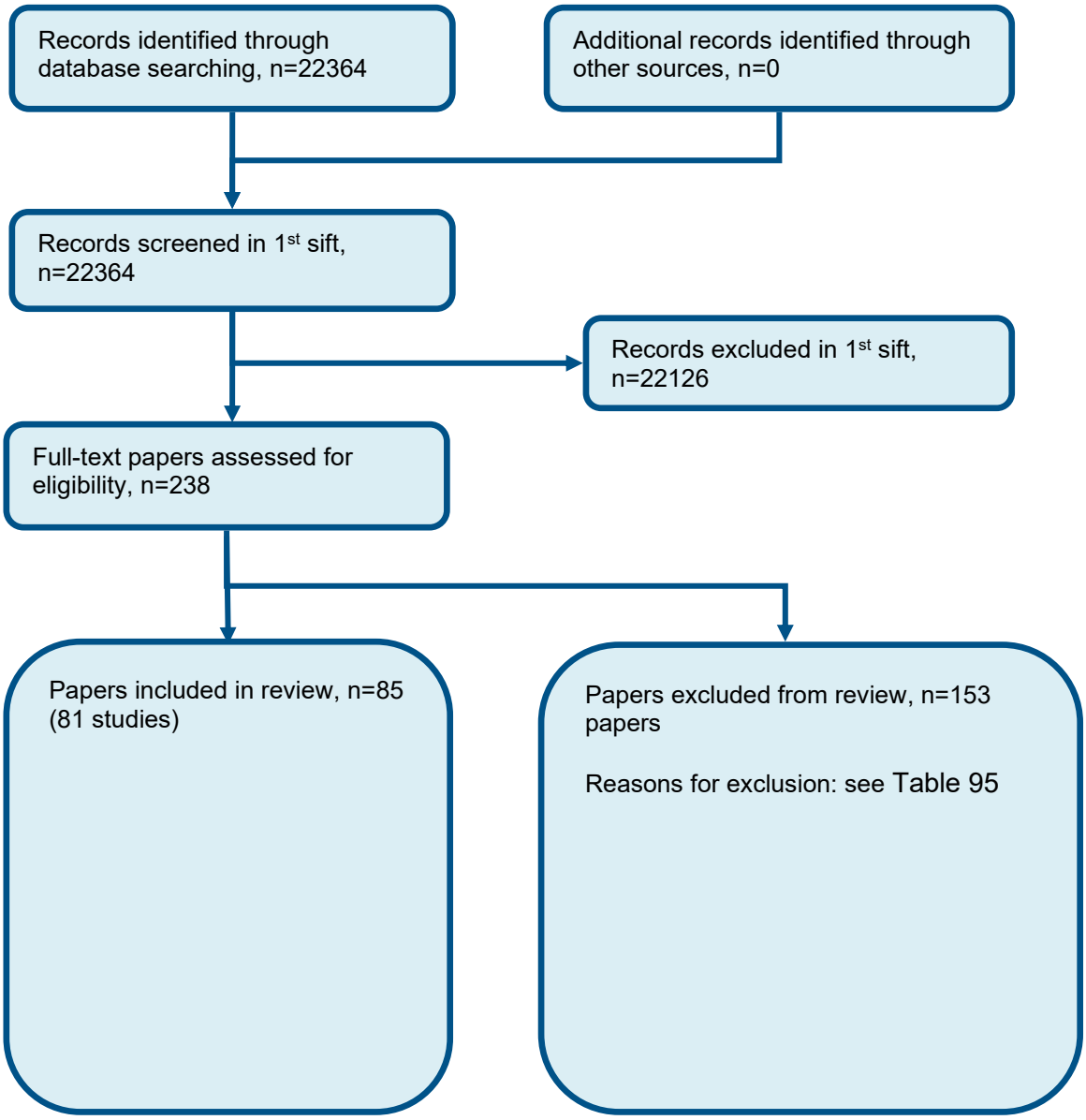
32.	cost*.ti.
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
38.	or/25-37
39.	quality adjusted life year/
40.	"quality of life index"/
41.	short form 12/ or short form 20/ or short form 36/ or short form 8/
42.	sickness impact profile/
43.	(quality adj2 (wellbeing or well being)).ti,ab.
44.	sickness impact profile.ti,ab.
45.	disability adjusted life.ti,ab.
46.	(qal* or qtime* or qwb* or daly*).ti,ab.
47.	(euroqol* or eq5d* or eq 5*).ti,ab.
48.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
49.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
50.	(hui or hui1 or hui2 or hui3).ti,ab.
51.	(health* year* equivalent* or hye or hyes).ti,ab.
52.	discrete choice*.ti,ab.
53.	rosser.ti,ab.
54.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
55.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
56.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
57.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
58.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
59.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
60.	or/39-59
61.	24 and (38 or 60)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Osteoarthritis EXPLODE ALL TREES
#2.	((osteoarthriti* or osteo-arthriti* or osteoarthrotic or osteoarthros*))
#3.	((degenerative adj2 arthritis))
#4.	(coxarthrosis)
#5.	(gonarthrosis)
#6.	#1 OR #2 OR #3 OR #4 OR #5
#7.	(#6) IN NHSEED
#8.	(#6) IN HTA

Appendix C – Effectiveness evidence study selection

Figure 1: Flow chart of clinical study selection for the review of the clinical and cost-effectiveness of electrotherapy for osteoarthritis



Appendix D Effectiveness evidence

Study	Akyol 2010[6]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 4 months (intervention for 4 weeks)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Bilateral knee osteoarthritis according to the American College of Rheumatology criteria with confirmation in standing anteroposterior and lateral radiographs of both knees
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with a diagnosis of bilateral knee osteoarthritis
Exclusion criteria	Serious systemic medical conditions for whom exercises would be contraindicated; neuromuscular or dermatologic disease that involves the lower extremities; exercise program that may cause increase of muscle strength within the previous months; inflammatory arthropathy; contracture; history of trauma and physiotherapy within previous 6 months; metallic implant around knee joint implanted cardiac pacemaker; grade 4 osteoarthritis and inability to understand how to score the symptoms
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 57.2 (9.5). Gender (M:F): 0:40. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grades <4 Duration of symptoms (mean [SD]): 71.03 (60.98) months
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. Short-wave diathermy and isokinetic exercise. Treatments with a Curapulse 419 machine operating at a frequency of 27.12 MHz. The panel was directed out of

	the person's view. The person was positioned supine and comfortably on the treatment plinth with the affected knee extended. A towel was wrapped around the knee joint, and then the induction coil cable was applied circularly along the affected leg. The intensity of the current was set based on each person's sensation of warm (a mild but pleasant sensation). Each session lasted 20 minutes. This was applied to each knee separately (therefore a total time of 40 minutes). The exercise program was completed three times a week on each knee including concentric contractions in a variety of angular velocities.. Duration 4 weeks. Concurrent medication/care: The use of NSAID, other analgesic drugs and antidepressant drugs was not permitted during the study period. Any pretreatment with these drugs had to be discontinued 7 days before the start of study. The use of other medication for comorbid diseases was permitted during study period.. Indirectness: No indirectness (n=20) Intervention 2: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. Isokinetic exercise program. The exercise program was completed three times a week on each knee including concentric contractions in a variety of angular velocities.. Duration 4 weeks. Concurrent medication/care: The use of NSAID, other analgesic drugs and antidepressant drugs was not permitted during the study period. Any pretreatment with these drugs had to be discontinued 7 days before the start of study. The use of other medication for comorbid diseases was permitted during study period.. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: SF-36 physical function at 4 weeks; Group 1: mean 25.25 (SD 18.17); n=20, Group 2: mean 19 (SD 20.55); n=20; SF-36 physical function 0-100 Top=High is good outcome; Comments: Baseline electrotherapy: 27.50 (25.26). Baseline control: 27.00 (16.81).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, height, weight, BMI, duration of symptoms, education and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 social function at 4 weeks; Group 1: mean 67.65 (SD 18.29); n=20, Group 2: mean 59.4 (SD 17.98); n=20; SF-36 social function 0-100 Top=High is good outcome; Comments: Baseline electrotherapy: 53.35 (19.31). Baseline control: 51.70 (23.15).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, height, weight, BMI, duration of symptoms, education and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 pain at 4 weeks; Group 1: mean 25.85 (SD 24.53); n=20, Group 2: mean 28.35 (SD 19.38); n=20; SF-36 pain 0-100 Top=High is

good outcome; Comments: Baseline electrotherapy: 35.75 (21.96). Baseline control: 25.00 (13.33).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, height, weight, BMI, duration of symptoms, education and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 general health at 4 weeks; Group 1: mean 5.5 (SD 19.92); n=20, Group 2: mean 6.5 (SD 8.75); n=20; SF-36 general health 0-100 Top=High is good outcome; Comments: Baseline electrotherapy: 48.00 (16.89). Baseline control: 42.75 (14.91).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, height, weight, BMI, duration of symptoms, education and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 energy at 4 weeks; Group 1: mean 6.5 (SD 14.51); n=20, Group 2: mean 7 (SD 10.68); n=20; SF-36 energy 0-100 Top=High is good outcome; Comments: Baseline electrotherapy: 53.50 (15.48). Baseline control: 49.75 (16.97).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, height, weight, BMI, duration of symptoms, education and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Health-related quality of life at > 3 months
- Actual outcome: SF-36 physical function at 16 weeks; Group 1: mean 24.25 (SD 21.16); n=20, Group 2: mean 17 (SD 18.52); n=20; SF-36 physical function 0-100 Top=High is good outcome; Comments: Baseline electrotherapy: 27.50 (25.26). Baseline control: 27.00 (16.81).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, height, weight, BMI, duration of symptoms, education and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 social function at 16 weeks; Group 1: mean 65.45 (SD 20.95); n=20, Group 2: mean 59.95 (SD 21.84); n=20; SF-36 social function 0-100 Top=High is good outcome; Comments: Baseline electrotherapy: 53.35 (19.31). Baseline control: 51.70 (23.15).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, height, weight, BMI, duration of symptoms, education and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 pain at 16 weeks; Group 1: mean 16.05 (SD 29.84); n=20, Group 2: mean 28.45 (SD 24.2); n=20; SF-36 pain 0-100 Top=High is good outcome; Comments: Baseline electrotherapy: 35.75 (21.96). Baseline control: 25.00 (13.33).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, height, weight, BMI, duration of symptoms, education and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 general health at 16 weeks; Group 1: mean 1 (SD 19.77); n=20, Group 2: mean 5.75 (SD 13.98); n=20; SF-36 general health 0-100 Top=High is good outcome; Comments: Baseline electrotherapy: 48.00 (16.89). Baseline control: 42.75 (14.91).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, height, weight, BMI, duration of symptoms, education and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 energy at 16 weeks; Group 1: mean -1.25 (SD 13.26); n=20, Group 2: mean -0.75 (SD 14.71); n=20; SF-36 energy 0-100 Top=High is good outcome; Comments: Baseline electrotherapy: 53.50 (15.48). Baseline control: 49.75 (16.97).

Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, height, weight, BMI, duration of symptoms, education and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: Pain at </= 3 months
- Actual outcome: WOMAC pain at 4 weeks; Group 1: mean -5.55 (SD 4.5); n=20, Group 2: mean -5.3 (SD 3.35); n=20; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline electrotherapy: 11.50 (4.02). baseline control: 11.65 (2.87).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, height, weight, BMI, duration of symptoms, education and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 4: Pain at > 3 months
- Actual outcome: WOMAC pain at 16 weeks; Group 1: mean -5.5 (SD 4.33); n=20, Group 2: mean -5 (SD 3.85); n=20; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline electrotherapy: 11.50 (4.02). baseline control: 11.65 (2.87).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, height, weight, BMI, duration of symptoms, education and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 5: Physical function at </= 3 months
- Actual outcome: WOMAC physical function at 4 weeks; Group 1: mean -19.4 (SD 11.03); n=20, Group 2: mean -15.1 (SD 12.23); n=20; WOMAC physical function 0-68 Top=High is poor outcome; Comments: Baseline electrotherapy: 41.00 (10.67). baseline control: 39.65 (8.30).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, height, weight, BMI, duration of symptoms, education and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 6: Physical function at > 3 months
- Actual outcome: WOMAC physical function at 16 weeks; Group 1: mean -16.9 (SD 15.63); n=20, Group 2: mean -15.35 (SD 11.27); n=20; WOMAC physical function 0-68 Top=High is poor outcome; Comments: Baseline electrotherapy: 41.00 (10.67). baseline control: 39.65 (8.30).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, height, weight, BMI, duration of symptoms, education and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 7: Psychological distress at </= 3 months
- Actual outcome: Beck depression score at 4 weeks; Group 1: mean -2.45 (SD 3.74); n=20, Group 2: mean -2.3 (SD 3.29); n=20; Beck depression score 0-63 Top=High is poor outcome; Comments: Baseline electrotherapy: 8.50 (4.68). Baseline control: 9.45 (5.23).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, height, weight, BMI, duration of symptoms, education and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 8: Psychological distress at > 3 months - Actual outcome: Beck depression score at 16 weeks; Group 1: mean -1.15 (SD 4.98); n=20, Group 2: mean -1.25 (SD 3.68); n=20; Beck depression score 0-68 Top=High is poor outcome; Comments: Baseline electrotherapy: 8.50 (4.68). Baseline control: 9.45 (5.23). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, height, weight, BMI, duration of symptoms, education and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Alayat 2017[8]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=75)
Countries and setting	Conducted in Saudi Arabia; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 3 months (6 weeks of treatment with laser and exercise, 3 months of treatment with glucosamine)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with a degenerative osteoarthritic knee of grade 3 or less based on the Kellgren and Lawrence classification
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Degenerative osteoarthritic knee of grade 3 or less based on Kellgren and Lawrence classification; persistent pain of at least 4 on the VAS for more than 3 months in one or both knees; body mass index of no more than 30kg/m²; self-reported disability due to knee pain with a score of at least 25 on the WOMAC
Exclusion criteria	Rheumatoid arthritis; fracture; knee joint surgery; knee deformity (genu varum or genu valgum of more than 20 degrees); ligament tears; meniscus injury; a knee corticosteroid injection; if they had participated in any form of resistance training int he previous 3 months; people with any problems that might interfere with participation in exercise (such as hip or ankle/foot joint pathology, an uncontrolled medical condition [e.g. heart, blood or respiratory disease); or central or peripheral neuropathy
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 53.9 (4.5). Gender (M:F): 67:0. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 3 or less Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=25) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. High-intensity laser therapy with glucosamine sulphate and exercises. Pulsed Nd:YAG laser, produced by the HIRO 3.0 device, providing the following options: pulsed emission of Nd:YAG laser with wavelength (1064nm), very high peak powers (3kw), average power (10.5W), high levels of fluency (510-1780mJ/cm²), pulse duration

	<120µs, lower frequency 910-30Hz), duty cycle of about 0.1%, probe diameter of 0.5cm and spot size of 0.2cm². Applied while the knee was flexed to 90 degrees. Each phase delivered 750J with 1500J delivered to either anterior or posterior knee surface. The scanning level and energy density was increased through stages with the final phase being similar to the initial phase. Glucosamine was given at 500mg glucosamine sulfate and 400mg chondroitin sulfate (given as salts with potassium chloride and sodium respectively) three times daily for 3 months. Exercise was based on range of motion, flexibility, stretching and strengthening exercises. This took place twice a week for 6 weeks.. Duration 6 weeks (for laser therapy and exercise), 3 months for glucosamine. Concurrent medication/care: Hot packs were allowed after exercise in cases of muscle soreness or pain. Indirectness: No indirectness (n=25) Intervention 2: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. Glucosamine was given at 500mg glucosamine sulfate and 400mg chondroitin sulfate (given as salts with potassium chloride and sodium respectively) three times daily for 3 months. Exercise was based on range of motion, flexibility, stretching and strengthening exercises. This took place twice a week for 6 weeks.. Duration 6 weeks (for exercise), 3 months for glucosamine. Concurrent medication/care: Hot packs were allowed after exercise in cases of muscle soreness or pain. Indirectness: No indirectness (n=25) Intervention 3: Sham electrotherapy. Sham electrotherapy with exercise. Duration 6 weeks. Concurrent medication/care: Hot packs were allowed after exercise in cases of muscle soreness or pain. Indirectness: No indirectness Comments: This group was not included in the final analysis as it did not fulfill the inclusion criteria in the protocol
Funding	Academic or government funding (The authors received research grants from the Institute of Scientific Research and Revival of Islamic Heritage at Umm Al-Qura University, Mecca, Saudi Arabia (project #43409008))

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 12 weeks; Group 1: mean 4.77 (SD 0.92); n=23, Group 2: mean 4.14 (SD 0.71); n=22; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline laser: 9.47 (1.28). Baseline no treatment: 9.86 (1.39).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, weight, height, bmI, osteoarthritis

grades, and baseline values of outcomes; Group 1 Number missing: 2, Reason: Not clearly explained; Group 2 Number missing: 3 Protocol outcome 2: Physical function at </= 3 months - Actual outcome: WOMAC physical function at 12 weeks; Group 1: mean 14.78 (SD 1.2); n=23, Group 2: mean 21.82 (SD 1.8); n=22; WOMAC function 0-68 Top=High is poor outcome; Comments: Baseline laser: 31.4 (2.9). Baseline no treatment: 32.36 (4.34). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, weight, height, bmI, osteoarthritis grades, and baseline values of outcomes; Group 1 Number missing: 2, Reason: Not clearly explained; Group 2 Number missing: 3	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study (subsidiary papers)	Alfredo 2012[10] (Alfredo 2018[11])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in Brazil; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 11 weeks (3 weeks of laser, 11 weeks of exercise), additional follow up for 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Knee osteoarthritis with levels 2-4 according to the Kellgren Lawrence grade
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with knee osteoarthritis with osteoarthritis Kellgren Lawrence grade 2-4, age between 50 and 75 years, of any gender, have knee pain and functional disability for at least three months and fulfill the criteria of the American College of Rheumatology
Exclusion criteria	If they had cancer, diabetes, symptomatic hip osteoarthritis or used antidepressants, anti-inflammatory medications or anxiolytics during six months prior to enrollment
Recruitment/selection of patients	People were recruited from the special rehabilitation services in Taboao da Serra-SP Brazil
Age, gender and ethnicity	Age - Mean (SD): 61.7 (7.2). Gender (M:F): 9:31. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Osteoarthritis grade 2-4, median grade 3 Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=24) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. Low level laser therapy three times a week for three weeks (energy irradiated over the joint line onto five points of the synovial region on the medial side of the knee and in four points at the lateral side, at 3J per point) and then exercise (strengthening, three phases, three sessions per week lasting 45 minutes). The laser pen was built on a gallium arsenide semi-conductor with a wavelength of 904nm, frequency of 700Hz, average power of 60mW, peak power of 20W, pulse duration 4.3ms, 50 seconds per point (area 0.5cm²). Duration 11 weeks (3 weeks of laser therapy then 8 weeks of exercise). Concurrent medication/care: No additional information. Indirectness: No

	indirectness (n=22) Intervention 2: Sham electrotherapy. Placebo laser therapy three times a week for three weeks and then exercise (strengthening, three phases, three sessions per week lasting 45 minutes).. Duration 11 weeks (3 weeks of placebo therapy then 8 weeks of exercise). Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Academic or government funding (The study was supported financially by FAPESP and CAPES)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 11 weeks; Group 1: mean 4.8 (SD 4.36); n=20, Group 2: mean 6.35 (SD 3.48); n=20; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline laser: 9.10 (4.92). baseline placebo: 7.30 (3.54).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, weight, height, BMI, gender, osteoarthritis grade and baseline values of outcomes; Group 1 Number missing: 4, Reason: 4 discontinued intervention; Group 2 Number missing: 2, Reason: 2 discontinued intervention

Protocol outcome 2: Pain at > 3 months
- Actual outcome: WOMAC pain at 6 months; Group 1: mean 5.3 (SD 4.68); n=20, Group 2: mean 5.35 (SD 4.38); n=20; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline laser: 9.10 (4.92). baseline placebo: 7.30 (3.54).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, weight, height, BMI, gender, osteoarthritis grade and baseline values of outcomes; Group 1 Number missing: 4, Reason: 4 discontinued intervention; Group 2 Number missing: 2, Reason: 2 discontinued intervention

Protocol outcome 3: Physical function at </= 3 months
- Actual outcome: WOMAC physical function at 11 weeks; Group 1: mean 19.5 (SD 14.04); n=20, Group 2: mean 23.35 (SD 12.18); n=20; WOMAC function 0-68 Top=High is poor outcome; Comments: Baseline laser: 33.85 (16.94). Baseline placebo: 27.15 (11.32).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, weight, height, BMI, gender, osteoarthritis grade and baseline values of outcomes; Group 1 Number missing: 4, Reason: 4 discontinued intervention; Group 2 Number missing: 2, Reason: 2 discontinued intervention

Protocol outcome 4: Physical function at > 3 months
- Actual outcome: WOMAC physical function at 6 months; Group 1: mean 19.8 (SD 15.56); n=20, Group 2: mean 22.85 (SD 15.55); n=20; WOMAC function

0-68 Top=High is poor outcome; Comments: Baseline laser: 33.85 (16.94). Baseline placebo: 27.15 (11.32). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, weight, height, BMI, gender, osteoarthritis grade and baseline values of outcomes; Group 1 Number missing: 4, Reason: 4 discontinued intervention; Group 2 Number missing: 2, Reason: 2 discontinued intervention	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	**Alfredo 2020[12]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=100)
Countries and setting	Conducted in Brazil; Setting: Physiotherapy clinic at the Pontifical Catholic University- Bareuri campus.
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 8 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	OA levels 2-4 according to the K-L classification system, aged between 50 and 75 years and who had knee pain and functional disabilities for at least three months, according to ACR criteria.
Exclusion criteria	Knee oedema, cancer, diabetes, or symptomatic hip OA, or the use of antidepressants, anti-inflammatory medications or anxiolytics for six months prior to enrollment.
Recruitment/selection of patients	not stated
Age, gender and ethnicity	Age - Range: 50-75 years. Gender (M:F): 28M/ 72F. Ethnicity: Not reported

Further population details	1. Age (≤/> 75 years): </=75 years (50-75 years). 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: K-L grades 2-4 Duration: not reported
Indirectness of population	No indirectness
Interventions	(n=80) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. Continuous/ pulsed ultrasound. The continuous ultrasound parameters were as follows: a frequency of 1 MHz, an intensity of 1.5 W/cm2 (spatial average, temporal average (SATA)), a duty cycle of 100% and an application time of 5 minutes on the medial side and 5 minutes on the lateral side of the knee. The pulsed ultrasound parameters were as follows: a frequency of 1 MHz, an intensity of 2.5 W/cm2 (SATA), a pulsed mode of 25% and an application time of 5 minutes on the medial side and 5 minutes on the lateral side of the knee. Group 1 received continuous ultrasound 3 times per week for the first month, and exercise 3 times per week for the second month. Group 2 received pulsed ultrasound 3 times per week for the first month, and exercise 3 times per week for the second month. Group 3 received continuous ultrasound 3 times per week for the first month, and continuous ultrasound associated with exercises 3 times per week for the second month. Group 4 received pulsed ultrasound 3 times per week for the first month, and pulsed ultrasound associated with exercises 3 times per week for the second month. The continuous and pulsed ultrasound groups were combined due to the class effect as agreed in the protocol. All patients followed the same training programme. The intervention was divided into three phases. Phase 1 (week 5)- objectives: range of motion, motor learning, balance, co-ordination. Each exercise had 30 repetitions and two sets. Sitting on the chair with a weight on the ankle, knee and stretch the foot to rotate alternately in and out then change legs. Lying prone. Bend the knee slowly as much as possible. Stretch the knee slowly. Standing with support. Bend the knees to approx. 60 degrees. Push up again. Walk on a 3m line without stepping beside the line. Walk-standing. Transfer body weight from one leg to the other. Phase 2 (week 6-7)- objective: strengthening. Each exercise had 30 repetitions and two sets. Standing. Bend knees to approx 60 degrees and push up again. Walk sideward by crossing legs to right and left. Standing on a balance board. Hold the balance. Lying prone, bend one knee as much as possible. One foot standing on a step, bend knee until the other foot touches the floor, push up again. Phase 3 (week 8)- objective: strengthening. Each exercise had 30 repetitions and two sets. Walk sideward by crossing steps to right and left. Standing on one leg, bend the knee to approx. 60 degrees and push up again. Standing on a balance board. Keep the balance. More difficult if eyes are closed. Standing on the floor. Get up on toes, hold 1-2 seconds and get down again. Standing with weight around the ankle. Stretch the knee slowly, hold the stretch 3-4 seconds and slowly down again. The total duration of the intervention was 8 weeks and there were three sessions per week. Each session lasted 45 minutes: 10 minutes for a warm-up (treadmill, ergometer bike or rowing machine); 30 minutes for two to three sets of P1, P2 or P3 exercises; 5 minutes for stretching exercises (hamstrings, quadriceps, adductors and gastrocnemius).. Duration 8 weeks. Concurrent

	medication/care: Participants were instructed not to use analgesic medications other than paracetamol (500mg/ day) or anti-inflammatory drugs during the study and not to perform any other type of physical exercise in addition to the treatment. (n=20) Intervention 2: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. All patients followed the same training programme. The intervention was divided into three phases. Phase 1 (week 5)- objectives: range of motion, motor learning, balance, co-ordination. Each exercise had 30 repetitions and two sets. Sitting on the chair with a weight on the ankle, knee and stretch the foot to rotate alternately in and out then change legs. Lying prone. Bend the knee slowly as much as possible. Stretch the knee slowly. Standing with support. Bend the knees to approx. 60 degrees. Push up again. Walk on a 3m line without stepping beside the line. Walk-standing. Transfer body weight from one leg to the other. Phase 2 (week 6-7)- objective: strengthening. Each exercise had 30 repetitions and two sets. Standing. Bend knees to approx 60 degrees and push up again. Walk sideward by crossing legs to right and left. Standing on a balance board. Hold the balance. Lying prone, bend one knee as much as possible. One foot standing on a step, bend knee until the other foot touches the floor, push up again. Phase 3 (week 8)- objective: strengthening. Each exercise had 30 repetitions and two sets. Walk sideward by crossing steps to right and left. Standing on one leg, bend the knee to approx. 60 degrees and push up again. Standing on a balance board. Keep the balance. More difficult if eyes are closed. Standing on the floor. Get up on toes, hold 1-2 seconds and get down again. Standing with weight around the ankle. Stretch the knee slowly, hold the stretch 3-4 seconds and slowly down again. The total duration of the intervention was 8 weeks and there were three sessions per week. Each session lasted 45 minutes: 10 minutes for a warm-up (treadmill, ergometer bike or rowing machine); 30 minutes for two to three sets of P1, P2 or P3 exercises; 5 minutes for stretching exercises (hamstrings, quadriceps, adductors and gastrocnemius).. Duration 8 weeks. Concurrent medication/care: Participants were instructed not to use analgesic medications other than paracetamol (500mg/ day) or anti-inflammatory drugs during the study and not to perform any other type of physical exercise in addition to the treatment.
Funding	Academic or government funding (Institutional Scientific Initiation Scholarship Program (PIBIC))

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC- pain subscale at 8 weeks; Group 1: mean -6.5 (SD 4.8946); n=80, Group 2: mean -0.8 (SD 3.1); n=20; WOMAC- pain subscale 0-20 Top=High is poor outcome; Comments: Continuous and pulsed ultrasound groups were pooled.
Reported pain results: group 1: -5.8 (5.11), group 2: -4.8 (4.0), group 3: -10.65 (4.4), group 4: -4.75 (3.27)
Baseline values not reported.
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: WOMAC pain/ function not reported; Group 1 Number missing: 0, Reason: N/A; Group 2 Number missing: 0, Reason: N/A

Protocol outcome 2: Physical function at </= 3 months - Actual outcome: WOMAC- function subscale at 8 weeks; Group 1: mean -14.8 (SD 12.465); n=80, Group 2: mean -2.4 (SD 7.44); n=20; WOMAC- function subscale 0-68 Top=High is poor outcome; Comments: Continuous and pulsed ultrasound groups were pooled. Reported pain results: group 1: -8.3 (12.16), group 2: -11.05 (8.49), group 3: -25.5 (10.87), group 4: -14.35 (10.6) Baseline values not reported. Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: WOMAC pain/ function not reported; Group 1 Number missing: 0, Reason: N/A; Group 2 Number missing: 0, Reason: N/A	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Alghadir 2014[13]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=42)
Countries and setting	Conducted in Saudi Arabia; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Knee osteoarthritis according to the American College of Rheumatology criteria with knee osteoarthritis of grade 2-3 according to the Kellgren and Lawrence grade
Stratum	Overall
Subgroup analysis within study	Not applicable:
Inclusion criteria	People with knee osteoarthritis according to the American College of Rheumatology criteria; knee osteoarthritis of grade 2-3 according to the Kellgren-Lawrence grade; a minimum score of 25 on the WOMAC total score; knee pain of at least 4 on a visual analogue scale in the previous 3 months; willingness to participate and follow the treatment schedule
Exclusion criteria	Concomitant disease affecting the knee (such as rheumatoid arthritis, injury and/or surgery to the knee); had received physical therapy and/or intra-articular corticosteroid or hyaluronic acid injections during the last 6 months; people with a history of cancer, dementia, neurological deficits, heart pacemaker, diabetes mellitus, uncontrolled hypertension or morbid obesity (BMI at least 40)
Recruitment/selection of patients	Conducted in the physical therapy department of King Saud Medical City, Riyadh, Saudi Arabia
Age, gender and ethnicity	Age - Mean (SD): 56.1 (8.0). Gender (M:F): 22:18. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 2-3, median grade 2 Duration of symptoms (mean [SD]): 9.6 (4.0) months
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. Irradiation with a Ga-As laser device that had a wavelength of 850nm, power of 100mW, and sport size of 1.0mm. Eight points were irradiated with low level laser therapy; three on the medial side of the knee, three on the lateral side of the knee, and

	two on the medial edge of the tendon of the biceps femoris muscle and semitendinosus muscle in the popliteal fossa. Each point received energy of 6 J/point for 60 seconds and a total dose of 48 J/cm². . Duration 4 weeks. Concurrent medication/care: Hot packs were wrapped in toweling and placed on the target knees for 20 minutes followed by laser therapy. All people were given an isometric knee extension and straight leg raising exercise program to complete at home for 10 times/set, for 3 sets. All people were advised to keep their activity level and medication unchanged (paracetamol 2g daily) throughout the study period. Indirectness: No indirectness (n=20) Intervention 2: Sham electrotherapy. Placebo laser therapy. Duration 4 weeks. Concurrent medication/care: Hot packs were wrapped in toweling and placed on the target knees for 20 minutes followed by laser therapy. All people were given an isometric knee extension and straight leg raising exercise program to complete at home for 10 times/set, for 3 sets. All people were advised to keep their activity level and medication unchanged (paracetamol 2g daily) throughout the study period. Indirectness: No indirectness
Funding	Academic or government funding (Funding from the Deanship of Scientific Research at King Saud University (NO RGP-VPP-209))

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 4 weeks; Group 1: mean 3.25 (SD 2.61); n=20, Group 2: mean 5.5 (SD 2.5); n=20; WOMAC 0-20 Top=High is poor outcome; Comments: Baseline laser: 9.15 (3.32). Baseline placebo: 9.6 (3.33).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, BMI, gender, duration of symptoms, radiographic grade, sides affected and baseline values of outcomes; Group 1 Number missing: 0, Reason: A little unclear but 4 refused to participate in the study, potentially 2 were randomized and registered but no information to determine which groups they were in. Unlikely to affect results.; Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC physical function at 4 weeks; Group 1: mean 10 (SD 7.39); n=20, Group 2: mean 18.2 (SD 9); n=20; WOMAC function 0-68 Top=High is poor outcome; Comments: Baseline laser: 25.95 (9.23). Baseline placebo: 18.2 (9).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, BMI, gender, duration of symptoms, radiographic grade, sides affected and baseline values of outcomes; Group 1 Number missing: 0, Reason: A little unclear but 4 refused to participate in the study, potentially 2 were randomized and registered but no information to determine which groups they were in. Unlikely to affect results.;

Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	**NCT02892025 trial: Alqualo-costa 2021[15]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=168)
Countries and setting	Conducted in Brazil; Setting: Physiotherapy clinic of City University of Sao Paolo.
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 4 week intervention, 6 month follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Knee OA according to ACR criteria, aged between 50 and 8- years, with pain ranging from 3 to 8 on a 0-10 NRS for at least 6 months, Lequesne Algofunctional Index ranging from 5 to 15, L-L index equal or greater than 2, no complain of pain in other joints of the lower limbs, without neurological and cognitive disorders, no loss of sensation in the lower limbs, no surgery on the knee(s) in the last 6 months, no infiltration(s) knee(s) in the last 4 weeks, no use of analgesics 4 hours before treatment.
Exclusion criteria	Age <18 or over 80 years, complaints from other diseases of the lower limbs, knee prosthesis and/ or hip joint instabilities and/ or surgery in lowerlimbs, heart disease, uncontrolled hypertension and diabetes, coagulation disorders in anticoagulant therapy, pregnant women, fibromyalgia and individuals who can not perform isokinetic test who have difficulty performing the tUG, and those that are experiencing abnormal sensitivity to algometry.
Recruitment/selection of patients	Consecutive recruitment of patients from a waiting list at a physiotherapy clinic.

Age, gender and ethnicity	Age - Mean (SD): IFC group: 64.5(7.8), PBM group: 61.3 (9.4), IFC+PBM group: 65.7 (10.1), placebo group: 65.3 (8.5). Gender (M:F): Male: 45, Female: 123. Ethnicity: IFC group: Caucasian: 41, Black: 1, Brown: 0, PBM group: Caucasian: 33, Black: 8, Brown: 1, IFC+PBM group: Caucasian: 38, Black: 4, Brown: 0, Placebo group: Caucasian: 37, Black: 5, Brown: 0
Further population details	1. Age (≤/> 75 years): Systematic review: mixed (age 18-80 years). 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity (Kellgren-Lawrence): (Score 2): IFC group: 24, PBM group: 23, IFC+PBM group: 27, placebo group: 24 (Score 3): IFC group: 17, PBM group: 19, IFC+PBM group: 15, placebo group: 18 (Score 4): IFC group: 1, PBM group: 1, IFC+PBM group: 0, placebo group: 0 Duration: not reported
Indirectness of population	No indirectness
Interventions	(n=42) Intervention 1: Non-invasive electrotherapy interventions - Interferential therapy. Interferential current (IFC) and sham photobiomodulation (PBM) Three times a week for 4 week (12 sessions). Duration of each session ranged from 40 to 50 minutes, with the first session taking a slightly longer time until all patients had received guidance about the disease, joint protection and energy conservation before receiving the IFC and PBM. Interventions were applied according to the following sequence: 1) IFC and 2) PBM for both the active and placebo groups. The patient was informed that during the passage of the current he/she may not feel some tingling and that during PBM no sensation would be perceived. A towel was placed on the devices for all groups of patients. IFC was applied using the equipment Neurovector (Industra Basileira de Equipamentos Medicos- iBRAMED, Amparo, Sao Paolo, Brazil); and four standard square self-adhesive electrodes (5x5cm) (ValuTrode, Axelgaard, Fallbrook, CA) were also used. The technique used was a quadripolar electrode configuration with automatic vector, covering the area of pain. Parameters were used as follows: carrier current frequency of 4000Hz; amplitude-modulated frequency of 50Hz; sweep frequency of 50Hz; swing pattern of 1:1 second, and the current amplitude was increased until the patient reported strong but comfortable and non-painful stimulation paraesthesia. IFC was applied for 30 minutes, and every 5 minutes the patient was asked of the current sensation had decreased, and then, the pulse amplitude was increased until a strong but comfortable paraesthesia intensity level returned. Placebo PBM was performed with the device switched on, with the energy emission button not activated. The panel light of equipment was constantly on. . Duration 4 weeks. Concurrent medication/care: No use of analgesics 4 hours before treatment.. Indirectness: No indirectness (n=42) Intervention 2: Non-invasive electrotherapy interventions - Laser therapy. Photobiomodulation (PBM) and sham IFC. Three times a week for 4 week (12 sessions). Duration of each session ranged from 40 to 50 minutes, with the first session taking a slightly longer time until all patients had received guidance about the disease, joint protection and energy conservation before receiving the IFC and PBM. Interventions were applied according to the following sequence: 1) IFC and

	2) PBM for both the active and placebo groups. The patient was informed that during the passage of the current he/she may not feel some tingling and that during PBM no sensation would be perceived. A towel was placed on the devices for all groups of patients. PBM was performed using the low level laser (Laserpulse- Industrica Brasileira de Equipamentos Medicos- IBRAMED, Amparo, Sao Paolo, Brazil) with a Gallium Arsenide (AsGa) probe with a wavelength of 904nm, with a dose of 3J per point, totalling 9 points, total energy of 27J per session, peak power of 70W, pulse repetition frequency of 9500Hz, pulse duration of 60ns, average power of 40mW, application time of 75 seconds per point, and beam cross-sectional area of 0.5cm². The intervention of the placebo PBM was performed with the device switched on, with the energy emission button not activated. The panel light of equipment was constantly on. Patients were informed that during the PBM application, no sensation would be perceived. A towel was placed on the devices for all groups of patients. Placebo application of IFC was performed with the device switched on, with the energy emission button not activated. The electrodes were positioned for 30 minutes and every 5 minutes the patient was asked regarding any possible discomfort. . Duration 4 weeks. Concurrent medication/care: No use of analgesics 4 hours before treatment.. Indirectness: No indirectness (n=42) Intervention 3: Non-invasive electrotherapy interventions - Combination therapy (e.g. ultrasound and interferential therapy). IFC plus PBM (interferential current plus photobiomodulation). Three times a week for 4 week (12 sessions). Duration of each session ranged from 40 to 50 minutes, with the first session taking a slightly longer time until all patients had received guidance about the disease, joint protection and energy conservation before receiving the IFC and PBM. Interventions were applied according to the following sequence: 1) IFC and 2) PBM for both the active and placebo groups. The patient was informed that during the passage of the current he/she may not feel some tingling and that during PBM no sensation would be perceived. A towel was placed on the devices for all groups of patients. IFC was applied using the equipment Neurovector (Industra Basileira de Equipamentos Medicos- iBRAMED, Amparo, Sao Paolo, Brazil); and four standard square self-adhesive and photobiomodulation (PBM)electrodes (5x5cm) (ValuTrode, Axelgaard, Fallbrook, CA) were also used. The technique used was a quadripolar electrode configuration with automatic vector, covering the area of pain. Parameters were used as follows: carrier current frequency of 4000Hz; amplitude-modulated frequency of 50Hz; sweep frequency of 50Hz; swing pattern of 1:1 second, and the current amplitude was increased until the patient reported strong but comfortable and non-painful stimulation paraesthesia. IFC was applied for 30 minutes, and every 5 minutes the patient was asked of the current sensation had decreased, and then, the pulse amplitude was increased until a strong but comfortable paraesthesia intensity level returned. PBM was performed using the low level laser (Laserpulse- Industrica Brasileira de Equipamentos Medicos- IBRAMED, Amparo, Sao Paolo, brazil) with a GAllium Arsenide (AsGa) probe with a wavelength of 904nm, with a dose of 3J per point, totalling 9 points, total energy of 27J per session, peak power of 70W, pulse repetition frequency of 9500Hz, pulse duration of 60ns, average power of 40mW, application time of 75 seconds per point, and beam cross-sectional area of 0.5cm². . Duration 4 weeks. Concurrent medication/care: No use of analgesics 4 hours before treatment.. Indirectness: No indirectness (n=42) Intervention 4: Sham electrotherapy. Sham IFC and PBM. Three times a week for 4 week (12 sessions). Duration of each session ranged from 40 to 50 minutes, with the first session

	taking a slightly longer time until all patients had received guidance about the disease, joint protection and energy conservation before receiving the IFC and PBM. Interventions were applied according to the following sequence: 1) IFC and 2) PBM for both the active and placebo groups. The patient was informed that during the passage of the current he/she may not feel some tingling and that during PBM no sensation would be perceived. A towel was placed on the devices for all groups of patients. Placebo application of IFC was performed with the device switched on, with the energy emission button not activated. The electrodes were positioned for 30 minutes and every 5 minutes the patient was asked regarding any possible discomfort. The patient was informed that during the passage of the current he/she may not feel some tingling. The intervention of the placebo PBM was performed with the device switched on, with the energy emission button not activated. The panel light of equipment was constantly on. Patients were informed that during the PBM application, no sensation would be perceived. . Duration 4 weeks. Concurrent medication/care: No analgesics 4 hours before the intervention. Indirectness: No indirectness
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTERFERENTIAL THERAPY versus PHOTOBIOMODULATION

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: Pain on movement at 3 months; Group 1: mean 3.55 (SD 2.9364); n=42, Group 2: mean 3.15 (SD 2.8004); n=42; NRS 0-10 Top=High is poor outcome; Comments: Values reported are averages of the results of pain on movement when performing the timed up and go (TUG) and sit and lift (SLT) tests.
Values for the TUG test: IFC: 3.1 (2.8), PBM: 3.1 (2.8). Values for the SLT test: IFC: 4.0 (3.0), PBM: 3.2 (2.8)
Baseline values: IFC group (TUG): 4.7 (3.1),(SLT):6.0 (2.9). PBM group (TUG): 5.0 (3.2), (SLT): 5.9 (3.5)
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: declined to participate (5), death (1); Group 2 Number missing: 0

Protocol outcome 2: Pain at > 3 months
- Actual outcome: Pain on movement at 6 months; Group 1: mean 3.65 (SD 2.8614); n=42, Group 2: mean 2.95 (SD 2.5323); n=42; NRS 0-10 Top=High is poor outcome; Comments: Values reported are averages of the results of pain on movement when performing the timed up and go (TUG) and sit and lift (SLT) tests.
Values for the TUG test: IFC: 3.4 (2.8), PBM: 2.6 (2.3). Values for the SLT test: IFC: 3.9 (2.9), PBM: 3.3 (2.7)
Baseline values: IFC group (TUG): 4.7 (3.1),(SLT):6.0 (2.9). PBM group (TUG): 5.0 (3.2), (SLT): 5.9 (3.5)
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 7, Reason: declined to participate (5), death (1), no reasons given (1); Group 2 Number missing: 1, Reason: declined to participate (1)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTERFERENTIAL THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: Pain on movement at 3 months; Group 1: mean 3.55 (SD 2.9364); n=42, Group 2: mean 3.85 (SD 2.921); n=42; NRS 0-10 Top=High is poor outcome; Comments: Values reported are averages of the results of pain on movement when performing the timed up and go (TUG) and sit and lift (SLT) tests.
Values for the TUG test: IFC: 3.1 (2.8), placebo: 3.5 (2.9). Values for the SLT test: IFC: 4.0 (3.0), placebo: 4.2 (2.9)
Baseline values: IFC group (TUG): 4.7 (3.1),(SLT):6.0 (2.9). Placebo group (TUG): 4.6 (3.0), (SLT): 5.7 (3.1)
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: declined to participate (5), death (1); Group 2 Number missing: 4, Reason: declined to participate (2), health problems (1), drop (1)

Protocol outcome 2: Pain at > 3 months
- Actual outcome: Pain on movement at 6 months; Group 1: mean 3.65 (SD 2.8614); n=42, Group 2: mean 4.1 (SD 3.1064); n=42; NRS 0-10 Top=High is poor outcome; Comments: Values reported are averages of the results of pain on movement when performing the timed up and go (TUG) and sit and lift (SLT) tests.
Values for the TUG test: IFC: 3.4 (2.8), placebo: 3.9 (3.1). Values for the SLT test: IFC: 3.9 (2.9), placebo: 4.3 (3.1)
Baseline values: IFC group (TUG): 4.7 (3.1),(SLT):6.0 (2.9). Placebo group (TUG): 4.6 (3.0), (SLT): 5.7 (3.1)
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 7, Reason: declined to participate (5), death (1), no reasons given (1); Group 2 Number missing: 5, Reason: declined to participate (2), health problems (1), drop (1), decreased symptoms (1)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PHOTOBIOMODULATION versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: Pain on movement at 3 months; Group 1: mean 3.15 (SD 2.8004); n=42, Group 2: mean 3.85 (SD 2.921); n=42; NRS 0-10 Top=High is poor outcome; Comments: Values reported are averages of the results of pain on movement when performing the timed up and go (TUG) and sit and lift (SLT) tests.
Values for the TUG test: PBM: 3.1 (2.8), Placebo: 3.5 (2.9). Values for the SLT test: PBM: 3.2 (2.8), Placebo: 4.2 (2.9)
Baseline values: PBM group (TUG): 5.0 (3.2), (SLT): 5.9 (3.5), Placebo group (TUG): 4.6 (3.0), (SLT): 5.7 (3.1)

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 4, Reason: declined to participate (2), health problems (1), drop (1)

Protocol outcome 2: Pain at > 3 months
- Actual outcome: Pain on movement at 6 months; Group 1: mean 2.95 (SD 2.5323); n=42, Group 2: mean 4.1 (SD 3.1064); n=42; NRS 0-10 Top=High is poor outcome; Comments: Values reported are averages of the results of pain on movement when performing the timed up and go (TUG) and sit and lift (SLT) tests.
Values for the TUG test: PBM: 2.6 (2.3), Placebo: 3.9 (3.1). Values for the SLT test: PBM: 3.3 (2.7), Placebo: 4.3 (3.1)
Baseline values: PBM group (TUG): 5.0 (3.2), (SLT): 5.9 (3.5), Placebo group (TUG): 4.6 (3.0), (SLT): 5.7 (3.1)

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1, Reason: declined to participate; Group 2 Number missing: 5, Reason: declined to participate (2), health problems (1), drop (1), decreased symptoms (1)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINATION THERAPY (E.G. ULTRASOUND AND INTERFERENTIAL THERAPY) versus INTERFERENTIAL THERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: Pain on movement at 3 months; Group 1: mean 2.45 (SD 2.8004); n=42, Group 2: mean 3.55 (SD 2.9364); n=42; NRS 0-10 Top=High is poor outcome; Comments: Values reported are averages of the results of pain on movement when performing the timed up and go (TUG) and sit and lift (SLT) tests.Values
for the TUG test: combination: 2.4 (2.8), IFC: 3.1 (2.8). Values for the SLT test: combination: 2.5 (2.8), IFC: 4.0 (3.0)
Baseline values: IFC group (TUG): 4.7 (3.1),(SLT):6.0 (2.9). combination group (TUG): 4.5 (3.0), (SLT): 5.2 (2.7)

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: declined to participate (1), no reasons given (1); Group 2 Number missing: 6, Reason: declined to participate (5), death (1)

Protocol outcome 2: Pain at > 3 months
- Actual outcome: Pain on movement at 6 months; Group 1: mean 2.5 (SD 2.2383); n=42, Group 2: mean 3.65 (SD 2.8614); n=42; NRS 0-10 Top=High is

poor outcome; Comments: Values reported are averages of the results of pain on movement when performing the timed up and go (TUG) and sit and lift (SLT) tests.Values
for the TUG test: combination: 2.1 (2.1), IFC: 3.4 (2.8). Values for the SLT test: combination: 2.9 (2.3), IFC: 3.9 (2.9)
Baseline values: IFC group (TUG): 4.7 (3.1),(SLT):6.0 (2.9). combination group (TUG): 4.5 (3.0), (SLT): 5.2 (2.7)

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: declined to participate (2), no reasons given (1); Group 2 Number missing: 7, Reason: declined to participate (5), unable to contact (1), death (1)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINATION THERAPY (E.G. ULTRASOUND AND INTERFERENTIAL THERAPY) versus PHOTOBIOMODULATION

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: Pain on movement at 3 months; Group 1: mean 2.45 (SD 2.8004); n=42, Group 2: mean 3.15 (SD 2.8004); n=42; NRS 0-10 Top=High is poor outcome; Comments: Values reported are averages of the results of pain on movement when performing the timed up and go (TUG) and sit and lift (SLT) tests.
Values for the TUG test: combination: 2.4 (2.8), PBM: 3.1 (2.8). Values for the SLT test: combination: 2.5 (2.8), PBM: 3.2 (2.8)
Baseline values: combination group (TUG): 4.5 (3.0), (SLT): 5.2 (2.7), PBM group (TUG): 5.0 (3.2), (SLT): 5.9 (3.5)

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: declined to participate (1), no reasons given (1); Group 2 Number missing: 0

Protocol outcome 2: Pain at > 3 months
- Actual outcome: Pain on movement at 6 months; Group 1: mean 2.5 (SD 2.2383); n=42, Group 2: mean 2.95 (SD 2.323); n=42; NRS 0-10 Top=High is poor outcome; Comments: Values reported are averages of the results of pain on movement when performing the timed up and go (TUG) and sit and lift (SLT) tests.
Values for the TUG test: combination: 2.1 (2.1), PBM: 2.6 (2.3). Values for the SLT test: combination: 2.9 (2.3), PBM: 3.3 (2.7)
Baseline values: combination group (TUG): 4.5 (3.0), (SLT): 5.2 (2.7), PBM group (TUG): 5.0 (3.2), (SLT): 5.9 (3.5)

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: declined to participate (2), no

	reasons given (1); Group 2 Number missing: 1, Reason: declined to participate (1) RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINATION THERAPY (E.G. ULTRASOUND AND INTERFERENTIAL THERAPY) versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: Pain on movement at 3 months; Group 1: mean 2.45 (SD 2.8004); n=42, Group 2: mean 3.85 (SD 2.921); n=42; NRS 0-10 Top=High is poor outcome; Comments: Values reported are averages of the results of pain on movement when performing the timed up and go (TUG) and sit and lift (SLT) tests. Values for the TUG test: combination: 2.4 (2.8), Placebo: 3.5 (2.9). Values for the SLT test: combination: 2.5 (2.8), Placebo: 4.2 (2.0) Baseline values: combination group (TUG): 4.5 (3.0), (SLT): 5.2 (2.7), Placebo group (TUG): 4.6 (3.0), (SLT): 5.7 (3.1) Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: declined to participate (1), no reasons given (1); Group 2 Number missing: 4, Reason: declined to participate (2), health problems (1), drop (1) Protocol outcome 2: Pain at > 3 months - Actual outcome: Pain on movement at 6 months; Group 1: mean 2.5 (SD 2.2383); n=42, Group 2: mean 4.1 (SD 3.1064); n=42; NRS 0-10 Top=High is poor outcome; Comments: Values reported are averages of the results of pain on movement when performing the timed up and go (TUG) and sit and lift (SLT) tests. Values for the TUG test: combination: 2.1 (2.1), Placebo: 3.9 (3.1). Values for the SLT test: combination: 2.9 (2.3), Placebo: 4.3 (3.1) Baseline values: combination group (TUG): 4.5 (3.0), (SLT): 5.2 (2.7), Placebo group (TUG): 4.6 (3.0), (SLT): 5.7 (3.1) Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: declined to participate (2), no reasons given (1); Group 2 Number missing: 5, Reason: declined to participate (2), health problems (1), drop (1), decreased symptoms (1)
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	**Altas 2020[16]**
Study type	RCT (Patient randomised; Parallel)

Number of studies (number of participants)	(n=40)
Countries and setting	Conducted in Turkey; Setting: Katip Celebi University Ataturk Training and Research Hospital Physical Therapy and Rehabilitation outpatient clinic.
Line of therapy	Unclear
Duration of study	Intervention + follow up: Unclear, but at least 3 weeks.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: 1986 ACR criteria and K-L grade 2-3.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients who were admitted with knee pain and diagnosed with knee OA according to the 1986 ACR criteria and were in K-L grade 2-3.
Exclusion criteria	Patients with knee effusion, secondary OA, severe knee trauma history within the past 6 months, previous intra-articular hyaluronic acid or steroid injection, meniscal or connective tissue damage, and those receiving physical therapy within the past year for knee pain were excluded from the study. Those with joint pathologies other than knee OA in the lower extremity, previous lower extremity surgery including knee surgery, severe circulatory problems in lower extremity, restless leg syndrome, fibromyalgia, inflammatory disease, active infectious disease, severe systemic disease such as asthma or cardiac failure, neurological disease, psychiatric disease, malignancy or pregnant women and those with a pacemaker were also excluded.
Recruitment/selection of patients	Not reported.
Age, gender and ethnicity	Age - Mean (SD): 56.6 (8.9). Gender (M:F): 9M/31F. Ethnicity: Not reported
Further population details	1. Age (≤/> 75 years): </=75 years (age 40-70 years). 2. Diagnosis : Diagnosis with imaging (Included K-L grading.). 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity (K-L grade 2): combination therapy group: 10, exercise group: 13 Severity (K-L grade 3): combination therapy group: 10, exercise group: 7 Duration (years): 3.13 (1.3), range 1-5 years
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Non-invasive electrotherapy interventions - Combination therapy (e.g. ultrasound and interferential therapy). Ten therapy sessions using the same instruments and exercise treatment five days a week and a single session each day were performed by a single physiotherapist. Hot pack (HP) was used as a surface warmer for 20 minutes. Also, TENS was applied using the Enraf (Enraf-Nonius B.V., Rotterdam, Holland) TENS instrument with 0-100Hz, dual 5x7cm electrodes for 20 minutes. The patient was laid in the

	supine position and two surface electrodes were used on upper part of the knee, while two surface electrodes were used on the lower part of the knee in full extension. The current intensity used was set as not to cause muscle contractions and based on the patient perception of 'strong, but tolerable'. As deep warmer, therapeutic US was applied for five minutes in the continuous mode at 1.5 watt/cm² with 100% productivity in 1mHz. The Enraf US with a 3 cm² head was used. Similarly, it was applied in the supine position with knees extended into the periarticular area in the circular motions. Both groups received the same home-based exercise program as in 30 sessions with 10 reps a day for three times a week. The exercise programme was demonstrated and explained by a single physiotherapist. Visual exercise guides were also provided for patients. The exercise programme consisted of isometric and isotonic exercises. The patient was asked to insert a rolled towel under his/her knee, while sitting upright on the bed and push his/her knees towards the ground, adn, then, relax the knee and, then, to put the same towel between the knees and squeeze it for 5 seconds and release. Another exercise was to life his/her leg 10cm above the ground, while lying in the supine position and one knee bent for 5 seconds, and, then, lower it back down. In addition, the patient was asked to raise his/ her knee by 90 degrees while sitting on a chair and wait for 5 seconds and, then, lower the knee and to add 0.5kg in the second and 1kg weight in the third week. Hamstring stretching exercises were also prescribed as flexing the body during ankle dorsiflexion and lying ankle dorsi- and plantar flexion exercises.. Duration ?3 weeks. Concurrent medication/care: All patients were allowed to use paracetamol at a dose ≤3000mg/day for pain during the assessment. However, they were instructed not to use any other analgesics except for paracetamol. In addition, all patients were allowed to use other medications for their concomitant systemic diseases.. Indirectness: No indirectness (n=20) Intervention 2: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. Both groups received the same home-based exercise program as in 30 sessions with 10 reps a day for three times a week. The exercise programme was demonstrated and explained by a single physiotherapist. Visual exercise guides were also provided for patients. The exercise programme consisted of isometric and isotonic exercises. The patient was asked to insert a rolled towel under his/her knee, while sitting upright on the bed and push his/her knees towards the ground, adn, then, relax the knee and, then, to put the same towel between the knees and squeeze it for 5 seconds and release. Another exercise was to life his/her leg 10cm above the ground, while lying in the supine position and one knee bent for 5 seconds, and, then, lower it back down. In addition, the patient was asked to raise his/ her knee by 90 degrees while sitting on a chair and wait for 5 seconds and, then, lower the knee and to add 0.5kg in the second and 1kg weight in the third week. Hamstring stretching exercises were also prescribed as flexing the body during ankle dorsiflexion and lying ankle dorsi- and plantar flexion exercises.. Duration ?3 weeks. Concurrent medication/care: All patients were allowed to use paracetamol at a dose ≤3000mg/day for pain during the assessment. However, they were instructed not to use any other analgesics except for paracetamol. In addition, all patients were allowed to use other medications for their concomitant systemic diseases.. Indirectness: No indirectness
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINATION THERAPY (ULTRASOUND AND TENS THERAPY) PLUS EXERCISE versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: SF-36 physical function at 3 weeks (post intervention); Group 1: mean 83 (SD 13.8); n=20, Group 2: mean 59 (SD 13.6); n=20; SF-36 physical function 0-100 Top=High is good outcome; Comments: baseline values: combination group: 65.3 (18.5), exercise group: 50.3 (15.8)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Combination therapy group: 65.3 (18.5), exercise group: 50.3 (15.8); Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 role physical at 3 weeks (post intervention); Group 1: mean 66.3 (SD 29.6); n=20, Group 2: mean 28.75 (SD 3); n=20; SF-36 role physical 0-100 Top=High is good outcome; Comments: baseline values: combination group: 21.3 (33.7), exercise group: 20 (26.4)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 pain at 3 weeks (post intervention); Group 1: mean 55.6 (SD 12.6); n=20, Group 2: mean 45.4 (SD 15.1); n=20; SF-36 pain 0-100 Top=High is good outcome; Comments: baseline values: combination group: 35.6 (12.7), exercise group: 38.7 (17.9)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 general health at 3 weeks (post intervention); Group 1: mean 43.8 (SD 9.2); n=20, Group 2: mean 40.9 (SD 16.7); n=20; SF-36 general health 0-100 Top=High is good outcome; Comments: baseline values: combination group: 26.9 (13.2), exercise group: 33.1 (13.5)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 vitality at 3 weeks (post intervention); Group 1: mean 62 (SD 15.3); n=20, Group 2: mean 40 (SD 13.7); n=20; SF-36 vitality 0-100 Top=High is good outcome; Comments: baseline values: combination group: 42.8 (20.7), exercise group: 41.8 (19.1)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 social function at 3 weeks (post intervention); Group 1: mean 76.2 (SD 17.1); n=20, Group 2: mean 50 (SD 21.5); n=20; SF-36 social function 0-100 Top=High is good outcome; Comments: baseline values: combination group: 53.1 (19.8), exercise group: 45 (24.1)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Combination therapy group: 53.1 (19.8), exercise group: 45 (24.1); Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 role emotion at 3 weeks (post intervention); Group 1: mean 79.7 (SD 22.9); n=20, Group 2: mean 47.9 (SD 22.8); n=20; SF-36 role emotion 0-100 Top=High is good outcome; Comments: baseline values: combination group: 23.1 (26.4), exercise group: 29 (30.2)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 mental health at 3 weeks (post intervention); Group 1: mean 69 (SD 9.4); n=20,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Pain at </= 3 months
- Actual outcome: VAS pain at 3 weeks (post intervention); Group 1: mean 4.1 (SD 1.3); n=20, Group 2: mean 6.4 (SD 1.4); n=20; VAS 0-10 Top=High is poor outcome; Comments: baseline values: combination group: 7.3 (1.0), exercise group: 7.3 (1.1)

Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 3: Psychological distress at </= 3 months - Actual outcome: Beck Depression Inventory at 3 weeks (post intervention); Group 1: mean 6.8 (SD 2.2); n=20, Group 2: mean 8.4 (SD 2.9); n=20; BDI 0-51 Top=High is poor outcome; Comments: baseline values: combination group: 10.3 (3.0), exercise group: 9.2 (3.3) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Altay 2010[17]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 3 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Primary knee osteoarthritis according to the American college of Rheumatology criteria confirmed with standing anteroposterior and lateral radiographs of both knees
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People aged between 40-70 years and diagnsosed with primary knee osteoarthritis according to the American College of Rheumatology criteria. Standing anteroposterior and lateral radiographs of both knees were obtained in each person and the severity of osteoarthritis in the tibiofemoral compartment was graded according to the criteria of Kellgren Lawrence.
Exclusion criteria	People younger than 40 and older than 70 years; people with a serious medical condition (diabetes mellitus, heart disease, uncontrolled hypertension; neuromuscular disease that involves the lower extremities; a history of previous knee surgery; trauma and physical therapy within the last 6 months; implanted cardiac pacemaker; inflammatory arthropathy; contracture or grade 4 osteoarthritis
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 59.5 (9.0). Gender (M:F): 30:10. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade <4 Duration of symptoms (mean [SD]): 7.9 (5.9) years.
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Non-invasive electrotherapy interventions - Transcutaneous electrical nerve stimulation (TENS). Active TENS using an Elettronica Pagani Class1 type BF branded device. Two electrodes were attached to the painful areas in both knees. Stimulation was applied in a conventional mode with a dose tolerated well by the person and a frequency of 100Hz, pulse time of 200 and current strength between

	20-35 mA. The duration of TENS treatment was 40 mins.. Duration 3 weeks. Concurrent medication/care: All people received an exercise program for 30 minutes and hot packs for 15 minutes in a day for 3 weeks. Indirectness: No indirectness (n=20) Intervention 2: Sham electrotherapy. Sham TENS 9same device, but device was switched on while delivering not current).. Duration 3 weeks. Concurrent medication/care: All people received an exercise program for 30 minutes and hot packs for 15 minutes in a day for 3 weeks. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) versus SHAM ELECTROTHERAPY

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: SF-36 physical function at 3 weeks; Group 1: mean 0.61 (SD 0.16); n=20, Group 2: mean 0.45 (SD 0.14); n=20; SF-36 physical function 0-1 Top=High is good outcome; Comments: Baseline TENS: 0.25 (0.12). Baseline sham: 0.30 (0.07).
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, BMI, duration of symptoms, sex, job, education, and baseline values of outcomes. SF-36 energy is different at baseline.; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 social function at 3 weeks; Group 1: mean 0.83 (SD 0.14); n=20, Group 2: mean 0.72 (SD 0.15); n=20; SF-36 social function 0-1 Top=High is good outcome; Comments: Baseline TENS: 0.62 (0.22). Baseline sham: 0.64 (0.14).
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, BMI, duration of symptoms, sex, job, education, and baseline values of outcomes. SF-36 energy is different at baseline.; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 mental health at 3 weeks; Group 1: mean 0.72 (SD 0.16); n=20, Group 2: mean 0.7 (SD 0.15); n=20; SF-36 mental health 0-1 Top=High is good outcome; Comments: Baseline TENS: 0.60 (0.18). Baseline sham: 0.67 (0.18).
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, BMI, duration of symptoms, sex, job, education, and baseline values of outcomes. SF-36 energy is different at baseline.; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 general health at 3 weeks; Group 1: mean 0.73 (SD 0.14); n=20, Group 2: mean 0.67 (SD 0.1); n=20; SF-36 general health 0-1 Top=High is good outcome; Comments: Baseline TENS: 0.60 (0.15). Baseline sham: 0.67 (0.09).
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, BMI, duration of symptoms, sex, job, education, and baseline values of outcomes. SF-36 energy is different at baseline.; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: SF-36 energy at 3 weeks; Group 1: mean 0.7 (SD 0.18); n=20, Group 2: mean 0.72 (SD 0.14); n=20; SF-36 energy 0-1 Top=High is good outcome; Comments: Baseline TENS: 0.58 (0.19). Baseline sham: 0.68 (0.18).
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, BMI, duration of symptoms, sex,

job, education, and baseline values of outcomes. SF-36 energy is different at baseline.; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at > 3 months; Pain at </= 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	**Arslan 2020[21]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=38)
Countries and setting	Conducted in Turkey; Setting: Faculty of Medicine at Kirikkale Univeristy.
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 2 weeks
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: ? stage 2 or 3 on K-L staging.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Admitted to hospital for knee pain and who had been diagnosed with stage 2 or stage 3 bilateral knee osteoarthritis at least 6 months earlier in accordance with K-L radiological staging
Exclusion criteria	Non- inclusion criteria involved a neurological disease, a cardiopulmonary or systemic disease that prevented receiving a physiotherapy programme and exercise, inflammatory arthritis, not being independently mobilised, history of knee or hip replacement surgery, a pathology other than knee OA that might cause knee pain, any pathology of the back and hip that might cause pain reflected in the knee, having received an intra-knee injection for any reason in the previous year, and cognitive problems.
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): NMES group; 64.85 (8.90), physio group: 60.58 (7.92). Gender (M:F): 21F/ 17M. Ethnicity: Not reported

Further population details	1. Age (≤/> 75 years): Not applicable (Age 50-78 years). 2. Diagnosis : Diagnosis with imaging (Diagnosed using K-L staging). 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity (VAS activity pain at baseline): NMES group: 48.43 (28.85), physio group: 52.29 (30.20) Duration: not reported
Indirectness of population	No indirectness
Interventions	(n=21) Intervention 1: Non-invasive electrotherapy interventions - Neuromuscular electrical stimulation. NMES and combined physiotherapy. Both groups received a combined physiotherapy programme, with 5 sessions per week. It included a hot pack, therapeutic ultrasound, TENS and exercise programme. At the beginning of the treatment session, the hot pack (23.1-41cm), which is a superficial heat agent, was applied on both knees for 20 mi9nutes when the patient was in a sitting position. To provide deep heat, the Chattanooga Intelect device was used(full-contact technique with 1 MHz set). Conventional tests were performed for 20 minutes with the Intelect brand TENS device. The frequency was set at 100Hz and the pulse width at 60ms. The intensity was raised until the patient felt. the NMES Chattanooga Intelect device was employed with the quadriceps muscle in a sitting-up position for 10 minutes at 10-40Hz, 250ms, with a 5 second warning, 15 second resting time with 3 beats a minute. As the exercise programme, the quadriceps muscle isometric strengthening exercises, and adductor muscle isometric strengthening exercises were given under the supervision of a physiotherapist at the end of each session. All exercises were performed in 3 sets of 10 repetitions.. Duration 2 weeks. Concurrent medication/care: Not reported (n=17) Intervention 2: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. Combined physiotherapy. Both groups received a combined physiotherapy programme, with 5 sessions per week. It included a hot pack, therapeutic ultrasound, TENS and exercise programme. At the beginning of the treatment session, the hot pack (23.1-41cm), which is a superficial heat agent, was applied on both knees for 20 minutes when the patient was in a sitting position. To provide deep heat, the Chattanooga Intelect device was used(full-contact technique with 1 MHz set). Conventional tests were performed for 20 minutes with the Intelect brand TENS device. The frequency was set at 100Hz and the pulse width at 60ms. The intensity was raised until the patient felt. As the exercise programme, the quadriceps muscle isometric strengthening exercises, and adductor muscle isometric strengthening exercises were given under the supervision of a physiotherapist at the end of each session. All exercises were performed in 3 sets of 10 repetitions.. Duration 2 weeks. Concurrent medication/care: Not reported
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NEUROMUSCULAR ELECTRICAL STIMULATION versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: Nottingham Health Profile- pain at post-intervention (2 weeks); Group 1: mean 37.76 (SD 24.47); n=21, Group 2: mean 51.11 (SD 30.95); n=17; Nottingham Health Profile- pain subscale unclear Top=High is poor outcome; Comments: Baseline values: NMES group: 60.58 (31.20), physio group: 72.48 (27.16)

Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: NMES group: 60.58 (31.20), physio group: 72.48 (27.16); Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: Nottingham Health Profile- physical mobility at post-intervention (2 weeks); Group 1: mean 38.2 (SD 17.83); n=21, Group 2: mean 33.53 (SD 26.43); n=17; Nottingham Health Profile- physical mobility subscale unclear Top=High is poor outcome; Comments: Baseline values: NMES group: 45.85(17.31), physio group: 34.80(21.42)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: NMES: 45.85 (17.31), physio: 34.80(21.42); Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: Nottingham Health Profile- energy level at post-intervention (2 weeks); Group 1: mean 36.61 (SD 43.25); n=21, Group 2: mean 56.84 (SD 36.26); n=17; Nottingham Health Profile- energy level subscale unclear Top=High is poor outcome; Comments: Baseline values: NMES group: 46.18(44.22), physio group: 67.34(32.33)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: NMES: 46.18 (44.22), physio: 67.34(32.33); Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: Nottingham Health Profile- sleep at post-intervention (2 weeks); Group 1: mean 32.06 (SD 29.39); n=21, Group 2: mean 34.23 (SD 32.21); n=17; Nottingham Health Profile- sleep subscale unclear Top=High is poor outcome; Comments: Baseline values: NMES group: 42.23(30.28), physio group: 44.92(31.83)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: Nottingham Health Profile- social isolation at post-intervention (2 weeks); Group 1: mean 9.09 (SD 19.64); n=21, Group 2: mean 10.38 (SD 23.25); n=17; Nottingham Health Profile- social isolation subscale unclear Top=High is poor outcome; Comments: Baseline values: NMES group: 11.10(21.04), physio group: 16.81(24.07)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: Nottingham Health Profile- emotional reaction at post-intervention (2 weeks); Group 1: mean 14.49 (SD 19.77); n=21, Group 2: mean 21.01 (SD 28.65); n=17; Nottingham Health Profile- emotional reaction subscale unclear Top=High is poor outcome; Comments: Baseline values: NMES group: 23.61(28.06), physio group: 32.08 (31.20)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: NMES: 23.61 (28.06), physio: 32.08(31.20); Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: Nottingham Health Profile- total score at post-intervention (2 weeks); Group 1: mean 167.58 (SD 105.33); n=21, Group 2: mean 213.07 (SD 139.18); n=17; Nottingham Health Profile- total score unclear Top=High is poor outcome; Comments: Baseline values: NMES group: 227.00 (127.64), physio group: 267.27(125.72)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: NMES group: 227 (127.64), physio group: 267.27(125.72); Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Pain at </= 3 months - Actual outcome: WOMAC- pain at post-intervention (2 weeks); Group 1: mean 6.23 (SD 3.3); n=21, Group 2: mean 7.78 (SD 9.65); n=17; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline values: NMES group: 8.53 (3.96), physio group: 9.67(3.59) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 3: Physical function at </= 3 months - Actual outcome: WOMAC- physical function at post-intervention (2 weeks); Group 2: mean 19.24 (SD 12.91); n=17; WOMAC physical function 0-68 Top=High is poor outcome; Comments: Baseline values: NMES group: 28.64(13.86), physio group: 29.10(14.83) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Atamaz 2012[22]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=203)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 3 weeks of treatment, 6 months of follow up in total
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with knee osteoarthritis according to the American College of Rheumatology criteria with radiologically confirmation with a Kellgren Lawrence grade of 2 or 3
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People aged 50-80 ymerican College of Rheumatology criteria; radiologically confirmed with a Kellgren Lawrence grade of 2 or 3; and symptomatic with at least 40mm severity of pain on the VAS for at least 6 months
Exclusion criteria	Any experience with electrotherapy; had history of any contraindication to electrotherapy; had received corticosteroid therapy or chondroprotective agents during the 30 days prior to the study or viscosupplementation treatment within 6 months prior to the study; had undergone previous major surgery such as joint replacement or arthroscopy, within 6 months prior to the study; diagnosis of joint infection, a specific condition (neoplasm, diabetes mellitus, paresis, osteonecrosis, recent trauma etc), ascertained/suspected pregnancy or lactation, and poor general health status that would interfere with the functional assessments during the study.
Recruitment/selection of patients	Multicenter trial
Age, gender and ethnicity	Age - Mean (SD): 61.5 (7.5). Gender (M:F): 36:167. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 2-3 Duration of symptoms (mean [SD]): 43.7 (49.1) months.
Indirectness of population	No indirectness
Interventions	(n=37) Intervention 1: Non-invasive electrotherapy interventions - Transcutaneous electrical nerve stimulation (TENS). TNES administered at a frequency of 80Hz with 10- to 30-mA intensity for 20 minutes. Four surface electrodes are placed over the painful area in the knee region with intensity in the tactile sensation threshold..

	Duration 3 weeks. Concurrent medication/care: All people had an exercise program conducted in groups of 4-5 people three times a week for 3 weeks involving stretching, isometric quadriceps exercises and chair lift/minisquats. This was supplemented with additional instruction for home exercise. All people also attended an education program consisting of one 1 hour session discussing the functional anatomy of the knee, ergonomic principles, and understanding of osteoarthritis. Indirectness: No indirectness (n=37) Intervention 2: Sham electrotherapy. Sham TENS. Duration 3 weeks. Concurrent medication/care: All people had an exercise program conducted in groups of 4-5 people three times a week for 3 weeks involving stretching, isometric quadriceps exercises and chair lift/minisquats. This was supplemented with additional instruction for home exercise. All people also attended an education program consisting of one 1 hour session discussing the functional anatomy of the knee, ergonomic principles, and understanding of osteoarthritis. Indirectness: No indirectness Comments: For comparisons, this group will only be compared to the TENS group (n=31) Intervention 3: Non-invasive electrotherapy interventions - Interferential therapy. Interferential currents administered at a frequency of 100Hz generated by 4kHz sinusoidal waves. Two electrodes were placed onto the knee region with intensity in the tactile sensation threshold.. Duration 3 weeks. Concurrent medication/care: All people had an exercise program conducted in groups of 4-5 people three times a week for 3 weeks involving stretching, isometric quadriceps exercises and chair lift/minisquats. This was supplemented with additional instruction for home exercise. All people also attended an education program consisting of one 1 hour session discussing the functional anatomy of the knee, ergonomic principles, and understanding of osteoarthritis. Indirectness: No indirectness (n=35) Intervention 4: Sham electrotherapy. Sham interferential currents. Duration 3 weeks. Concurrent medication/care: All people had an exercise program conducted in groups of 4-5 people three times a week for 3 weeks involving stretching, isometric quadriceps exercises and chair lift/minisquats. This was supplemented with additional instruction for home exercise. All people also attended an education program consisting of one 1 hour session discussing the functional anatomy of the knee, ergonomic principles, and understanding of osteoarthritis. Indirectness: No indirectness Comments: For comaprisons, this group will only be compared to the interferential

	therapy group (n=32) Intervention 5: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. Shortwave diathermy. People were targeted with continued shortwave diathermy with a 10cm diameter condenser plate operating at a frequency of 27.12mHz, an input of 300W and a mean output of 3.2W.. Duration 3 weeks. Concurrent medication/care: All people had an exercise program conducted in groups of 4-5 people three times a week for 3 weeks involving stretching, isometric quadriceps exercises and chair lift/minisquats. This was supplemented with additional instruction for home exercise. All people also attended an education program consisting of one 1 hour session discussing the functional anatomy of the knee, ergonomic principles, and understanding of osteoarthritis. Indirectness: No indirectness (n=31) Intervention 6: Sham electrotherapy. Sham short wave therapy. Duration 3 weeks. Concurrent medication/care: All people had an exercise program conducted in groups of 4-5 people three times a week for 3 weeks involving stretching, isometric quadriceps exercises and chair lift/minisquats. This was supplemented with additional instruction for home exercise. All people also attended an education program consisting of one 1 hour session discussing the functional anatomy of the knee, ergonomic principles, and understanding of osteoarthritis. Indirectness: No indirectness Comments: For comparisons, this group will only be compared to the short wave therapy group
Funding	Academic or government funding (Supported by Ege, Dokuz Eylul, and Adnan Menderes University, and Sisli Etfal Education and Research Hospital)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) versus SHAM ELECTROTHERAPY - TENS

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 3 months; Group 1: mean 2.8 (SD 3.4); n=37, Group 2: mean 3.6 (SD 3); n=37; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported TENS: 3.6 (2.6-4.5). Reported sham TENS: 2.8 (1.7-3.9). Baseline TENS: 14.0 (4.3). Baseline sham TENS: 14.5 (4.0).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 6, Reason: TENS: 6 withdrawals by 3 months, 8 by 6 months. Reasons: Worsening of symptoms (3), health problems not related to knee pain (2), not enough time to attend (3).; Group 2 Number missing: 3, Reason: Sham TENS: 3 withdrawals by 3 months, 4 by 6 months.

Reasons: Worsening of symptoms (3), health problems not related to knee pain (1).

Protocol outcome 2: Pain at > 3 months
- Actual outcome: WOMAC pain at 6 months; Group 1: mean 3.7 (SD 3.7); n=37, Group 2: mean 3 (SD 3.1); n=37; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported TENS: 3.7 (2.7-4.7). Reported sham TENS: 3 (1.8-4.2). Baseline TENS: 14.0 (4.3). Baseline sham TENS: 14.5 (4.0).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 8, Reason: TENS: 6 withdrawals by 3 months, 8 by 6 months. Reasons: Worsening of symptoms (3), health problems not related to knee pain (2), not enough time to attend (3).; Group 2 Number missing: 4, Reason: Sham TENS: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (3), health problems not related to knee pain (1).

Protocol outcome 3: Physical function at </= 3 months
- Actual outcome: WOMAC function at 3 months; Group 1: mean 8.7 (SD 11.6); n=37, Group 2: mean 9.4 (SD 10.7); n=37; WOMAC function 0-68 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported TENS: 8.7 (5.0-12.5). Reported sham TENS: 9.4 (5.9-12.8). Baseline TENS: 41.3 (13.1). Baseline sham TENS: 43.4 (11.7).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 6, Reason: TENS: 6 withdrawals by 3 months, 8 by 6 months. Reasons: Worsening of symptoms (3), health problems not related to knee pain (2), not enough time to attend (3).; Group 2 Number missing: 3, Reason: Sham TENS: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (3), health problems not related to knee pain (1).

Protocol outcome 4: Physical function at > 3 months
- Actual outcome: WOMAC function at 6 months; Group 1: mean 9.5 (SD 11.5); n=37, Group 2: mean 9.1 (SD 10.7); n=37; WOMAC function 0-68 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported TENS: 9.5 (5.8-13.2). Reported sham TENS: 9.1 (5.6-12.5). Baseline TENS: 41.3 (13.1). Baseline sham TENS: 43.4 (11.7).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 8, Reason: TENS: 6 withdrawals by 3 months, 8 by 6 months. Reasons: Worsening of symptoms (3), health problems not related to knee pain (2), not enough time to attend (3).; Group 2 Number missing: 4, Reason: Sham TENS: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (3), health problems not related to knee pain (1).

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) versus INTERFERENTIAL THERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 3 months; Group 1: mean 3.6 (SD 3); n=37, Group 2: mean 3.3 (SD 3.1); n=31; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported TENS: 3.6 (2.6-4.5). Reported IFCs: 3.6 (2.6-4.6). Baseline TENS: 14.0 (4.3).

Baseline IFCs: 13.6 (4.3).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 6, Reason: TENS: 6 withdrawals by 3 months, 8 by 6 months. Reasons: Worsening of symptoms (3), health problems not related to knee pain (2), not enough time to attend (3).; Group 2 Number missing: 3, Reason: IFC: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (1), not enough time to attend (3).

Protocol outcome 2: Pain at > 3 months
- Actual outcome: WOMAC pain at 6 months; Group 1: mean 3.7 (SD 3.7); n=37, Group 2: mean 3.4 (SD 3.4); n=31; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported TENS: 3.7 (2.7-4.7). Reported IFCs: 3.4 (2.2-4.6). Baseline TENS: 14.0 (4.3). Baseline IFCs: 13.6 (4.3).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 8, Reason: TENS: 6 withdrawals by 3 months, 8 by 6 months. Reasons: Worsening of symptoms (3), health problems not related to knee pain (2), not enough time to attend (3).; Group 2 Number missing: 4, Reason: IFC: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (1), not enough time to attend (3).

Protocol outcome 3: Physical function at </= 3 months
- Actual outcome: WOMAC function at 3 months; Group 1: mean 8.7 (SD 11.6); n=37, Group 2: mean 8.1 (SD 11.1); n=31; WOMAC function 0-68 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported TENS: 8.7 (5.0-12.5). Reported IFCs: 8.1 (4.0-12.0). Baseline TENS: 41.3 (13.1). Baseline IFCs: 42.7 (12.9).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 6, Reason: TENS: 6 withdrawals by 3 months, 8 by 6 months. Reasons: Worsening of symptoms (3), health problems not related to knee pain (2), not enough time to attend (3).; Group 2 Number missing: 3, Reason: IFC: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (1), not enough time to attend (3).

Protocol outcome 4: Physical function at > 3 months
- Actual outcome: WOMAC function at 6 months; Group 1: mean 9.5 (SD 11.5); n=37, Group 2: mean 8.5 (SD 11.1); n=31; WOMAC function 0-68 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported TENS: 9.5 (5.8-13.2). Reported IFCs: 8.5 (4.6-12.4). Baseline TENS: 41.3 (13.1). Baseline IFCs: 42.7 (12.9).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 8, Reason: TENS: 6 withdrawals by 3 months, 8 by 6 months. Reasons: Worsening of symptoms (3), health problems not related to knee pain (2), not enough time to attend (3).; Group 2 Number missing: 4, Reason: IFC: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (1), not enough time to attend (3).

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) versus

PULSED SHORT-WAVE THERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 3 months; Group 1: mean 3.6 (SD 3); n=37, Group 2: mean 4.9 (SD 4); n=32; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported TENS: 3.6 (2.6-4.5). Reported SWD: 4.9 (3.5-6.3). Baseline TENS: 14.0 (4.3). Baseline SWD: 14.0 (4.5).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 6, Reason: TENS: 6 withdrawals by 3 months, 8 by 6 months. Reasons: Worsening of symptoms (3), health problems not related to knee pain (2), not enough time to attend (3).; Group 2 Number missing: 3, Reason: SWD: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (2), health problems not related to knee pain (2).

Protocol outcome 2: Pain at > 3 months
- Actual outcome: WOMAC pain at 6 months; Group 1: mean 3 (SD 3.1); n=37, Group 2: mean 4.5 (SD 4); n=32; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported TENS: 3.7 (2.7-4.7). Reported SWD: 4.5 (3.1-5.9). Baseline TENS: 14.0 (4.3). Baseline SWD: 14.0 (4.5).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 8, Reason: TENS: 6 withdrawals by 3 months, 8 by 6 months. Reasons: Worsening of symptoms (3), health problems not related to knee pain (2), not enough time to attend (3).; Group 2 Number missing: 4, Reason: SWD: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (2), health problems not related to knee pain (2).

Protocol outcome 3: Physical function at </= 3 months
- Actual outcome: WOMAC function at 3 months; Group 1: mean 8.7 (SD 11.6); n=37, Group 2: mean 11.4 (SD 12.4); n=32; WOMAC function 0-68 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported TENS: 8.7 (5.0-12.5). Reported SWD: 11.4 (7.1-15.8). Baseline TENS: 41.3 (13.1). Baseline SWD: 41.1 (10.7).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 6, Reason: TENS: 6 withdrawals by 3 months, 8 by 6 months. Reasons: Worsening of symptoms (3), health problems not related to knee pain (2), not enough time to attend (3).; Group 2 Number missing: 3, Reason: SWD: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (2), health problems not related to knee pain (2).

Protocol outcome 4: Physical function at > 3 months
- Actual outcome: WOMAC function at 6 months; Group 1: mean 9.5 (SD 11.5); n=37, Group 2: mean 9.9 (SD 13.2); n=32; WOMAC function 0-68 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported TENS: 9.5 (5.8-13.2). Reported SWD: 9.9 (5.3-14.6). Baseline TENS: 41.3 (13.1). Baseline SWD: 41.1 (10.7).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of

outcomes; Group 1 Number missing: 8, Reason: TENS: 6 withdrawals by 3 months, 8 by 6 months. Reasons: Worsening of symptoms (3), health problems not related to knee pain (2), not enough time to attend (3).; Group 2 Number missing: 4, Reason: SWD: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (2), health problems not related to knee pain (2).

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTERFERENTIAL THERAPY versus SHAM ELECTROTHERAPY - IFC

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 3 months; Group 1: mean 3.3 (SD 3.1); n=31, Group 2: mean 3.6 (SD 3); n=35; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals.Reported IFCs: 3.6 (2.6-4.6). Reported sham IFCs: 3.3 (2.2-4.4). Baseline IFCs: 13.6 (4.3). Baseline sham IFCs: 14.8 (3.3).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 3, Reason: IFC: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (1), not enough time to attend (3).; Group 2 Number missing: 0, Reason: Sham IFC: 0 withdrawals by 3 months, 1 by 6 months. Reason: Worsening of symptoms (1)

Protocol outcome 2: Pain at > 3 months
- Actual outcome: WOMAC pain at 6 months; Group 1: mean 3.4 (SD 3.4); n=31, Group 2: mean 3.2 (SD 3.2); n=35; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported IFCs: 3.4 (2.2-4.6). Reported sham IFCs: 3.2 (2.2-4.3). Baseline IFCs: 13.6 (4.3). Baseline sham IFCs: 14.8 (3.3).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 4, Reason: IFC: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (1), not enough time to attend (3).; Group 2 Number missing: 1, Reason: Sham IFC: 0 withdrawals by 3 months, 1 by 6 months. Reason: Worsening of symptoms (1)

Protocol outcome 3: Physical function at </= 3 months
- Actual outcome: WOMAC function at 3 months; Group 1: mean 8.1 (SD 11.1); n=31, Group 2: mean 11 (SD 8.9); n=35; WOMAC function 0-68 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported IFCs: 8.1 (4.0-12.0). Reported sham IFCs: 11 (8.0-13.9). Baseline IFCs: 42.7 (12.9). Baseline sham IFCs: 45.3 (11.8).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 3, Reason: IFC: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (1), not enough time to attend (3).; Group 2 Number missing: 0, Reason: Sham IFC: 0 withdrawals by 3 months, 1 by 6 months. Reason: Worsening of symptoms (1)

Protocol outcome 4: Physical function at > 3 months
- Actual outcome: WOMAC function at 6 months; Group 1: mean 8.5 (SD 11.1); n=31, Group 2: mean 11.5 (SD 9.1); n=35; WOMAC function 0-68 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported IFCs: 8.5 (4.6-12.4). Reported sham IFCs: 11.5 (8.5-14.5). Baseline IFCs: 42.7 (12.9). Baseline sham IFCs: 45.3 (11.8).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover -

Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 4, Reason: IFC: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (1), not enough time to attend (3).; Group 2 Number missing: 1, Reason: Sham IFC: 0 withdrawals by 3 months, 1 by 6 months. Reason: Worsening of symptoms (1)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTERFERENTIAL THERAPY versus PULSED SHORT-WAVE THERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 3 months; Group 1: mean 3.3 (SD 3.1); n=31, Group 2: mean 4.9 (SD 4); n=32; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported IFCs: 3.6 (2.6-4.6). Reported SWD: 4.9 (3.5-6.3). Baseline IFCs: 13.6 (4.3). Baseline SWD: 14.0 (4.5).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 3, Reason: IFC: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (1), not enough time to attend (3).; Group 2 Number missing: 3, Reason: SWD: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (2), health problems not related to knee pain (2).

Protocol outcome 2: Pain at > 3 months
- Actual outcome: WOMAC pain at 6 months; Group 1: mean 3.4 (SD 3.4); n=31, Group 2: mean 4.5 (SD 4); n=32; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported IFCs: 3.4 (2.2-4.6). Reported SWD: 4.5 (3.1-5.9). Baseline IFCs: 13.6 (4.3). Baseline SWD: 14.0 (4.5).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 4, Reason: IFC: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (1), not enough time to attend (3).; Group 2 Number missing: 4, Reason: SWD: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (2), health problems not related to knee pain (2).

Protocol outcome 3: Physical function at </= 3 months
- Actual outcome: WOMAC function at 3 months; Group 1: mean 8.1 (SD 11.1); n=31, Group 2: mean 11.4 (SD 12.4); n=32; WOMAC function 0-68 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported IFCs: 8.1 (4.0-12.0). Reported SWD: 11.4 (7.1-15.8). Baseline IFCs: 42.7 (12.9). Baseline SWD: 41.1 (10.7).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 3, Reason: IFC: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (1), not enough time to attend (3).; Group 2 Number missing: 3, Reason: SWD: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (2), health problems not related to knee pain (2).

Protocol outcome 4: Physical function at > 3 months
- Actual outcome: WOMAC function at 6 months; Group 1: mean 8.5 (SD 11.1); n=31, Group 2: mean 9.9 (SD 13.2); n=32; WOMAC function 0-68 Top=High

is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported IFCs: 8.5 (4.6-12.4). Reported SWD: 9.9 (5.3-14.6). Baseline IFCs: 42.7 (12.9). Baseline SWD: 41.1 (10.7).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 4, Reason: IFC: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (1), not enough time to attend (3).; Group 2 Number missing: 4, Reason: SWD: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (2), health problems not related to knee pain (2).

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus SHAM ELECTROTHERAPY - SWD

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 3 months; Group 1: mean 3.6 (SD 3.5); n=32, Group 2: mean 4.9 (SD 4); n=31; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported SWD: 4.9 (3.5-6.3). Reported sham SWD: 3.6 (2.4-4.8). Baseline SWD: 14.0 (4.5). Baseline sham SWD: 13.7 (3.8).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 3, Reason: SWD: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (2), health problems not related to knee pain (2).; Group 2 Number missing: 3, Reason: Sham SWD: 3 withdrawals by 3 months, 7 by 6 months. Reasons: Worsening of symptoms (5), not enough time to attend (2)

Protocol outcome 2: Pain at > 3 months
- Actual outcome: WOMAC pain at 6 months; Group 1: mean 4.5 (SD 4); n=32, Group 2: mean 3.5 (SD 3.8); n=31; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported SWD: 4.5 (3.1-5.9). Reported sham SWD: 3.5 (2.2-4.8). Baseline SWD: 14.0 (4.5). Baseline sham SWD: 13.7 (3.8).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 4, Reason: SWD: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (2), health problems not related to knee pain (2).; Group 2 Number missing: 7, Reason: Sham SWD: 3 withdrawals by 3 months, 7 by 6 months. Reasons: Worsening of symptoms (5), not enough time to attend (2)

Protocol outcome 3: Physical function at </= 3 months
- Actual outcome: WOMAC function at 3 months; Group 1: mean 11.4 (SD 12.4); n=32, Group 2: mean 10.3 (SD 10.7); n=31; WOMAC function 0-68 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported SWD: 11.4 (7.1-15.8). Reported sham SWD: 19.3 (6.6-14.0). Baseline SWD: 41.1 (10.7). Baseline sham SWD: 41.2 (10.7).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 3, Reason: SWD: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (2), health problems not

related to knee pain (2).; Group 2 Number missing: 3, Reason: Sham SWD: 3 withdrawals by 3 months, 7 by 6 months. Reasons: Worsening of symptoms (5), not enough time to attend (2) Protocol outcome 4: Physical function at > 3 months - Actual outcome: WOMAC function at 6 months; Group 1: mean 9.9 (SD 13.2); n=32, Group 2: mean 9.9 (SD 10.1); n=31; WOMAC function 0-68 Top=High is poor outcome; Comments: Reported MD and 95% confidence intervals. Reported SWD: 9.9 (5.3-14.6). Reported sham SWD: 9.9 (6.4-13.4). Baseline SWD: 41.1 (10.7). Baseline sham SWD: 41.2 (10.7). Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 4, Reason: SWD: 3 withdrawals by 3 months, 4 by 6 months. Reasons: Worsening of symptoms (2), health problems not related to knee pain (2).; Group 2 Number missing: 7, Reason: Sham SWD: 3 withdrawals by 3 months, 7 by 6 months. Reasons: Worsening of symptoms (5), not enough time to attend (2)	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Bagnato 2016[27]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=60)
Countries and setting	Conducted in Italy; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 1 month
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: A diagnosis of primary osteoarthritis of the knee according to the American College of Rheumatology criteria, including radiological evidence of osteoarthritis
Stratum	Overall
Subgroup analysis within study	Not applicable:
Inclusion criteria	A diagnosis of primary osteoarthritis of the knee according to the American College of Rheumatology criteria, including radiological evidence of osteoarthritis; age >40 years; symptomatic disease for at least 6 months prior to enrolment; persistent pain despite receiving the maximal tolerated doses of conventional medical therapy, including paracetamol and/or an NSAID; with persistent pain defined as a minimal score of 40mm on a 0-100 VAS; daily pain during the month prior to study enrolment; ability to attend follow-up appointments; no change in pain medication during the last month
Exclusion criteria	People with secondary causes of osteoarthritis; DIP joint osteoarthritis; local or systemic injection; secondary fibromyalgia; diabetes mellitus; systemic arthritis; coagulopathy; people on anti-coagulant therapy and people who had received previous intra-articular steroid injection or with avascular necrosis of the bone.
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 67.7 (10.9). Gender (M:F): 17:43. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Not stated Duration of symptoms (mean [SD]): 12.1 (8.2) years.
Indirectness of population	No indirectness
Interventions	(n=33) Intervention 1: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. Pulsed electromagnetic field therapy using an ActiPatch device that emits a safe form of non-ionizing electromagnetic radiation with a carrier frequency of 27.12MHz. The pulse rate was 100Hz with a 100 µs burst width. The peak burst

	output power of the 12cm antenna was around 0.0098W covering a surface area of 103cm². The circuit was low voltage (3V). . Duration 4 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=33) Intervention 2: Sham electrotherapy. Sham electrotherapy (using a device that did not emit any fields). Duration 4 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Equipment / drugs provided by industry (Bioelectronics Corporation provided both the pulsed electromagnetic fields and placebo devices)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: SF-36 physical health component at 4 weeks; Group 1: mean 55.8 (SD 6.1); n=30, Group 2: mean 53.1 (SD 6.2); n=33; SF-36 physical component 0-100 Top=High is good outcome; Comments: Baseline PEMF: 52 (7.4). Baseline placebo: 52.2 (6.2).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, gender, BMI, analgesic use, disease duration and baseline values of outcomes; Group 1 Number missing: 3, Reason: 3 lost to follow up; Group 2 Number missing: 3, Reason: 3 lost to follow up
- Actual outcome: SF-36 mental health component at 4 weeks; Group 1: mean 43.8 (SD 3.6); n=30, Group 2: mean 43.6 (SD 4.7); n=30; SF-36 mental component 0-100 Top=High is good outcome; Comments: Baseline PEMF: 40.4 (5.8). Baseline placebo: 41.8 (6.0).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, gender, BMI, analgesic use, disease duration and baseline values of outcomes; Group 1 Number missing: 3, Reason: 3 lost to follow up; Group 2 Number missing: 3, Reason: 3 lost to follow up

Protocol outcome 2: Pain at </= 3 months
- Actual outcome: WOMAC pain at 4 weeks; Group 1: mean 21.6 (SD 9.6); n=30, Group 2: mean 26.8 (SD 8.2); n=30; WOMAC pain 0-50 Top=High is poor outcome; Comments: Baseline PEMF: 28.2 (9.9). Baseline placebo: 27.6 (7.4).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, gender, BMI, analgesic use, disease duration and baseline values of outcomes; Group 1 Number missing: 3, Reason: 3 lost to follow up; Group 2 Number missing: 3, Reason: 3 lost to follow up

Protocol outcome 3: Physical function at </= 3 months
- Actual outcome: WOMAC function at 4 weeks; Group 1: mean 81.7 (SD 37.9); n=30, Group 2: mean 89.7 (SD 34.4); n=30; WOMAC function 0-180 Top=High is poor outcome; Comments: Baseline PEMF: 97.6 (39.9). Baseline placebo: 91.2 (36.7).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, gender, BMI, analgesic use, disease duration and baseline values of outcomes; Group 1 Number missing: 3, Reason: 3 lost to follow up; Group 2 Number missing: 3, Reason: 3 lost to follow up

Protocol outcomes not reported by the study	Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Basford 1987[29]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=81)
Countries and setting	Conducted in USA; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 3 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Symptomatic osteoarthritis of the thumb
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with symptomatic osteoarthritis of the thumb who had been on the same medication schedule for at least 2 months and had a stable level of activity
Exclusion criteria	Pregnancy, light sensitivity, unavailable for treatment three times a week for three consecutive weeks
Recruitment/selection of patients	People were recruited by advertisements in local newsletters
Age, gender and ethnicity	Age - Other: Mean: 59.1. Gender (M:F): Not stated. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis without imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Thumb
Extra comments	Severity: Not stated Duration of symptoms (mean): 9.1 years
Indirectness of population	No indirectness
Interventions	(n=47) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. Irradiation with a 0.9mw continuous wave Helium-Neon (632.8nm) laser via fiberoptic delivery system. This took place three times a week for three weeks.. Duration 3 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=34) Intervention 2: Sham electrotherapy. Sham laser therapy (a concealed switch is switched to make it turn the laser off). Duration 3 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Equipment / drugs provided by industry (Equipment supplied by Dynatronics and Glendale Optical Company)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Mild adverse events at </= 3 months - Actual outcome: Tingling over the distal superficial radial nerve distribution and mild erythema at 3 weeks; Group 1: 1/47, Group 2: 1/34; Comments: 1 person experienced tingling over the distal superficial radial nerve distrubtion. 1 experienced mild erythema in the treated area that lasted less than a day. No information about which person (and which group) the effects belong to. Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, duration of symptoms and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at </= 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Brosseau 2005[35]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=88)
Countries and setting	Conducted in Canada; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 6 weeks, additional follow up to 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis made by rheumatologists and consistent with the clinical criteria as set out by the American College of Rheumatology classification of osteoarthritis of the hand, the radiologic criteria according to Kallman and the disease activity criteria according to the Doyle Articular Index
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Met the diagnostic criteria of definite osteoarthritis of the hand and have experienced pain symptoms for at least 3 months; be between 45 and 80 years old; have a level of pain of at least 4/10 on a VAS at the time of study entry; display X-ray evidence of joint space narrowing of the hands; be ambulatory and able to be treated as an out-patient; be available for the study treatment schedule; be able to understand English or French instructions, have adequate concentration, and be oriented with respect to time and to place
Exclusion criteria	Participants' unwillingness or an inability to cooperate; other orthopaedic, rheumatological diseases or evidence of chondrocalcinosis; any prior surgery for the finger joints; any acute disease, uncontrolled diabetes mellitus, untreated hypertension, neurological deficits (motor or sensory), or other mental disorders; any anticipated start, stop or change in type or dosage of prescribed initial analgesic medication during the study; current rehabilitation treatment or any other pain-related treatment besides medication for osteoarthritis; previous experience with low level laser therapy; corticosteroid injection of finger joints within the last 12 months; pregnancy, photosensitivity, or cancer; plans to move within 6 months
Recruitment/selection of patients	People were recruited from different rheumatology treatment facilities in the Ottawa-Carleton area including the Ottawa Hospital, private clinics and the Arthritis Society
Age, gender and ethnicity	Age - Mean (SD): 64.7 (10.1). Gender (M:F): 19:69. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Hand

Extra comments	Severity: Not stated Duration of symptoms (mean [SD]): 8.0 (8.3) years
Indirectness of population	No indirectness
Interventions	(n=42) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. Active low level laser therapy using a gallium aluminium arsenide laser on painful joints and superficial nerves innervating the painful joints. Used an Eriel laser, top laser 250, class IIIb. The active medium produced a wavelength of 860nm with a programmable pulse repetition rate from 1 to 9999Hz. The chosen modulation was 20Hz. At the end of the aperture, the average output power was 60mW with the size of the area treated being 0.01cm². The power density of the laser apparatus delivered in a modulated mode was 3W/cm². The energy density per point irradiated was 3J/cm². A total of 15 points were irradiated on three specific nerves (three points respectively for the proximal and distal aspects of each nerve, except the radial nerve which is deep in the distal aspect). In addition, each painful joint received four 1 second treatments in the 12, 3, 6 and 9 o'clock positions. Treatment sessions were three times a week for 6 weeks, each session lasted 20 minutes.. Duration 6 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=46) Intervention 2: Sham electrotherapy. Sham laser therapy using the same device with the emitter replaced with a dummy emitter. Duration 6 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Academic or government funding (Funding from the Ontario Arthritis Society (contract grant number TAS-302), Ontario Ministry of Health and Long-Term Care (contract grant number HRPD-05225), University Research Chair, Ministry of Human Resources)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: AUSCAN pain score at 3 months; Group 1: mean -0.48 (SD 0.71); n=41, Group 2: mean -0.29 (SD 0.71); n=45; AUSCAN pain 0-4 Top=High is poor outcome; Comments: Baseline laser: 2.36 (0.63). Baseline sham: 2.10 (0.65).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, dominant hand, affected hand, family history of arthritis, taking medication for arthritis, diagnosis time, and baseline values of outcomes; Group 1 Number missing: 1, Reason: Reasons not given; Group 2 Number missing: 1, Reason: Reasons not given

Protocol outcome 2: Pain at > 3 months

- Actual outcome: AUSCAN pain score at 6 months; Group 1: mean -0.41 (SD 0.83); n=41, Group 2: mean -0.35 (SD 0.71); n=45; AUSCAN pain 0-4 Top=High is poor outcome; Comments: Baseline laser: 2.36 (0.63). Baseline sham: 2.10 (0.65). Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, dominant hand, affected hand, family history of arthritis, taking medication for arthritis, diagnosis time, and baseline values of outcomes; Group 1 Number missing: 1, Reason: Reasons not given; Group 2 Number missing: 1, Reason: Reasons not given Protocol outcome 3: Physical function at </= 3 months - Actual outcome: AUSCAN function score at 3 months; Group 1: mean -0.35 (SD 0.71); n=41, Group 2: mean -0.31 (SD 0.82); n=45; AUSCAN function 0-4 Top=High is poor outcome; Comments: Baseline laser: 2.22 (0.86). Baseline sham: 2.06 (0.70). Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, dominant hand, affected hand, family history of arthritis, taking medication for arthritis, diagnosis time, and baseline values of outcomes; Group 1 Number missing: 1, Reason: Reasons not given; Group 2 Number missing: 1, Reason: Reasons not given Protocol outcome 4: Physical function at > 3 months - Actual outcome: AUSCAN function score at 6 months; Group 1: mean -0.38 (SD 0.74); n=41, Group 2: mean -0.34 (SD 0.75); n=45; AUSCAN function 0-4 Top=High is poor outcome; Comments: Baseline laser: 2.22 (0.86). Baseline sham: 2.06 (0.70). Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, dominant hand, affected hand, family history of arthritis, taking medication for arthritis, diagnosis time, and baseline values of outcomes; Group 1 Number missing: 1, Reason: Reasons not given; Group 2 Number missing: 1, Reason: Reasons not given Protocol outcome 5: Mild adverse events at </= 3 months - Actual outcome: Experienced any adverse events at 6 weeks; Group 1: 2/31, Group 2: 0/33 Risk of bias: All domain - Very high, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, dominant hand, affected hand, family history of arthritis, taking medication for arthritis, diagnosis time, and baseline values of outcomes; Group 1 Number missing: 11, Reason: Reasons not given; Group 2 Number missing: 13, Reason: Reasons not given Protocol outcome 6: Mild adverse events at > 3 months - Actual outcome: Experienced any adverse events at 6 months; Group 1: 0/32, Group 2: 0/34 Risk of bias: All domain - Very high, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, dominant hand, affected hand, family history of arthritis, taking medication for arthritis, diagnosis time, and baseline values of outcomes; Group 1 Number missing: 10, Reason: Reasons not given; Group 2 Number missing: 12, Reason: Reasons not given	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months;

	Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Bruce-brand 2012[36]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=41)
Countries and setting	Conducted in Irish Republic; Setting: Outpatient follow up
Line of therapy	1st line
Duration of study	Intervention + follow up: 14 weeks (6 weeks of intervention)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Symptomatic moderate to severe knee osteoarthritis confirmed radiographically as Kellgren Lawrence grade 3-4
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with arthroscopically diagnosed grade 3 or 4 osteoarthritis on the Outerbridge scale within the last 2 years, or were placed within the last 6 months on the waiting list for knee replacement surgery with the indication of osteoarthritis, confirmed radiographically with kellgren-Lawrence severity grades of 3 or 4.
Exclusion criteria	Medical co-morbidities precluding participation in an exercise program; implanted electrical devices; neurological disorders; inflammatory arthritis; non-ambulatory status; significant cognitive impairment; participation in an exercise program within the last 6 months; involvement in a previous similar study; anticoagulant therapy; recent or imminent surgery (within 3 months).
Recruitment/selection of patients	People were recruited from the arthroscopy database and knee arthroplasty waiting list from Cappagh National Orthopaedic Hospital
Age, gender and ethnicity	Age - Mean (SD): 64.0 (5.4). Gender (M:F): 15:11. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 3-4 Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=14) Intervention 1: Non-invasive electrotherapy interventions - Neuromuscular electrical stimulation. Neuromuscular electrical stimulation. The group undertook a single 20 minute unsupervised session of the affected quadriceps femoris muscle, 5 days per week for 6 weeks. Bilateral NMES was available for bilateral symptoms. People were instructed to train at the same time of day to ensure adequate muscle recovery. Each stimulation cycle comprised a 10s contraction period, and a 50s

	relaxation period, excluding the 1s ramp-up and 0.5s ramp-down. This provided a total contraction time of 3 min 20s in each 20 min session. This was provided through a portable, battery powered garment based stimulator. The stimulator provided a symmetrical bi-phasic square waveform, with a maximum root mean square output current of 18mA and an output frequency of 50Hz. Pulse width changes dynamically during the stimulation cycle between 100-400 microseconds. Four reusable adhesive hydrogel electrodes, having surface areas of 194cm², 83cm², 74cm², 66cm² respectively were attached to the deep surface of the garment and conduct impulses to the vasti and rectus femoris muscles. People wee instructed to perform the training in the seated position with the knee flexed to 60 degrees, the foot flat on the floor and the toes pressed against a wall to achieve isometric muscle contraction and to increase the stimulation intensity to the maximally tolerated level.. Duration 6 weeks (follow up for 14 weeks). Concurrent medication/care: Standard care was available to all including osteoarthritis education, weight loss, pharmacologic therapy and physical therapy. Indirectness: No indirectness (n=13) Intervention 2: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. No treatment. Duration 14 weeks. Concurrent medication/care: Standard care was available to all including osteoarthritis education, weight loss, pharmacologic therapy and physical therapy. Indirectness: No indirectness (n=14) Intervention 3: No intervention - No treatment. Supervised strength exercise. Duration 14 weeks. Concurrent medication/care: Standard care was available to all including osteoarthritis education, weight loss, pharmacologic therapy and physical therapy. Indirectness: No indirectness Comments: This group was not included in this review as it was not a comparison stated i n the protocol
Funding	Study funded by industry (This study was supported by a grant from the Cappagh Hospital Trust. The Kneehab stimulators were provided by Bio-Medical Research Ltd, Galway, Ireland. Neither sponsor had any involvement in the design of the study, in the collection, analysis and interpretation of data; in the writing of the manuscript; or in the decision to submit the manuscript for publication)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NEUROMUSCULAR ELECTRICAL STIMULATION versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT

Protocol outcome 1: Health-related quality of life at </= 3 months

- Actual outcome: SF-36 physical health at 14 weeks; Group 1: mean 47.6 (SD 10.73); n=10, Group 2: mean 67.83 (SD 21.71); n=6; SF-36 physical health 0-100 Top=High is good outcome; Comments: Baseline NMES: 39.25 (6.95). Baseline no treatment: 51.78 (24.34). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in SF-36 physical health and WOMAC scores; Group 1 Number missing: 4, Reason: 1 unwell, 1 spouse hospitalised, 2 underwent TKR; Group 2 Number missing: 7, Reason: 3 unwell, 1 personal reason, 2 underwent TKR, 1 away abroad - Actual outcome: SF-36 mental health at 14 weeks; Group 1: mean 65.4 (SD 12.98); n=10, Group 2: mean 70.5 (SD 22.4); n=6; SF-36 mental health 0-100 Top=High is good outcome; Comments: Baseline NMES: 60.67 (26.45). Baseline no treatment: 62.00 (25.41). Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in SF-36 physical health and WOMAC scores; Group 1 Number missing: 4, Reason: 1 unwell, 1 spouse hospitalised, 2 underwent TKR; Group 2 Number missing: 7, Reason: 3 unwell, 1 personal reason, 2 underwent TKR, 1 away abroad Protocol outcome 2: Pain at </= 3 months - Actual outcome: WOMAC pain at 14 weeks; Group 1: mean 8.5 (SD 2.72); n=10, Group 2: mean 8.33 (SD 4.08); n=6; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline NMES: 11.50 (3.50). Baseline no treatment: 9.00 (3.65). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in SF-36 physical health and WOMAC scores; Group 1 Number missing: 4, Reason: 1 unwell, 1 spouse hospitalised, 2 underwent TKR; Group 2 Number missing: 7, Reason: 3 unwell, 1 personal reason, 2 underwent TKR, 1 away abroad Protocol outcome 3: Physical function at </= 3 months - Actual outcome: WOMAC physical function at 14 weeks; Group 1: mean 31.5 (SD 12.63); n=10, Group 2: mean 21.67 (SD 18.9); n=6; WOMAC function 0-68 Top=High is poor outcome; Comments: Baseline NMES: 41.04 (11.60). Baseline no treatment: 31.67 (17.95). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in SF-36 physical health and WOMAC scores; Group 1 Number missing: 4, Reason: 1 unwell, 1 spouse hospitalised, 2 underwent TKR; Group 2 Number missing: 7, Reason: 3 unwell, 1 personal reason, 2 underwent TKR, 1 away abroad	
Protocol outcomes not reported by the study	Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Bulow 1994[37]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=27)
Countries and setting	Conducted in Denmark; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 9 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Clinically and x-ray verified uni- or bilateral osteoarthritis of the knee with exercise induced pain for at least 6 months
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Clinically and x-ray verified uni- or bilateral osteoarthritis of the knee suffering from exercise induced pain of at least 6 months duration. The x-ray verification was based on the assessment by a radiologist of a standard anteroposterior radiograph. The people had to have at least five periarticular tender points and demonstrate ability to fill in the pain questionnaire.
Exclusion criteria	People who had received intra- or periarticular injection therapy, physiotherapy or who had changed medication (NSAID/analgesics) during the last 5 weeks. People with secondary arthrosis due to inflammatory joint disease and people in whom routine medical examination indicated other causes for knee-related pain (osteoarthritis of the hip, arterial insufficiency, lumbar root compression).
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Median (range): 74 (60-86). Gender (M:F): 5:24. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years (Mixed realistically). 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Not stated Duration of symptoms: At least 6 months
Indirectness of population	No indirectness
Interventions	(n=13) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. An active laser that was a Ga-Al-As infra-red laser, class 3B, wavelength 830nm, mean effect 25mW, continuous beam, with an irradiation area of the diodes of 0.28cm². The people received a total of nine treatments, 2-4 per week over 3 weeks.. Duration 3 weeks. Concurrent medication/care: Analgesics and NSAIDs were permitted including weak simple analgesics, NSAIDs and dextropropoxifen and opioids. These were noted

	for each participant.. Indirectness: No indirectness (n=14) Intervention 2: Sham electrotherapy. Placebo laser (laser was switched off). Duration 3 weeks. Concurrent medication/care: Analgesics and NSAIDs were permitted including weak simple analgesics, NSAIDs and dextropropoxifen and opioids. These were noted for each participant.. Indirectness: No indirectness
Funding	Academic or government funding (This study was sponsored by Henny and Helge Holgersen's Foundation and the Bodil Petersen Foundation)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Mild adverse events at </= 3 months - Actual outcome: Adverse events at 9 weeks; Group 1: 0/13, Group 2: 0/14 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at </= 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Burch 2008[38]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=116)
Countries and setting	Conducted in USA; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 8 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Evidence of osteoarthritis in more than one joint based on a physician's assessment of patient-reported symptoms and a differential diagnosis of radiographic evidence
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Evidence of osteoarthritis in more than one joint based on a physician's assessment of patient-reported symptoms and a differential diagnosis or radiographic evidence; radiographic evidence indicative of cartilage remaining in the entire knee and no bone-on-bone contact within 6 months of enrollment; osteoarthritis pain present more days than not in the knee chosen to receive electrical stimulation, and the overall pain VAS rating of at least 40mm on a 100mm line; osteoarthritis stiffness present more days than not in the knee chosen to receive electrical stimulation, and typically lasting less than 30 minutes; agreement to follow the treatment plan and to use the stimulation device; older than 18; signing the informed consent form
Exclusion criteria	Hypersensitivity to electrostimulation; had intra-articular injections within 3 months to the knee to receive electrostimulation; if taking medications (e.g. oral steroids, on-steroidal anti-inflammatories or paracetamol), the dosage had not been stable for at least 3 months prior to enrollment; if taking chondroprotective supplements (e.g. glucosamine and chondroitin sulfate)m, the dosage had not been stable for at least 3 months prior to enrollment; had pathologic processes causing a structural defect in or instability of the knee at the knee to receive electrostimulation (e.g. congenital defects, anatomical or mechanical deformities, blunt trauma); had cartilage-related surgery in the last 2 years; was pregnant or intended to become pregnant; had known current or remittent malignancy or cancer; had implanted cardiac pacemaker or defibrillator; had a body mass index >45; had serious or uncontrolled systemic illness such as autoimmune disease, rheumatoid arthritis, diabetes mellitus or renal failure; concurrently used another electrical stimulation device for treatment of knee symptoms; previously or concurrently used an RS Medical stimulation device; was recently in another clinical trial for medical devices or biologic agents; had a

	relationship other than medical with principal investigators and their staff; had a relationship other than medical with principal investigators and their staff; had a relationship with another enrolled patient; was unable to complete the study or the case report forms
Recruitment/selection of patients	People were recruited by self-selection (advertisements) and by referral from patient databases from four study sites in the United States
Age, gender and ethnicity	Age - Mean (SD): 61.7 (11.0). Gender (M:F): 30:79. Ethnicity: "American Indian or Alaska native" = 2, African American = 3, Caucasian = 81, Asian = 2, Other = 21
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Not stated / Unclear (Mixed, may have been clinical or radiographic). 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Other (All had knee, around 61% had other types of osteoarthritis as well).
Extra comments	Severity: Not stated Duration of symptoms (mean [SD]): 8.3 (7.9) years
Indirectness of population	No indirectness
Interventions	(n=57) Intervention 1: Non-invasive electrotherapy interventions - Interferential therapy. Interferential therapy plus patterned stimulation. 15 minutes of IF stimulation with a base frequency of 500Hz and a premodulated beat frequency sweeping between 1 and 150Hz. Followed by 20 minutes of patterned muscle stimulation, delivered as 50Hz impulses for 200ms every 1500ms with a biphasic square waveform with a fixed amplitude of 50mA, stimulation intensity controlled by varied pulse width ranging from 3.39 to 102.2 microseconds. The electrodes were placed in the same position for both. One session daily.. Duration 8 weeks. Concurrent medication/care: Stable doses of medications were permitted. Indirectness: No indirectness (n=59) Intervention 2: Non-invasive electrotherapy interventions - Transcutaneous electrical nerve stimulation (TENS). Low current TENS for 35 minutes. Delivered as a biphasic square wave with a 0.2Hz frequency and a fixed amplitude of 60mA, and a pulse width adjusted to provide a net output of 73nC. Delivered across 300 microseconds, equivalent to a peak output of 0.5mA. The stimulation might be perceived but would not produce a muscular contraction. One session daily.. Duration 8 weeks. Concurrent medication/care: Stable doses of medications were permitted. Indirectness: No indirectness
Funding	Study funded by industry (The study was funded by RS Medical)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTERFERENTIAL THERAPY versus TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS)

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 8 weeks; MD; -2.02 (Standard error: 0.64) WOMAC pain 0-20 Top=High is poor outcome, Comments: Reported mean difference and 98.5% confidence intervals. Instead used change score to calculate SE. Reported: 2.02 (0.60-3.57) (in high is good form). P- value = 0.002. n1 = 52. n2 = 53.;
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports gender, age, weight, height, BMI, race, work status, knee treated, length of treatment, osteoarthritis in other joints, prior treatments and baseline values of outcomes; Group 1 Number missing: 7, Reason: 7 dropped out due to a mixture of adverse events, lack of adherence to treatment, lack of efficacy, loss to follow-up and patient decision; Group 2 Number missing: 9, Reason: 9 dropped out due to a mixture of adverse events, lack of adherence to treatment, lack of efficacy, loss to follow-up and patient decision

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function at 8 weeks; MD; -6.12 (Standard error: 2.01) WOMAC 0-68 Top=High is poor outcome, Comments: Reported mean difference and 98.5% confidence intervals. Instead used change score to calculate SE. Reported: 6.12 (1.57-10.66) (in high is good form). P- value = 0.003. n1 = 52. n2 = 53.;
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports gender, age, weight, height, BMI, race, work status, knee treated, length of treatment, osteoarthritis in other joints, prior treatments and baseline values of outcomes; Group 1 Number missing: 7, Reason: 7 dropped out due to a mixture of adverse events, lack of adherence to treatment, lack of efficacy, loss to follow-up and patient decision; Group 2 Number missing: 9, Reason: 9 dropped out due to a mixture of adverse events, lack of adherence to treatment, lack of efficacy, loss to follow-up and patient decision

Protocol outcome 3: Mild adverse events at </= 3 months
- Actual outcome: Skin irritation, skin burns, muscle soreness, electrical shock and unanticipated adverse events at 8 weeks; Group 1: 5/57, Group 2: 9/59
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports gender, age, weight, height, BMI, race, work status, knee treated, length of treatment, osteoarthritis in other joints, prior treatments and baseline values of outcomes; Group 1 Number missing: 7, Reason: 7 dropped out due to a mixture of adverse events, lack of adherence to treatment, lack of efficacy, loss to follow-up and patient decision; Group 2 Number missing: 9, Reason: 9 dropped out due to a mixture of adverse events, lack of adherence to treatment, lack of efficacy, loss to follow-up and patient decision

Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months;

	Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Cakir 2014[40]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=60)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: Treatment for 2 weeks, follow up for 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosed knee osteoarthritis according to the American College of Rheumatology, confirmed with radiologically grade 2-3 Kellgren Lawrence changes
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Outpatients with knee pain for at least 6 months, diagnosed with knee osteoarthritis, confirmed with radiological grade 2-3 Kellgren Lawrence changes, aged 40-80 years
Exclusion criteria	An experience of any physical therapy agent, intra-articular corticosteroid therapy or chondroprotective agents during the 30 days prior to the study or viscosupplementation treatment within 6 months prior to the study; people with a diagnosis of joint infection, neoplasm, diabetes mellitus, paresis, osteonecrosis, recent trauma, ascertained/suspected pregnancy or lactating and poor general health; history of contraindication of heat therapy or previous major surgery
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 57.4 (8.9). Gender (M:F): 13:47. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 2-3 Duration of symptoms (mean [SD]): 4.5 (3.7) years
Indirectness of population	No indirectness
Interventions	(n=40) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. Continuous ultrasound or pulsed ultrasound using a 5cm² head ultrasound device for 5 times a week for 2 weeks by the same device and physiotherapist. Continuous ultrasound was administered at the frequency of 1MHz with an intensity of 1W/cm². Pulse ultrasound was used for same frequency and intensity on 1:4 pulse ratios. Each treatment was continued for approximately 12 minutes over the painful area in the knee region with full contact in a supine position.. Duration 2 weeks. Concurrent

	medication/care: All people were instructed to perform a home exercise program (including quadriceps isometric exercise, muscle strength exercises and stretching exercises of the lower extremity muscles) at least 3 times per week. During the therapy period and within 1 week before people weren't allowed to take non-steroid antiinflammatory drugs. Paracetamol up to 2000mg/day was allowed. Other drugs for systemic diseases were not stopped.. Indirectness: No indirectness Comments: These two groups were combined together due to class effect as agreed in the protocol (n=20) Intervention 2: Sham electrotherapy. Sham ultrasound using a 5cm² head ultrasound device for 5 times a week for 2 weeks by the same device and physiotherapist. The same as the other procedures except the power switch was off.. Duration 2 weeks. Concurrent medication/care: All people were instructed to perform a home exercise program (including quadriceps isometric exercise, muscle strength exercises and stretching exercises of the lower extremity muscles) at least 3 times per week. During the therapy period and within 1 week before people weren't allowed to take non-steroid antiinflammatory drugs. Paracetamol up to 2000mg/day was allowed. Other drugs for systemic diseases were not stopped.. Indirectness: No indirectness
Funding	Academic or government funding (Equipment and financial support were provided by Ege University for this project)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 2 weeks; Group 1: mean -6.2 (SD 6); n=40, Group 2: mean -4.3 (SD 7.2); n=20; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported mean differences and 95% confidence intervals. Continuous and pulsed ultrasound groups were pooled. Reported continuous ultrasound: 7.4 (4.8-10.0). Reported pulsed ultrasound: 5.0 (2.4-7.6). Reported sham: 4.3 (1.4-7.7). Baseline continuous ultrasound: 15.9 (4.3). Baseline pulsed ultrasound: 14.5 (3.1). Baseline sham ultrasound: 14.9 (4.3).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI, duration, side affected and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Pain at > 3 months
- Actual outcome: VAS pain on movement at 6 months; Group 1: mean -35.5 (SD 15.1); n=40, Group 2: mean -34.1 (SD 12.3); n=20; VAS pain on movement 0-100 Top=High is poor outcome; Comments: Reported mean differences and 95% confidence intervals. Continuous and pulsed ultrasound groups were pooled. Reported continuous ultrasound: 36.8 (26.8-42.0). Reported pulsed ultrasound: 35.5 (29.8-39.2). Reported sham: 34.1 (28.6-39.4). Baseline continuous ultrasound: 75.5 (18.3). Baseline pulsed ultrasound: 73.0 (19.9). Baseline sham ultrasound: 72.2 (21.8). Does not report the mean difference for WOMAC pain for the continuous ultrasound group only, so extracted VAS pain on movement instead.

Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI, duration, side affected and baseline values of outcomes; Group 1 Number missing: 1, Reason: 1 withdrew due to health problems not related to knee pain; Group 2 Number missing: 1, Reason: 1 not enough time to attend Protocol outcome 3: Physical function at </= 3 months - Actual outcome: WOMAC function at 2 weeks; Group 1: mean -17.7 (SD 6); n=40, Group 2: mean -13.6 (SD 5.9); n=20; WOMAC function 0-68 Top=High is poor outcome; Comments: Reported mean differences and 95% confidence intervals. Continuous and pulsed ultrasound groups were pooled. Reported continuous ultrasound: 20.1 (17.8-22.4). Reported pulsed ultrasound: 15.2 (12.7-17.7). Reported sham: 13.6 (11.0-16.2). Baseline continuous ultrasound: 55.7 (13.4). Baseline pulsed ultrasound: 52.4 (11.9). Baseline sham ultrasound: 52.5 (15.4). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI, duration, side affected and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 4: Physical function at > 3 months - Actual outcome: WOMAC function at 6 months; Group 1: mean -19.2 (SD 10.6); n=40, Group 2: mean -17 (SD 6.6); n=20; WOMAC function 0-68 Top=High is poor outcome; Comments: Reported mean differences and 95% confidence intervals. Continuous and pulsed ultrasound groups were pooled. Reported continuous ultrasound: 23.1 (17.9-28.3). Reported pulsed ultrasound: 15.3 (12.1-18.5). Reported sham: 17.0 (14.2-20.0). Baseline continuous ultrasound: 55.7 (13.4). Baseline pulsed ultrasound: 52.4 (11.9). Baseline sham ultrasound: 52.5 (15.4). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI, duration, side affected and baseline values of outcomes; Group 1 Number missing: 1, Reason: 1 withdrew due to health problems not related to knee pain; Group 2 Number missing: 1, Reason: 1 not enough time to attend	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Callaghan 2005[41]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=30)
Countries and setting	Conducted in United Kingdom; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Primary generalised osteoarthritis and a diagnosis of osteoarthritis knee with radiographic evidence (Kellgren Lawrence grade 3-4)
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Primary generalised osteoarthritis and a diagnosis of osteoarthritis knee with radiographs showing Kellgren Lawrence grade 3-4 changes.
Exclusion criteria	People with Kellgren Lawrence grades 0-2 changes; a diagnosis of inflammatory joint disease (confirmed by blood tests); or an intraarticular corticosteroid injection in any joint 8 weeks prior to the first scan that may suppress the classic features of inflammation
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 60.4 (7.7). Gender (M:F): 14:13. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 3-4 Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. Short wave therapy including two groups: active high frequency (27 mHz) pulsed shortwave for 20 minutes to the affected knee joint using a dose of 200 microseconds and 400 pulses per second with an output of 10W or active high frequency (27mHz) pulsed shortwave for 20 minutes at a dose of 400 microseconds and 400 pulses per second, with an output of 20W.. Duration 2 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=10) Intervention 2: Sham electrotherapy. Sham pulsed short-wave treatment for 20

	minutes. Duration 2 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Academic or government funding (Funding from RLUH Hospital Trust Fund, Physiotherapy Research Foundation, UK. Equipment from Robert Graham.)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Health-related quality of life at </= 3 months - Actual outcome: AIMS at 2 weeks; Group 1: mean 5.3 (SD 2.7); n=18, Group 2: mean 5.1 (SD 1.7); n=9; AIMS 0-10 Top=High is poor outcome; Comments: High dose and low dose groups merged. Reported high dose: 5.1 (2.3). Reported low dose: 5.5 (3). Reported placebo: 5.1 (1.7). Baseline high dose: 5.1 (2.1). Baseline low dose: 5.2 (2.8). Baseline placebo: 5.3 (1.4). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, BMI, test side, radiographic severity, and baseline values of outcomes; Group 1 Number missing: 2, Reason: Overall: 2 people failed to attend assessments, 1 person failed to attend scan and 2 people failed to attend treatment leading to 3 people being excluded; Group 2 Number missing: 1, Reason: Overall: 2 people failed to attend assessments, 1 person failed to attend scan and 2 people failed to attend treatment leading to 3 people being excluded Protocol outcome 2: Pain at </= 3 months - Actual outcome: VAS at 2 weeks; Group 1: mean 5.3 (SD 3); n=18, Group 2: mean 6.3 (SD 1.9); n=9; VAS 0-10 Top=High is poor outcome; Comments: High dose and low dose groups merged. Reported high dose: 5.5 (2.7). Reported low dose: 5 (3.2). Reported placebo: 6.3 (1.9). Baseline high dose: 6.5 (2.1). Baseline low dose: 5.2 (3.3). Baseline placebo: 5.8 (1.7). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, BMI, test side, radiographic severity, and baseline values of outcomes; Group 1 Number missing: 2, Reason: Overall: 2 people failed to attend assessments, 1 person failed to attend scan and 2 people failed to attend treatment leading to 3 people being excluded; Group 2 Number missing: 1, Reason: Overall: 2 people failed to attend assessments, 1 person failed to attend scan and 2 people failed to attend treatment leading to 3 people being excluded	
Protocol outcomes not reported by the study	Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	**Cantero-tellez 2020[42]**
Study type	RCT (Patient randomised; Parallel)

Number of studies (number of participants)	(n=43)
Countries and setting	Conducted in Spain; Setting: Private practice, Malaga, Spain.
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 4 week treatment period, 3 month follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR diagnosis of thumb CMC OA in dominant hand with a radiographic stage of 1-2.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Women >18 with a diagnosis of thumb CMC OA in their dominant hand with a radiographic stage of 1-2 according to the ACR, a reported pain intensity during activities of daily living of at least 4/10 on the VAS, the ability to read or understand the patient information leaflets, and the ability to sign a consent form to be included in the study.
Exclusion criteria	Participants were excluded if they had a neurologic disorder affecting the upper limb; had received previous treatment for their hand problem in the last 6 montths, including an intraarticular joint injection to wrist, fingers or thumb; had fractures or a significant hand injury or previous surgery to the wrist, thumb, or hand; had hand or finger tenosynovitis and/ or Dupuytren disease; or were undergoing psychological or medical treatment. Also excluded were participants who suffered a disease where laser treatment is contraindicated (cancer, uncontrolled diabetes mellitus, hypertension) and those whose current medications might interfere with LT treatment (e.g. corticosteroid injections).
Recruitment/selection of patients	Consecutively recruited from February 2017 to June 2017 from the waiting lists of different local hospitals.
Age, gender and ethnicity	Age - Mean (SD): 71 (12) years. Gender (M:F): all female. Ethnicity: not reported
Further population details	1. Age (≤/> 75 years): Not stated / Unclear 2. Diagnosis : Diagnosis with imaging (diagnosis with a radiographic stage of 1-2 according to ACR criteria). 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Thumb (thumb of dominant hand).
Extra comments	. Severity: VAS at baseline: laser group: 6.3 (1.2), sham group: 5.9 (1.1) Duration: not reported
Indirectness of population	No indirectness
Interventions	(n=22) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. The experimental group received the application of laser therapy on a painful, affected joint. A high-level, Class IV K-Laser, Mod. K1200 (Eltech K-Laser S.r.l., Treviso, Italy), was employed for the local laster therapy and placebo treatment. Delivery parameters were established according to the acknowledged guidelines and were peak power 3.0W (duty cycle of 50%, mean power 1.5W), with intense super pulse mode, combined wavelength of 800 +970nM, pulse frequency 2Hz, energy dose 75J per session, spot size 5cm2, and treatment frequency three times per week. The phase time was 15 seconds, with a total treatment time of 45 seconds. The procedure was performed by a physical therapist with experience in laser application in a reserved, noise-free

	room. Laser therapy was applied three times a week for four weeks. The participants were positioned in a seated position. Both the operator and participant wore protective glasses. The skin at the site to be irradiated was cleaned with 70% alcohol. Laser therapy was the only treatment intervention received by participants. The functioning of the laser was verified before the treatment of each patient, and energy source, application points, and energy measurement were checked each time. The laser probe (head size: 4cm2) was applied in a circular motion from the centre toward the outside over both the volar and dorsal aspects of the thumb CMC joint, with skin contact and no pressure. . Duration 4 weeks. Concurrent medication/care: No therapeutic exercises, modalities, or other complementary treatments were provided in order to not interfere with assessment of the individual effectiveness of laser therapy. . Indirectness: No indirectness (n=21) Intervention 2: Sham electrotherapy. The same equipment was used with a pen emitting a red guide light and a warning sound, but without the emission of a laser beam. All conditions including indicator lights and sounds in the laser application were therefore identical in both groups, except the laser irradiation, which was not visible. . Duration 4 weeks. Concurrent medication/care: No therapeutic exercises, modalities, or other complementary treatments were provided in order to not interfere with assessment of the individual effectiveness of laser therapy. . Indirectness: No indirectness
Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: Change in VAS score at 3 months; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: 'neither the investigator nor the participants were aware whether a placebo or active treatment was being administered'; Group 1 Number missing: 4, Reason: not reported; Group 2 Number missing: 4, Reason: notreported	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Cetin 2008[44]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=100)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 8 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Defined by the American College of Rheumatology with radiographic confirmation
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Women with clinical and radiologic diagnoses of knee osteoarthritis.
Exclusion criteria	History of knee surgery, lower-extremity arthroplasty, intra-articular hyaluronic acid or steroids in the last 6 months.
Recruitment/selection of patients	Consecutive outpatients at the department to physical medicine and rehabilitation at the Baskent University in Ankara, Turkey.
Age, gender and ethnicity	Age - Mean (SD): 59.8 (9.2). Gender (M:F): 0:100. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Radiographic grade 1-4, median grade 3
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. Short wave diathermy, hot packs and isokinetic exercise. Applied using a Curapulas 419 at the frequency of 27.12 MHz. The condenser field technique was used for 15 mins as each person sat on a chair and placed their legs on a table with both knees fully extended during treatment. Total of 24 sessions (three times a week for 8 weeks). Duration 8 weeks. Concurrent medication/care: After application of physical agents, each person underwent individual warm up exercises on a stationary bike set for 20 cycles/min for 5 mins before undergoing muscle-strengthening exercises. People were instructed to continue taking any current medications and not to start any new therapies for knee osteoarthritis during the 8 week studies.. Indirectness: No indirectness (n=20) Intervention 2: Non-invasive electrotherapy interventions - Transcutaneous

	electrical nerve stimulation (TENS). Short wave diathermy, hot packs and isokinetic exercise. Applied using a TENS unit set to 60-100Hz, and the pulse duration was set to 60milliseconds. The intensity was set at the point of seeing no contraction while the person felt comfortable. Total of 24 sessions (three times a week for 8 weeks). Duration 8 weeks. Concurrent medication/care: After application of physical agents, each person underwent individual warm up exercises on a stationary bike set for 20 cycles/min for 5 mins before undergoing muscle-strengthening exercises. People were instructed to continue taking any current medications and not to start any new therapies for knee osteoarthritis during the 8 week studies.. Indirectness: No indirectness (n=20) Intervention 3: Non-invasive electrotherapy interventions - Ultrasound. Ultrasound, hot packs and isokinetic exercise. Applied using a Sonopuls 590 us machine was used for continuous ultrasound therapy. A 1MHz US head was used, set to an intensity of 1.5W/cm². US was applied around the knee joint with full contact for 10 minutes. The person remained in the supine position with both knees fully extended while ultrasound was applied. Total of 24 sessions (three times a week for 8 weeks). Duration 8 weeks. Concurrent medication/care: After application of physical agents, each person underwent individual warm up exercises on a stationary bike set for 20 cycles/min for 5 mins before undergoing muscle-strengthening exercises. People were instructed to continue taking any current medications and not to start any new therapies for knee osteoarthritis during the 8 week studies.. Indirectness: No indirectness (n=20) Intervention 4: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. Hot packs and isokinetic exercises only. Duration 8 weeks. Concurrent medication/care: After application of physical agents, each person underwent individual warm up exercises on a stationary bike set for 20 cycles/min for 5 mins before undergoing muscle-strengthening exercises. People were instructed to continue taking any current medications and not to start any new therapies for knee osteoarthritis during the 8 week studies.. Indirectness: No indirectness (n=20) Intervention 5: No intervention - No treatment. Controls. Isokinetic exercise only.. Duration 8 weeks. Concurrent medication/care: After application of physical agents, each person underwent individual warm up exercises on a stationary bike set for 20 cycles/min for 5 mins before undergoing muscle-strengthening exercises. People were instructed to continue taking any current medications and not to start any

	new therapies for knee osteoarthritis during the 8 week studies.. Indirectness: No indirectness Comments: This group was not included as it was not comparable to the other groups.
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS)

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: VAS at 8 weeks; Group 1: mean -2.33 (SD 0.77); n=20, Group 2: mean -2.32 (SD 0.6); n=20; VAS 0-10 Top=High is poor outcome; Comments: Baseline pulsed short-wave: 5.69 (1.55). Baseline TENS: 5.85 (1.34).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, BMI, compliance, severity on radiography and baseline values of outcomes; Group 1 Number missing: -, Reason: 15 people in total throughout the study withdrew; Group 2 Number missing: -, Reason: 15 people in total throughout the study withdrew

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus ULTRASOUND

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: VAS at 8 weeks; Group 1: mean -2.33 (SD 0.77); n=20, Group 2: mean -2.34 (SD 0.94); n=20; VAS 0-10 Top=High is poor outcome; Comments: Baseline pulsed short-wave: 5.69 (1.55). Baseline ultrasound: 5.90 (1.45).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, BMI, compliance, severity on radiography and baseline values of outcomes; Group 1 Number missing: -, Reason: 15 people in total throughout the study withdrew; Group 2 Number missing: -, Reason: 15 people in total throughout the study withdrew

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: VAS at 8 weeks; Group 1: mean -2.33 (SD 0.77); n=20, Group 2: mean -2.27 (SD 0.88); n=20; VAS 0-10 Top=High is poor outcome; Comments: Baseline pulsed short-wave: 5.69 (1.55). Baseline no treatment: 5.76 (1.48).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, BMI, compliance, severity on radiography and baseline values of outcomes; Group 1 Number missing: -, Reason: 15 people in total throughout the study withdrew; Group 2 Number missing: -, Reason: 15 people in total throughout the study withdrew

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) versus

ULTRASOUND Protocol outcome 1: Pain at </= 3 months - Actual outcome: VAS at 8 weeks; Group 1: mean -2.32 (SD 0.6); n=20, Group 2: mean -2.34 (SD 0.94); n=20; VAS 0-10 Top=High is poor outcome; Comments: Baseline TENS: 5.85 (1.34). Baseline ultrasound: 5.90 (1.45). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, BMI, compliance, severity on radiography and baseline values of outcomes; Group 1 Number missing: -, Reason: 15 people in total throughout the study withdrew; Group 2 Number missing: -, Reason: 15 people in total throughout the study withdrew RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT Protocol outcome 1: Pain at </= 3 months - Actual outcome: VAS at 8 weeks; Group 1: mean -2.32 (SD 0.6); n=20, Group 2: mean -2.27 (SD 0.88); n=20; VAS 0-10 Top=High is poor outcome; Comments: Baseline TENS: 5.85 (1.34). Baseline no treatment: 5.76 (1.48). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, BMI, compliance, severity on radiography and baseline values of outcomes; Group 1 Number missing: -, Reason: 15 people in total throughout the study withdrew; Group 2 Number missing: -, Reason: 15 people in total throughout the study withdrew RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT Protocol outcome 1: Pain at </= 3 months - Actual outcome: VAS at 8 weeks; Group 1: mean -2.34 (SD 0.94); n=20, Group 2: mean -2.27 (SD 0.88); n=20; VAS 0-10 Top=High is poor outcome; Comments: Baseline ultrasound: 5.90 (1.45). Baseline no treatment: 5.76 (1.48). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, BMI, compliance, severity on radiography and baseline values of outcomes; Group 1 Number missing: -, Reason: 15 people in total throughout the study withdrew; Group 2 Number missing: -, Reason: 15 people in total throughout the study withdrew	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Cho 2016[58]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=18)
Countries and setting	Conducted in South Korea; Setting: Inpatient rehabilitation
Line of therapy	Unclear
Duration of study	Intervention + follow up: 4 weeks (intervention for 3 weeks)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Unilateral or bilateral knee osteoarthritis of at least Kellgren Lawrence grade 1
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Chronic stroke of at least 2 years duration; unilateral or bilateral knee osteoarthritis (at least Kellgren Lawrence grade 2); intact cognition (MMSE score >20); and ambulatory ability.
Exclusion criteria	People with other musculoskeletal conditions that can cause lower extremity pain; secondary causes of arthritis; history of intra-articular knee injection within the previous 6 months
Recruitment/selection of patients	People were recruited from an inpatient rehabilitation center
Age, gender and ethnicity	Age - Mean (SD): 74.1 (7.0). Gender (M:F): 15:3. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years (Realistically mixed). 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : High morbidity score (At least everyone had previously had a stroke). 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade (mean [SD]): 1.9 (1.1) Duration of symptoms: Not stated
Indirectness of population	Serious indirectness: People had a chronic stroke and knee osteoarthritis
Interventions	(n=9) Intervention 1: Non-invasive electrotherapy interventions - Extracorporeal shockwave therapy. Extracorporeal shockwave therapy administered as 1000 impulses of shockwave at 0.05mL/mm² on the proximal medial tibia of the affected knee.. Duration 2 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=9) Intervention 2: Sham electrotherapy. Sham extracorporeal shockwave therapy administered as 1000 impulses of shockwave at 0mL/mm² on the proximal medial tibia of the affected knee.. Duration 2 weeks. Concurrent medication/care: No additional

	information. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EXTRACORPOREAL SHOCKWAVE THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: VAS at 3 weeks; Group 1: mean 2.7 (SD 1.4); n=9, Group 2: mean 4.1 (SD 1.7); n=9; VAS 0-10 Top=High is poor outcome; Comments: Baseline EST: 4.5 (1.9). Baseline control: 4.3 (1.9). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, sex, height, body weight, MMSE, Kellgren Lawrence grade and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	NCT02636764 trial: De paula gomes 2020[66]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=100)
Countries and setting	Conducted in Brazil; Setting: Two physiotherapy clinics in Sao Paolo, Brazil.
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 8 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Unilateral knee OA according to ACR criteria, made through examination and the written opinion of a specialist in rheumatic disease.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Knee pain in the last 6 months, and confirmed diagnosis for unilateral knee OA, according to ACR criteria. Radiographic confirmation of the diagnosis and classified as grade 2 or 3 of the K-L classification.
Exclusion criteria	HIstory of knee trauma, signs of hip OA; lameness or use of any walking assist device; neurological disorder characterised as sensitive or motor; diagnosis of cancer, diabetes, or any adverse health condition characterised as acute; cognitive impairment or psychological disorder and cardiopulmonary disease that could compromise the performance of the therapeutic exercises used in this research.
Recruitment/selection of patients	Recruited from the waiting lists of two physiotherapy clinics and five basic health units.
Age, gender and ethnicity	Age - Mean (SD): Exercise group: 67.85 (4.49), exercise+placebo group: 69.4 (4.45), exercise+ICT group: 71.85 (2.62), exercise+SDT group: 68.45 (4.62), exercise+PHOTO group: 65.75(4.48). Gender (M:F): 8M/92F. Ethnicity: not reported
Further population details	1. Age (≤/> 75 years): Not applicable (age 40-80 years). 2. Diagnosis : Diagnosis with imaging (Radiographic confirmation of the diagnosis and classified as grade 2 or 3 of the K-L classification). 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity (NRS pain score): Exercise group: 6.55 (1.09), exercise+placebo group: 6.50 (0.68), exercise+ICT group: 6.65 (0.98), exercise+SDT group: 6.40 (0.99), exercise+PHOTO group: 6.70 (0.86) Duration: not reported
Indirectness of population	No indirectness

Interventions	(n=20) Intervention 1: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. Exercise. Exercises (commonly used in clinical practice and supported by findings of previous studies) were performed to enhance muscle strength (mainly the gluteus maximum, gluteus medius and quadriceps). All procedures for the definition and use of loads, repetitions and implementation of loads over time were based on a study by the author. 70% of a maximum painless repetition was instituted for each participant. For this, the maximum load was defined before the first treatment session and, when necessary, reviewed at the end of each week. The bogAssessment Relative Effort Scale (0-10 points) was used as a reference for monitoring and adjusting the load, in which 1kg was added to the initial load when the research participant attested a score between 0 (not at all difficult) up to 4 points (somewhat difficult). For the exercises involving elastic resistance, the load was determined individually, with 10 repetitions of the exercise without pain. The elastic bands used had 8 levels of resistance divided by colours, in which the more intense colouring indicated greater resistance. The sessions were held three times a week, over 8 weeks (24 sessions), on alternate days, lasting approximately 90 minutes each treatment session. The exercise programme was as follows: - warm up on a treadmill for 10 min with no change in grade and adopting a standardised velocity between 1.1 and 1.2 m/s; -supine bridge, five sets of 30s; - straight leg raise in supine position, two sets of 20 repetitions; - seated knee extension (90 to 45 degree knee flexion), two sets of 20 repetitions; - prone knee flexion, two sets of 20 repetitions; - wall squat (0 to 60 degrees of knee flexion), two sets of 20 repetitions with 5-s isometric contraction; - hip abduction/ lateral rotation/ extension in side-lying position, two sets of 20 repetitions with 5-s isometric contraction; - hip abduction in standing position two sets of 20 repetitions with 5-s isometric contraction; - hip extension/ lateral rotation in prone position, two sets of 20 repetitions with 5-s isometric contraction.. Duration 8 weeks. Concurrent medication/care: None of the participants undertook any form of physical therapy, in addition to the one stipulate. In addition, they did not use intra-articular, anti-inflammatory or chondroprotective corticosteroids. The use of medications for concomitant diseases was not controlled.Indirectness: No indirectness (n=20) Intervention 2: Sham electrotherapy. At the end of the exercise protocol intervention, an ultrasound device (Sonophays, EUS-0503; KLD BiosistemasEquipamentos Eletronics Ltda, Amparo, Sao Paolo.) was used to perform the placebo therapy. The therapy was considered a placebo as the device was turned on (so that participants could see lights flashing on the device) but no dosing was applied. For this, the individual was asked to lie supine on a stretcher, performing knee flexion of the affected leg. Slow circular movements of the transducer head were applied over the knee using transducer gel for 20 min per session.. Duration 8 weeks. Concurrent medication/care: None of the participants undertook any form of physical therapy, in addition to the one stipulate. In addition they did not use intra-articular, anti-inflammatory or chondroprotective corticosteroids. The use of medications for concomitant diseases was not controlled.. Indirectness: No indirectness (n=20) Intervention 3: Non-invasive electrotherapy interventions - Interferential therapy. At the end of each exercise session, participants received ICT using an ICT device (Sonophays, EUS-0503; KLD Biosistemas Equipamentos Eletronics Ltda, Amparo, Sao Paolo.). Four electrodes (8x6cm) were placed around the affected knee joint. The intensity adopted by the

	stimulator was kept at a level considered strong, but comfortable, throughout the treatment time. ICT was performed using a premodulated tetrapolar method with a carrier frequency of 4KHz, 1/1s sweep mode, 75 Hz frequency modulation amplitude, 25Hz delta frequency modulation amplitude, and automatic vector mode for 40 minutes. The parameters chosen were routinely used by the group for interventions involving knee OA.. Duration 8 weeks. Concurrent medication/care: None of the participants undertook any form of physical therapy, in addition to the one stipulate. In addition they did not use intra-articular, anti-inflammatory or chondroprotective corticosteroids. The use of medications for concomitant diseases was not controlled.. Indirectness: No indirectness (n=20) Intervention 4: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. In addition to the exercise protocol, a thermopulse (Ibramed, Amparo, Sao Paolo, Brazil) device set to continuous mode, 27.12MHz frequency and 150W input was used for 20 minutes, and the intensity was defined based on each participant reporting a warm sensation (one sensation, described as soft but pleasant heat). For SDT application, a standard sized malleable electrode (16x20 cm) was applied to the anterior area of the thigh, 5cm above the upper border of the patella, and a second electrode was applied on the posterior area of the leg. For this, the participant lay supine and the knee was kept in semi-flexion.. Duration 8 weeks. Concurrent medication/care: None of the participants undertook any form of physical therapy, in addition to the one stipulate. In addition they did not use intra-articular, anti-inflammatory or chondroprotective corticosteroids. The use of medications for concomitant diseases was not controlled.. Indirectness: No indirectness (n=20) Intervention 5: Non-invasive electrotherapy interventions - Laser therapy. Prior to the exercise protocol, participants in the exercise and photobiomodulation (PHOTO) group underwent photobiomodulation therapy using a laserpulse device (Ibramed, Amparo, SP, Brazil). The power of each infrared laser was as follows: wavelength of 904nm, frequency of 9500Hz, pulse duration of 60ns, peak power of 70W, average power of 0.04W, energy density of 6J/cm² applied on eight points, with a total dose of 48J/cm², each session. The eight points were: 1. the medial and lateral epicondyle of the tibia and femur, 2. the medial and lateral knee joint gap, 3. the medial edge of the tendon of the biceps femoris muscle and semitendinous muscle in the popliteal ditch.. Duration 8 weeks. Concurrent medication/care: None of the participants undertook any form of physical therapy, in addition to the one stipulate. In addition they did not use intra-articular, anti-inflammatory or chondroprotective corticosteroids. The use of medications for concomitant diseases was not controlled.. Indirectness: No indirectness
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTERFERENTIAL THERAPY+EXERCISE versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT (EXERCISE)

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain subscale at 8 weeks; Group 1: mean 11 (SD 1.16); n=20, Group 2: mean 9 (SD 1.41); n=20; Comments: Baselione values: ICT group: 14.75 (1.61), exercise group: 14.90 (1.86), SDT group: 15.20 (1.15), PHOTO group: 14.00 (1.49), placebo group: 15.30 (1.49)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: the exercise alone group received no electrotherapy or sham treatment therefore were not blinded, however the intervention group was blinded as to whether they were receiving active treatment or sham. ; Group

1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function subscale at 8 weeks; Group 1: mean 36.2 (SD 3.41); n=20, Group 2: mean 38.9 (SD 3.72); n=20; WOMAC function subscale 0-68 Top=High is poor outcome; Comments: Baseline values: ICT group: 47.60(3.76), exercise group: 53.70 (5.24), SDT group: 46.90 (3.27), PHOTO group: 48.50 (3.23), placebo group: 50.60 (2.92)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: the exercise alone group received no electrotherapy or sham treatment therefore were not blinded, however the intervention group was blinded as to whether they were receiving active treatment or sham. ; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTERFERENTIAL THERAPY+EXERCISE versus SHAM ELECTROTHERAPY+ EXERCISE

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain subscale at 8 weeks; Group 1: mean 11 (SD 1.16); n=20, Group 2: mean 10.9 (SD 1.55); n=20; Comments: Baseline values: ICT group: 14.75 (1.61), exercise group: 14.90 (1.86), SDT group: 15.20 (1.15), PHOTO group: 14.00 (1.49), placebo group: 15.30 (1.49)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function subscale at 8 weeks; Group 1: mean 36.2 (SD 3.41); n=20, Group 2: mean 41.35 (SD 2.96); n=20; WOMAC function subscale 0-68 Top=High is poor outcome; Comments: Baseline values: ICT group: 47.60(3.76), exercise group: 53.70 (5.24), SDT group: 46.90 (3.27), PHOTO group: 48.50 (3.23), placebo group: 50.60 (2.92)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTERFERENTIAL THERAPY+EXERCISE versus PULSED SHORT-WAVE THERAPY+ EXERCISE

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain subscale at 8 weeks; Group 1: mean 11 (SD 1.16); n=20, Group 2: mean 11.3 (SD 1.41); n=20; WOMAC pain subscale 0-20 Top=High is poor outcome; Comments: Baseline values: ICT group: 14.75 (1.61), exercise group: 14.90 (1.86), SDT group: 15.20 (1.15), PHOTO group: 14.00 (1.49), placebo group: 15.30 (1.49)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months

- Actual outcome: WOMAC function subscale at 8 weeks; Group 1: mean 36.2 (SD 3.41); n=20, Group 2: mean 36.85 (SD 2.28); n=20; WOMAC function subscale 0-68 Top=High is poor outcome; Comments: Baseline values: ICT group: 47.60(3.76), exercise group: 53.70 (5.24), SDT group: 46.90 (3.27), PHOTO group: 48.50 (3.23), placebo group: 50.60 (2.92)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTERFERENTIAL THERAPY+EXERCISE versus LASER THERAPY+ EXERCISE

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain subscale at 8 weeks; Group 1: mean 11 (SD 1.16); n=20, Group 2: mean 10.45 (SD 1.05); n=20; WOMAC pain subscale 0-20 Top=High is poor outcome; Comments: Baseline values: ICT group: 14.75 (1.61), exercise group: 14.90 (1.86), SDT group: 15.20 (1.15), PHOTO group: 14.00 (1.49), placebo group: 15.30 (1.49)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function subscale at 8 weeks; Group 1: mean 36.2 (SD 3.41); n=20, Group 2: mean 39.2 (SD 2.12); n=20; WOMAC function subscale 0-68 Top=High is poor outcome; Comments: Baseline values: ICT group: 47.60(3.76), exercise group: 53.70 (5.24), SDT group: 46.90 (3.27), PHOTO group: 48.50 (3.23), placebo group: 50.60 (2.92)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY+ EXERCISE versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT (EXERCISE)

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain subscale at 8 weeks; Group 1: mean 11.3 (SD 1.41); n=20, Group 2: mean 9 (SD 1.41); n=20; WOMAC pain subscale 0-20 Top=High is poor outcome; Comments: Baseline values: ICT group: 14.75 (1.61), exercise group: 14.90 (1.86), SDT group: 15.20 (1.15), PHOTO group: 14.00 (1.49), placebo group: 15.30 (1.49)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: the exercise alone group received no electrotherapy or sham treatment therefore were not blinded, however the intervention group was blinded as to whether they were receiving active treatment or sham. ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function subscale at 8 weeks; Group 1: mean 36.85 (SD 2.28); n=20, Group 2: mean 38.9 (SD 3.72); n=20; WOMAC function subscale 0-68 Top=High is poor outcome; Comments: Baseline values: ICT group: 47.60(3.76), exercise group: 53.70 (5.24), SDT group: 46.90 (3.27),

PHOTO group: 48.50 (3.23), placebo group: 50.60 (2.92)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: the exercise alone group received no electrotherapy or sham treatment therefore were not blinded, however the intervention group was blinded as to whether they were receiving active treatment or sham. ; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY+ EXERCISE versus SHAM ELECTROTHERAPY+ EXERCISE

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain subscale at 8 weeks; Group 1: mean 11.3 (SD 1.41); n=20, Group 2: mean 10.9 (SD 1.55); n=20; WOMAC pain subscale 0-20 Top=High is poor outcome; Comments: Baseline values: ICT group: 14.75 (1.61), exercise group: 14.90 (1.86), SDT group: 15.20 (1.15), PHOTO group: 14.00 (1.49), placebo group: 15.30 (1.49)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function subscale at 8 weeks; Group 1: mean 36.85 (SD 2.28); n=20, Group 2: mean 41.35 (SD 2.96); n=20; WOMAC function subscale 0-68 Top=High is poor outcome; Comments: Baseline values: ICT group: 47.60(3.76), exercise group: 53.70 (5.24), SDT group: 46.90 (3.27), PHOTO group: 48.50 (3.23), placebo group: 50.60 (2.92)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY+ EXERCISE versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT (EXERCISE)

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain subscale at 8 weeks; Group 1: mean 10.45 (SD 1.05); n=20, Group 2: mean 9 (SD 1.41); n=20; WOMAC pain subscale 0-20 Top=High is poor outcome; Comments: Baseline values: ICT group: 14.75 (1.61), exercise group: 14.90 (1.86), SDT group: 15.20 (1.15), PHOTO group: 14.00 (1.49), placebo group: 15.30 (1.49)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: the exercise alone group received no electrotherapy or sham treatment therefore were not blinded, however the intervention group was blinded as to whether they were receiving active treatment or sham. ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function subscale at 8 weeks; Group 1: mean 39.2 (SD 2.12); n=20, Group 2: mean 38.9 (SD 3.72); n=20; WOMAC function subscale 0-68 Top=High is poor outcome; Comments: Baseline values: ICT group: 47.60(3.76), exercise group: 53.70 (5.24), SDT group: 46.90 (3.27),

PHOTO group: 48.50 (3.23), placebo group: 50.60 (2.92)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: the exercise alone group received no electrotherapy or sham treatment therefore were not blinded, however the intervention group was blinded as to whether they were receiving active treatment or sham. ; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY+ EXERCISE versus SHAM ELECTROTHERAPY+ EXERCISE

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain subscale at 8 weeks; Group 1: mean 10.45 (SD 1.05); n=20, Group 2: mean 9 (SD 1.41); n=20; WOMAC pain subscale 0-20 Top=High is poor outcome; Comments: Baseline values: ICT group: 14.75 (1.61), exercise group: 14.90 (1.86), SDT group: 15.20 (1.15), PHOTO group: 14.00 (1.49), placebo group: 15.30 (1.49)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function subscale at 8 weeks; Group 1: mean 39.2 (SD 2.12); n=20, Group 2: mean 41.35 (SD 2.96); n=20; WOMAC function subscale 0-68 Top=High is poor outcome; Comments: Baseline values: ICT group: 47.60(3.76), exercise group: 53.70 (5.24), SDT group: 46.90 (3.27), PHOTO group: 48.50 (3.23), placebo group: 50.60 (2.92)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY+ EXERCISE versus PULSED SHORT-WAVE THERAPY+ EXERCISE

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain subscale at 8 weeks; Group 1: mean 10.45 (SD 1.05); n=20, Group 2: mean 11.3 (SD 1.41); n=20; WOMAC pain subscale 0-20 Top=High is poor outcome; Comments: Baseline values: ICT group: 14.75 (1.61), exercise group: 14.90 (1.86), SDT group: 15.20 (1.15), PHOTO group: 14.00 (1.49), placebo group: 15.30 (1.49)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function subscale at 8 weeks; Group 1: mean 39.2 (SD 2.12); n=20, Group 2: mean 36.85 (SD 2.28); n=20; WOMAC function subscale 0-68 Top=High is poor outcome; Comments: Baseline values: ICT group: 47.60(3.76), exercise group: 53.70 (5.24), SDT group: 46.90 (3.27), PHOTO group: 48.50 (3.23), placebo group: 50.60 (2.92)

Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Devrimsel 2019[69]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=60)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 3 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: American College of Rheumatology knee osteoarthritis with grade 2-3 Kellgren Lawrence changes
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with knee osteoarthritis with grade 2 or 3 Kellgren Lawrence changes
Exclusion criteria	People with cardiovascular, inflammatory, infectious diseases, causes of lower extremity weakness, tumoral diseases, participation in a strength training program on physiotherapy treatment for knee osteoarthritis in the past 6 months, knee surgery, and intra-articular injection in the past 6 months
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 62.1 (7.8). Gender (M:F): 13:47. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence (mean [SD]): 2.6 (0.5) Duration of symptoms (mean [SD]): 6.4 (3.5) years
Indirectness of population	No indirectness
Interventions	(n=30) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. Ultrasound therapy distributed over three weeks (five days per week). Continuous ultrasound therapy (Chattanooga, 1 watt/cm² dose, 1 MHz, 5 minutes) applied with a 5cm diameter applicator bilaterally to the knees of each subject for three weeks.. Duration 3 weeks. Concurrent medication/care: People received hot pack, exercise and analgesic treatment (paracetamol 1500mg/day). Indirectness: No indirectness (n=30) Intervention 2: Non-invasive electrotherapy interventions - Neuromuscular electrical stimulation. Neuromuscular electric stimulation through a Cefar device performed with two self-adhesive electrodes applied bilaterally to vastus lateralis and the quadriceps femoris muscles for 20 minutes/session, once daily, give days a week,

	for three weeks. The parameters used were as follows: frequency of 50Hz; pulse duration of 250 microseconds; time on: 10 seconds; time off: 30 seconds. The intensity was set to the maximum tolerated by each person.. Duration 3 weeks. Concurrent medication/care: People received hot pack, exercise and analgesic treatment (paracetamol 1500mg/day). Indirectness: No indirectness
Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus NEUROMUSCULAR ELECTRICAL STIMULATION Protocol outcome 1: Pain at </= 3 months - Actual outcome: WOMAC pain at 3 weeks; Group 1: mean 4.16 (SD 1.51); n=30, Group 2: mean 5.1 (SD 1.78); n=30; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline ultrasound: 9.16 (2.47). Baseline NMES: 8.93 (2.13). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, BMI, Kellgren Lawrence grade, disease duration and baseline values of outcomes; Group 1 Number missing: 1, Reason: Hypertension peak = 1; Group 2 Number missing: 0 Protocol outcome 2: Physical function at </= 3 months - Actual outcome: WOMAC physical function at 3 weeks; Group 1: mean 12.1 (SD 2.42); n=30, Group 2: mean 13.26 (SD 1.79); n=30; WOMAC physical function 0-68 Top=High is poor outcome; Comments: Baseline ultrasound: 34.26 (5.85). Baseline NMES: 32.73 (6.57). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, BMI, Kellgren Lawrence grade, disease duration and baseline values of outcomes; Group 1 Number missing: 1, Reason: Hypertension peak = 1; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Draper 2018[71]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=90)
Countries and setting	Conducted in USA; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 6 weeks (and 2 additional weeks of baseline examinations)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Moderate to severe knee pain negatively affecting their life with radiographically-confirmed mild to moderate changes
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People were 35 to 80 years of age; reported moderate to severe knee osteoarthritis pain negatively affecting their life; were radiographically-confirmed mild to moderate knee osteoarthritis (Kellgren-Lawrence grade 1-2) in one or both knees based on fixed-flexion x-ray radiological findings for osteophytes or joint space narrowing in any compartment in the previous 12 months; and reported average baseline pain score between 3 and 7 based on the numeric rating scale (0-10 NRS) the week preceding enrollment
Exclusion criteria	Presence of severe knee osteoarthritis (Kellgren Lawrence grade 3); having had a knee replacement; surgical intervention, or hyaluronic acid injection in the affected knee in the previous 6 months; being a non-ambulatory person; being unable to self-apply tohe device to their knee; having current treatment with corticosteroids; having had osteoarthritis develop secondary to a metabolic disorder
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 52.6 (9.0). Gender (M:F): 39:45. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 1-2 Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=55) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. The long-duration low-intensity ultrasound treatment phase lasted 6 weeks. Ultrasound was self-administered in the home-setting with a wearable SAM Sport device. The device was self-administered 4 hours per day, 7 days per week for 6 weeks. The

	device operates at 3MHz in continuous wave mode and delivers 1.3W output power divided evenly across two transducers. The average ultrasonic intensity from each transducer is 132 mW/cm² and the device delivers a total acoustic dose of 18,720J of energy over the 4 hour treatment period. The device is attached to the body with a disposable adhesive patch which comes pre-filled with ultrasonic coupling gel. . Duration 6 weeks. Concurrent medication/care: People were permitted to continue use of pain medications as long as those medication were maintained at a stable dose throughout the trial. Co-interventions were not assessed in this study.. Indirectness: No indirectness (n=35) Intervention 2: Sham electrotherapy. Sham ultrasound device - in all ways the same as the ultrasound device but the transducers were deactivated so it did not emit ultrasound energy. Duration 6 weeks. Concurrent medication/care: People were permitted to continue use of pain medications as long as those medication were maintained at a stable dose throughout the trial. Co-interventions were not assessed in this study.. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: WOMAC pain at 8 weeks; Group 1: mean -107.3 (SD 97.5); n=51, Group 2: mean -60.8 (SD 80.95); n=31; WOMAC pain 0-500 Top=High is poor outcome; Comments: Baseline ultrasound: 292 (89.1). Baseline sham: 276.5 (77.9). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI and baseline values of outcomes; Group 1 Number missing: 4, Reason: 2 dropped out for skin irritation, 2 dropped out for device damage; Group 2 Number missing: 3, Reason: 1 dropped out for no follow up, 1 dropped out for device damage, 1 dropped out for unrelated medical issue Protocol outcome 2: Physical function at </= 3 months - Actual outcome: WOMAC function at 8 weeks; Group 1: mean -352.3 (SD 309.6); n=51, Group 2: mean -220.1 (SD 233.6); n=31; WOmaC function 0-1800 Top=High is poor outcome; Comments: Baseline ultrasound: 975 (272.2). Baseline sham: 974 (218.3). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI and baseline values of outcomes; Group 1 Number missing: 4, Reason: 2 dropped out for skin irritation, 2 dropped out for device damage; Group 2 Number missing: 3, Reason: 1 dropped out for no follow up, 1 dropped out for device damage, 1 dropped out for unrelated medical issue	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3

	months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	**Eftekharsadat 2020[74]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=75)
Countries and setting	Conducted in Iran; Setting: Shohada hospital
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 3 week intervention plus 7 week follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: KOA diagnosed on the basis of ACR criteria.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Presence of KOA based on ACR criteria, including grades II and III KOA based on K-L radiologic criteria using knee x-ray, and the age range 50-70 years.
Exclusion criteria	Grade I (mild) or IV (severe) OA, history of other rheumatological diseases such as RA, history of knee surgery and lower limb fracture involving the knee articular surface, and electrical implants such as a pacemaker. Other criteria included a history of heart conduction block, epilepsy, pregnancy, DVT of lower limbs, intra-articular knee injection history over the last 6 months, and taking steroid medications during the last month, as well as balance disorder, neuropathic or impaired sensation disorders, and local infection.
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): ESWT group: 58.00 (5.97), PT group: 55.76 (6.06), exercise group: 58.16 (7.20). Gender (M:F): 70F/ 5M. Ethnicity: Not reported
Further population details	1. Age (≤/> 75 years): </=75 years (age range 50-70). 2. Diagnosis : Diagnosis with imaging (grades II and III KOA based on K-L radiologic criteria (x-ray)). 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity (VAS score at baseline): ESWT group: 7.00 (1.63), PT group: 7.16 (1.37), exercise group: 6.32(1.44) Duration: not reported

Indirectness of population	No indirectness
Interventions	(n=25) Intervention 1: Non-invasive electrotherapy interventions - Extracorporeal shockwave therapy. ESWT. Participants received 5 sessions of shock wave therapy through 3 weeks via a Zimmer enPulsPro Medizin SystemGmbH, Germany. Participants were placed in a sitting position, and the affected knee was exposed. Further, the knee was slightly flexed, the hip abducted and externally rotated, and the applicator was directed in the most tender point over the affected knee joint. Then, radial ESWT was used with shockwaves of 2000 pulses/session with an energy flux density of 0.18mJ/mm², the energy level of 2-4, a frequency of 10-16Hz, and pulse rate of 160/ minute were generally applied each session. . Duration 3 weeks. Concurrent medication/care: The exercise programme was applied to all 3 groups. It consisted of the isometric strengthening of the quadriceps muscle in the form of 3 submaximal isometric contractions with gradually increasing intensity combined with weight- bearing water and land based exercises. Additionally, participants were advised to only use acetaminophen for pain relief in the event of severe pain and activities of daily living modifications (e.g. weight loss and the avoidance of heavy lifting, long-distance walking, and high-impact exercises) were taught as well.. Indirectness: No indirectness (n=25) Intervention 2: Non-invasive electrotherapy interventions - Combination therapy (e.g. ultrasound and interferential therapy). Participants received 10 sessions (3 sessions, weekly) of physical therapy including hot pack, TENS and ultrasound (US, HP: 74.5 degrees C, 20 minutes on the affected knee, TENS: pulse duration 20-100 microseconds, 50% duty cycle, current amplitude, maximum tolerated tingling, frequency <200pps, US: frequency of 1 MHz, the intensity of 2.5 W/cm², and duty cycle of 25%,and the probe of USwas applied for 10 minutes.. Duration 3 weeks. Concurrent medication/care: The exercise programme was applied to all 3 groups. It consisted of the isometric strengthening of the quadriceps muscle in the form of 3 submaximal isometric contractions with gradually increasing intensity combined with weight- bearing water and land based exercises. Additionally, participants were advised to only use acetaminophen for pain relief in the event of severe pain and activities of daily living modifications (e.g. weight loss and the avoidance of heavy lifting, long-distance walking, and high-impact exercises) were taught as well.. Indirectness: No indirectness (n=25) Intervention 3: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. The exercise programme was applied to all 3 groups. It consisted of the isometric strengthening of the quadriceps muscle in the form of 3 submaximal isometric contractions with gradually increasing intensity combined with weight- bearing water and land based exercises. Additionally, participants were advised to only use acetaminophen for pain relief in the event of severe pain and activities of daily living modifications (e.g. weight loss and the avoidance of heavy lifting, long-distance walking, and high-impact exercises) were taught as well.. Duration 3 weeks. Concurrent medication/care: none. Indirectness: No indirectness
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EXTRACORPOREAL SHOCKWAVE THERAPY (PLUS EXERCISE) versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT (EXERCISE ONLY)

Protocol outcome 1: Pain at </= 3 months

- Actual outcome: WOMAC- pain subscale at 7 weeks; Group 1: mean 12.3 (SD 4.84); n=23, Group 2: mean 10.61 (SD 4.91); n=22; WOMAC-pain subscale 0-36 Top=High is poor outcome; Comments: Baseline values: ESWT group: 18.68 (3.90), combination group: 19.48 (4.34), exercise group: 16.84 (3.69) Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Comments - ; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: lost to follow-up (inability to attend); Group 2 Number missing: 3, Reason: lost to follow-up (inability to attend) Protocol outcome 2: Physical function at </= 3 months - Actual outcome: WOMAC- physical function subscale at 7 weeks; Group 1: mean 30.74 (SD 13.55); n=23, Group 2: mean 20 (SD 10.51); n=22; WOMAC-physical function subscale 0-68 Top=High is poor outcome; Comments: Baseline values: ESWT group: 38.44(11.46), combination group: 34.68 (10.41), exercise group: 31.20 (9.40) Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Comments - ; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: lost to follow-up (inability to attend); Group 2 Number missing: 3, Reason: lost to follow-up (inability to attend) RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINATION THERAPY (HOT PACK, TENS+ US PLUS EXERCISE) versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT (EXERCISE ONLY) Protocol outcome 1: Pain at </= 3 months - Actual outcome: WOMAC- pain subscale at 7 weeks; Group 1: mean 13.18 (SD 5.66); n=22, Group 2: mean 10.61 (SD 4.91); n=22; WOMAC-pain subscale 0-36 Top=High is poor outcome; Comments: Baseline values: ESWT group: 18.68 (3.90), combination group: 19.48 (4.34), exercise group: 16.84 (3.69) Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Comments - ; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: lost to follow-up (inability to attend); Group 2 Number missing: 3, Reason: lost to follow-up (inability to attend) Protocol outcome 2: Physical function at </= 3 months - Actual outcome: WOMAC- physical function subscale at 7 weeks; Group 1: mean 24.18 (SD 11.32); n=22, Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Comments - ; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: lost to follow-up (inability to attend); Group 2 Number missing: 3, Reason: lost to follow-up (inability to attend)	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Elboim-gabyzon 2013[76]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=63)
Countries and setting	Conducted in Israel; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 6 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Radiographic evidence of knee osteoarthritis at grade at least 2 according to the Kellgren Lawrence classification
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Radiographic evidence of knee osteoarthritis at a grade at least 2, according to the Kellgren and Lawrence classification; age above 50; compliance with the classification of the American College of Rheumatology; knee pain for at least three months, with pain presenting at least 2 days a week during the last month; ability to ambulate independently for at least 10 meters; ability to follow instructions
Exclusion criteria	Existence of a pacemaker; history of cardiovascular, neurological or orthopedic problems that could affect functional performance; previous knee surgery other than arthroscopy; injections to the knee joint during the previous six months; change in pain medication in the previous month; inability to tolerate electrical stimulation at a level of current sufficient to elicit full knee extension
Recruitment/selection of patients	People referred to an orthopedic outpatient physical therapy clinic
Age, gender and ethnicity	Age - Mean (SD): 68.2 (8.0). Gender (M:F): 11:52. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence at least grade 2 Duration of symptoms (mean [SD]): 4.3 (5.6) years.
Indirectness of population	No indirectness
Interventions	(n=33) Intervention 1: Non-invasive electrotherapy interventions - Neuromuscular electrical stimulation. Neuromuscular electrical stimulation. Electrodes secured to the thigh, one over the rectus femoris proximal muscle belly and the other over the vastus medialis muscle belly. The electrodes were connected to a high-voltage constant-current simulation. Two electrical pulses at submaximal intensity (300 and 600mA) were then given to familiarize the subjects with the electrical stimulation. This was

	followed by the application of a single electrical stimulus (150V, 100ms pulse duration and 1000mA intensity) to the resting muscle. After a 5 minute break, the person performed knee extension with maximal effort. The same stimulus was applied a second time at the point noted on the screen as the peak force. The procedure was repeated up to three times in cases where maximal effort was not captured. 12 biweekly treatments.. Duration 6 weeks. Concurrent medication/care: All people participated in a group exercise programme, with 6-8 subjects in each group. The exercise sessions involved muscle strengthening exercises, functional activities and balance training. They took 45 minutes to complete. Patient education was incorporated into each session including information on self-management, which included activity and exercise planning, and a discussion of pain-coping strategies.. Indirectness: No indirectness (n=30) Intervention 2: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. No electrotherapy treatment. Duration 6 weeks. Concurrent medication/care: All people participated in a group exercise programme, with 6-8 subjects in each group. The exercise sessions involved muscle strengthening exercises, functional activities and balance training. They took 45 minutes to complete. Patient education was incorporated into each session including information on self-management, which included activity and exercise planning, and a discussion of pain-coping strategies.. Indirectness: No indirectness
Funding	Academic or government funding (Research grant from the Ministry of Health, State of Isreal, Grant no. 3000004258)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NEUROMUSCULAR ELECTRICAL STIMULATION versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT Protocol outcome 1: Pain at </= 3 months - Actual outcome: VAS at 6 weeks; Group 1: mean 3.3 (SD 2.4); n=25, Group 2: mean 5 (SD 2.2); n=25; VAS 0-10 Top=High is poor outcome; Comments: Baseline NMES: 7.5 (2). Baseline no treatment: 7.4 (1.9). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports gender, age, height, weight, BMI, osteoarthritis durations and baseline values of outcomes; Group 1 Number missing: 8, Reason: 7 non-compliance, 1 pneumonia; Group 2 Number missing: 5, Reason: 1 no tolerance, 3 non-compliance, 1 pneumonia	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild

	adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study (subsidiary papers)	Fary 2011[79] (Fary 2008[80])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=70)
Countries and setting	Conducted in Australia; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 26 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis in accordance with the American College of Rheumatology modified clinical classification system with plain radiographs being available for all participants
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with osteoarthritis of the knee who had persistent and stable pain for a minimum of 3 months prior to the study of at least a baseline pain score of 25mm on a 100mm visual analog scale
Exclusion criteria	Coexisting inflammatory arthropathies; contraindications to electrical stimulation; skin disorders in the vicinity of the knee to be treated; total knee replacement scheduled during the study period; insufficient English to follow instructions and complete forms
Recruitment/selection of patients	Recruitment occurred through notices in published newsletters of community organisations, letters to medical general practices and word of mouth
Age, gender and ethnicity	Age - Mean (SD): 69.8 (10.3). Gender (M:F): 37:33. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years (Realistically probably a mix). 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grades 1-4, median grade 3 Duration of symptoms (mean [SD]): 12.0 (10.5) years
Indirectness of population	No indirectness
Interventions	(n=34) Intervention 1: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. A commercially available TENS stimulator (Metron Digit-10s) modified to deliver PES current parameters as follows: pulsed asymmetrically biphasic, exponentially decreasing waveform with a frequency of 100Hz and a pulse width of 4milliseconds. Current was delivered via 120mm x 80mm multiple-use conductive silicone electrodes inserted into larger calico pockets (175mm x 100mm) . Electrodes, positioned over the anterior distal thigh (anode) and anterior to the knee joint itself

	(cathode), were coupled to the skin using hypoallergenic conduction gel and secured with specially made neoprene wraps. People were instructed to wear the device 7 hours daily, preferably overnight, for 26 weeks. They were instructed to turn the intensity up until they could feel pins and needles or a prickling sensation under one or both electrodes. After achieving this, they were instructed to turn the intensity down until they could no longer feel it and then a locking mechanism was engaged that prevented subsequent adjustment without restarting the device.. Duration 26 weeks. Concurrent medication/care: People were instructed to continue their usual treatment for osteoarthritis throughout the study (including prescribed medications, health professional interventions such as exercise programs, and complementary therapies). However, they were counseled against starting any new treatments.. Indirectness: No indirectness (n=36) Intervention 2: Sham electrotherapy. Placebo device. Set up to be identical to the intervention group device,. However, it was set to switch off after 3 minutes of use.. Duration 26 weeks. Concurrent medication/care: People were instructed to continue their usual treatment for osteoarthritis throughout the study (including prescribed medications, health professional interventions such as exercise programs, and complementary therapies). However, they were counseled against starting any new treatments.. Indirectness: No indirectness
Funding	Academic or government funding (Supported by an Arthritis Australia and State & Territory Affiliate Grant and a Physiotherapy Research Foundation Seeding grant, and by a Curtin University School of Physiotherapy Early Career Researcher grant to Dr. Fary. Dr. Fary was recipient of an Australian Government Postgraduate PhD scholarship and a Curtin University School of PHysiotherapy movement Through Life Top-Up scholarship.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Health-related quality of life at > 3 months
- Actual outcome: SF-36 physical component summary at 26 weeks; Group 1: mean 1 (SD 5.6); n=34, Group 2: mean 2.6 (SD 7.3); n=36; SF-36 physical component summary 0-100 Top=High is good outcome; Comments: Baseline short-wave therapy: 37.0 (8.5). Baseline sham: 36.5 (9.1).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, BMI, duration of symptoms, time since diagnosis, Kellgren Lawrence grade, clinical features, laterality, medication use and baseline values of outcomes; Group 1 Number missing: 2, Reason: 2 people withdrew before the final analysis; Group 2 Number missing: 1, Reason: 1 person withdrew before the final analysis
- Actual outcome: SF-36 mental component summary at 26 weeks; Group 1: mean 1.2 (SD 9.3); n=34, Group 2: mean 2.4 (SD 8.1); n=36; SF-36 mental component summary 0-100 Top=High is good outcome; Comments: Baseline short-wave therapy: 52.7 (11.0). Baseline sham: 53.7 (11.2).

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, BMI, duration of symptoms, time since diagnosis, Kellgren Lawrence grade, clinical features, laterality, medication use and baseline values of outcomes; Group 1 Number missing: 2, Reason: 2 people withdrew before the final analysis; Group 2 Number missing: 1, Reason: 1 person withdrew before the final analysis Protocol outcome 2: Pain at > 3 months - Actual outcome: WOMAC pain at 26 weeks; Group 1: mean -5 (SD 20.4); n=34, Group 2: mean -10 (SD 18.4); n=36; WOMAC pain 0-100 Top=High is poor outcome; Comments: Baseline short-wave therapy: 35.0 (16.3). Baseline sham: 36.0 (18.1). Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, BMI, duration of symptoms, time since diagnosis, Kellgren Lawrence grade, clinical features, laterality, medication use and baseline values of outcomes; Group 1 Number missing: 2, Reason: 2 people withdrew before the final analysis; Group 2 Number missing: 1, Reason: 1 person withdrew before the final analysis Protocol outcome 3: Physical function at > 3 months - Actual outcome: WOMAC function at 26 weeks; Group 1: mean -5 (SD 16.5); n=34, Group 2: mean -7 (SD 16.2); n=36; WOMAC function 0-100 Top=High is poor outcome; Comments: Baseline short-wave therapy: 35 (17.6). Baseline sham: 34 (16.5). Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, BMI, duration of symptoms, time since diagnosis, Kellgren Lawrence grade, clinical features, laterality, medication use and baseline values of outcomes; Group 1 Number missing: 2, Reason: 2 people withdrew before the final analysis; Group 2 Number missing: 1, Reason: 1 person withdrew before the final analysis	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Pain at </= 3 months; Physical function at </= 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Fukuda 2011[83]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=121)
Countries and setting	Conducted in Brazil; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 3 weeks of treatment, 12 months of follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Primary grade 2-3 knee osteoarthritis based on Gupta and colleagues' radiographic criteria and have had joint or anterior knee pain for at least 3 months
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Over 40 years of age; had primary grade 2 or 3 knee osteoarthritis based on Gupta and colleagues' radiographic criteria; had joint or anterior knee pain for at least 3 months
Exclusion criteria	People with a history of surgery or any invasive procedure of the affected knee; physical therapy ofor knee injuries or any medication that had changed in the last 3 months; or other diseases affecting function and patients who presented any contraindication for application of PSW treatment, especially metallic implants, pacemakers, lack of sensitivity, or tumour
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 61.0 (9.3). Gender (M:F): 0:121. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Gupta and colleagues radiographic criteria: grade 2-3 Duration of symptoms: At least 3 months
Indirectness of population	No indirectness
Interventions	(n=63) Intervention 1: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. Low-dose or high-dose pulsed shortwave therapy using Diatermed II devices with a carrying frequency of 27.12 MHz, a peak power of 250 W, and a pulse duration of 400 microseconds. They used the maximum power provided by the machine in a pulsed form with a pulse frequency of 145 Hz, resulting in a mean power of 14.5 W. The settings were based on the fact that applications with a mean power below 20 W minimize the thermal effects. In the low dose group the treatment had a duration of 19

	minutes per session with approximately 17kJ of total energy. The high dose group received 38 minutes of treatment, with 33kJ of total energy. Both groups were given 3 applications per week, totaling 9 sessions. The electrodes were applied on the anterior area of the thigh 5cm above the superior border of the patella, and the posterior area of the leg, with the person positioned in supine. The knee was kept in semi-flexion at 20 degrees.. Duration 3 weeks, follow up for 12 months. Concurrent medication/care: No advice was given to participants in all groups in relation to physical activities, except to maintain their daily activities and to avoid using anti-inflammatory drugs.. Indirectness: No indirectness Comments: These two groups were combined due to class effect as agreed in the protocol (n=23) Intervention 2: Sham electrotherapy. Sham treatment where the device was turned on but kept in standby mode during 19 minutes without any electrical current being applied. Duration 3 weeks, follow up for 12 months. Concurrent medication/care: No advice was given to participants in all groups in relation to physical activities, except to maintain their daily activities and to avoid using anti-inflammatory drugs.. Indirectness: No indirectness (n=35) Intervention 3: No intervention - No treatment. No treatment control. Duration 3 weeks. Concurrent medication/care: No advice was given to participants in all groups in relation to physical activities, except to maintain their daily activities and to avoid using anti-inflammatory drugs.. Indirectness: No indirectness Comments: This group was not followed up for 12 months
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: KOOS quality of life at 3 weeks; Group 1: mean 38.2 (SD 17.5); n=59, Group 2: mean 29.7 (SD 13.7); n=23; KOOS quality of life 0-100 Top=High is good outcome; Comments: Reported low dose PSW: 37.0 (16.2). Reported high dose PSW: 39.4 (18.7). Baseline placebo: 27.8 (29.7). Baseline low dose PSW: 26.1 (12.0). Baseline high dose PSW: 32.4 (15.0).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, body mass, height, BMI, injured limb and baseline values of outcomes; Group 1 Number missing: 4, Reason: High dose: 2 missed 2 or more treatment sessions. Low dose: 2 missed 2 or more treatment sessions.; Group 2 Number missing: 2, Reason: 2 missed 2 or more treatment sessions

Protocol outcome 2: Health-related quality of life at > 3 months

- Actual outcome: KOOS quality of life at 12 months; Group 1: mean 36.4 (SD 17); n=37, Group 2: mean 33 (SD 12.8); n=14; KOOS quality of life 0-100 Top=High is good outcome; Comments: Reported low dose PSW: 31.8 (10.7). Reported high dose PSW: 41.2 (20.6). Baseline placebo: 27.8 (29.7). Baseline low dose PSW: 26.1 (12.0). Baseline high dose PSW: 32.4 (15.0).
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, body mass, height, BMI, injured limb and baseline values of outcomes; Group 1 Number missing: 26, Reason: High dose: 2 missed 2 or more treatment sessions, 5 lot to evaluation, 4 performed other treatment, 2 total knee replacement. Low dose: 2 missed 2 or more treatment sessions, 5 lost to evaluation, 5 performed other treatment, 1 total knee replacement; Group 2 Number missing: 9, Reason: 2 missed 2 or more treatment sessions, 3 lost to evaluation, 3 performed other treatment, 1 total knee replacement

Protocol outcome 3: Pain at </= 3 months
- Actual outcome: KOOS pain at 3 weeks; Group 1: mean 59.9 (SD 17.2); n=59, Group 2: mean 43.8 (SD 16.1); n=21; KOOS pain 0-100 Top=High is good outcome; Comments: Reported low dose PSW: 60.8 (18.6). Reported high dose PSW: 59.0 (15.5). Baseline placebo: 38.0 (13.5). Baseline low dose PSW: 37.4 (17.4). Baseline high dose PSW: 42.5 (16.0).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, body mass, height, BMI, injured limb and baseline values of outcomes; Group 1 Number missing: 4, Reason: High dose: 2 missed 2 or more treatment sessions. Low dose: 2 missed 2 or more treatment sessions.; Group 2 Number missing: 2, Reason: 2 missed 2 or more treatment sessions

Protocol outcome 4: Pain at > 3 months
- Actual outcome: KOOS pain at 12 months; Group 1: mean 57.6 (SD 18.8); n=37, Group 2: mean 33 (SD 9.9); n=14; KOOS pain 0-100 Top=High is good outcome; Comments: Reported low dose PSW: 57.5 (21.0). Reported high dose PSW: 57.6 (16.1). Baseline placebo: 38.0 (13.5). Baseline low dose PSW: 37.4 (17.4). Baseline high dose PSW: 42.5 (16.0).
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, body mass, height, BMI, injured limb and baseline values of outcomes; Group 1 Number missing: 26, Reason: High dose: 2 missed 2 or more treatment sessions, 5 lot to evaluation, 4 performed other treatment, 2 total knee replacement. Low dose: 2 missed 2 or more treatment sessions, 5 lost to evaluation, 5 performed other treatment, 1 total knee replacement; Group 2 Number missing: 9, Reason: 2 missed 2 or more treatment sessions, 3 lost to evaluation, 3 performed other treatment, 1 total knee replacement

Protocol outcome 5: Physical function at </= 3 months
- Actual outcome: KOOS daily activities subscale at 3 weeks; Group 1: mean 62.3 (SD 18.6); n=59, Group 2: mean 51.5 (SD 17.5); n=21; KOOS daily activities 0-100 Top=High is good outcome; Comments: Reported low dose PSW: 61.5 (20.3). Reported high dose PSW: 63.2 (16.5). Baseline placebo: 45.7 (16.3). Baseline low dose PSW: 45.8 (19.8). Baseline high dose PSW: 51.7 (19.1).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, body mass, height, BMI, injured limb and baseline values of outcomes; Group 1 Number missing: 4, Reason: High dose: 2 missed 2 or more treatment sessions. Low dose: 2 missed 2 or more treatment sessions.; Group 2 Number missing: 2, Reason: 2 missed 2 or more treatment sessions

Protocol outcome 6: Physical function at > 3 months
- Actual outcome: KOOS daily activities subscale at 12 months; Group 1: mean 60.6 (SD 19.8); n=37, Group 2: mean 41.6 (SD 16.9); n=14; KOOS daily activites 0-100 Top=High is good outcome; Comments: Reported low dose PSW: 68.9 (20.2). Reported high dose PSW: 51.9 (15.0). Baseline placebo: 45.7 (16.3). Baseline low dose PSW: 45.8 (19.8). Baseline high dose PSW: 51.7 (19.1).
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, body mass, height, BMI, injured limb and baseline values of outcomes; Group 1 Number missing: 26, Reason: High dose: 2 missed 2 or more treatment sessions, 5 lot to evaluation, 4 performed other treatment, 2 total knee replacement. Low dose: 2 missed 2 or more treatment sessions, 5 lost to evaluation, 5 performed other treatment, 1 total knee replacement; Group 2 Number missing: 9, Reason: 2 missed 2 or more treatment sessions, 3 lost to evaluation, 3 performed other treatment, 1 total knee replacement

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus NO TREATMENT

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: KOOS quality of life at 3 weeks; Group 1: mean 38.2 (SD 17.5); n=59, Group 2: mean 26.4 (SD 21.8); n=32; KOOS quality of life 0-100 Top=High is good outcome; Comments: Reported low dose PSW: 37.0 (16.2). Reported high dose PSW: 39.4 (18.7). Baseline no treatment: 27.9 (19.0). Baseline low dose PSW: 26.1 (12.0). Baseline high dose PSW: 32.4 (15.0).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, body mass, height, BMI, injured limb and baseline values of outcomes; Group 1 Number missing: 4, Reason: High dose: 2 missed 2 or more treatment sessions. Low dose: 2 missed 2 or more treatment sessions.; Group 2 Number missing: 3, Reason: 3 lost to posttreatment evaluation

Protocol outcome 2: Pain at </= 3 months
- Actual outcome: KOOS pain at 3 weeks; Group 1: mean 59.9 (SD 17.2); n=59, Group 2: mean 42.3 (SD 17.3); n=32; KOOS pain 0-100 Top=High is good outcome; Comments: Reported low dose PSW: 60.8 (18.6). Reported high dose PSW: 59.0 (15.5). Baseline no treatment: 40.9 (17.2). Baseline low dose PSW: 37.4 (17.4). Baseline high dose PSW: 42.5 (16.0).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, body mass, height, BMI, injured limb and baseline values of outcomes; Group 1 Number missing: 4, Reason: High dose: 2 missed 2 or more treatment sessions. Low dose: 2 missed 2 or more treatment sessions.; Group 2 Number missing: 3, Reason: 3 lost to posttreatment evaluation

Protocol outcome 3: Physical function at </= 3 months
- Actual outcome: KOOS daily activities subscale at 3 weeks; Group 1: mean 62.3 (SD 18.6); n=59, Group 2: mean 48.1 (SD 17.7); n=32; KOOS daily activities 0-100 Top=High is good outcome; Comments: Reported low dose PSW: 61.5 (20.3). Reported high dose PSW: 63.2 (16.5). Baseline no treatment: 49.0 (16.9). Baseline low dose PSW: 45.8 (19.8). Baseline high dose PSW: 51.7 (19.1).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, body mass, height, BMI, injured

limb and baseline values of outcomes; Group 1 Number missing: 4, Reason: High dose: 2 missed 2 or more treatment sessions. Low dose: 2 missed 2 or more treatment sessions.; Group 2 Number missing: 3, Reason: 3 lost to posttreatment evaluation	
Protocol outcomes not reported by the study	Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Fukuda 2011[84]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=47)
Countries and setting	Conducted in Brazil; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 3 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with knee pain and reduced functional ability over the preceding three months and a radiographic examination showing knee osteoarthritis of grade 2-4 according to the classification of Kellgren and Lawrence
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People of both sexes aged between 50 and 78 years with knee pain and reduced functional ability over the preceding three months and a radiographic examination showing knee osteoarthritis of grade 2-4 according to the classification of Kellgren and Lawrence
Exclusion criteria	History of cancer, dementia, neurological deficits (sensory or motor), heart pacemaker, type I or decompensated diabetes, uncontrolled system arterial hypertension, or morbid obesity (BMI no less than 40); use of antidepressants, anti-inflammatory agents, steroids or tranquilizers over the last six months; presenting with symptomatic hip osteoarthritis, acute diseases or other rheumatoid or orthopedic diseases that could interfere with the results; if they had undergone physiotherapy during the last 6 months
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 63.0 (8.6). Gender (M:F): 13:34. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 2-4, median grade 2 Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=25) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. Three weeks of treatment with low level laser therapy, consisting of three sessions per week and totaling nine sessions. The equipment used was an Irradia class 3B laser

	that had been previously measured and calibrated. The pen used was of AsGa type, with a wavelength of 904nm in the infrared spectrum, at a frequency of 700Hz, with mean power of 60mW and peak power of 20W; 50 seconds per point and beam area of 0.5cm². Five points were irradiated with LLLT on the medial face of the knee and four points on the lateral face, in the region of the joint capsule and synovial membrane, with energy of 3.0 J per point and total energy of 27.0 J per session.. Duration 3 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=22) Intervention 2: Sham electrotherapy. Placebo laser. Duration 3 weeks. Concurrent medication/care: People with knee pain and reduced functional ability over the preceding three months and a radiographic examination showing knee osteoarthritis of grade 2-4 according to the classification of Kellgren and Lawrence. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: VNPS for activities of daily living at 3 weeks; Group 1: mean 4.4 (SD 2.9); n=25, Group 2: mean 5.3 (SD 2.8); n=22; VNPS 0-10 Top=High is poor outcome; Comments: baseline laser: 6.1 (2.6). Baseline placebo: 6.2 (2.3). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, weight, height, BMI, gender, side affected, radiographic grade and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Garland 2007[86]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=58)
Countries and setting	Conducted in USA; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 12 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Moderate to severe osteoarthritis with persistence of pain on NSAID and/or analgesic therapy and the presence of Kellgren-Lawrence grade 3-4 changes on standing, weight bearing, and semiflexed x-ray views of the knees
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Moderate to severe osteoarthritis with persistence of pain on NSAID and/or analgesic therapy and the presence of Kellgren-Lawrence grade 3-4 changes on standing, weight bearing, and semiflexed x-ray views of the knees. Other inclusion criteria: age 18 years or greater, the intellectual ability to understand and sign an informed consent and complete the study questionnaire, and willingness to maintain stable doses of analgesics and NSAIDs for 1 month prior to study entry and during the 3 month double blind period.
Exclusion criteria	People with knee instability and/or valgus or varus deformities of >20 degrees; pregnancy; breastfeeding; intention to become pregnant; infectious arthritis; cardiac pacemakers or other implantable electronic devices; a diagnosis of gout; recurrent inflammatory episodes of pseudogout; malignancy (other than basal cell carcinoma) in the prior 3 years; inflammatory arthritis such as rheumatoid arthritis, psoriatic arthritis, Reiter's syndrome, hemochromatosis, inflammatory bowel disease, ankylosing spondylitis, other collagen vascular disease; Paget's disease adjacent to the treated knee; significant instability of the treated knee as determined by the investigator; a history of drug or alcohol abuse within the past 2 years; morbid obesity (BMI greater than 45); involvement in litigation or Wokers' Compensation; intra-articular injection of the target joint within the past month; previous arthroplasty of the treated knee; arthroscopy in the treated knee within he past 6 months
Recruitment/selection of patients	People were offered participation during regular office visits in two orthopedic surgery and one rheumatology practice
Age, gender and ethnicity	Age - Mean (SD): 66.1 (10.9). Gender (M:F): 20:38. Ethnicity: Not stated

Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 3-4 Duration of symptoms (mean [range]): 8.4 (0.2-44) years
Indirectness of population	No indirectness
Interventions	(n=39) Intervention 1: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. Pulsed electrical stimulation using a study device consisting of a knee garment with flexible, embedded electrodes and a small battery-operated generator that produced a 100Hz, negative pulsed signal. It weighs 8 ounces. People were asked to wear the device for 6 hours or more each day, usually at night. They first applied a conducting gel to each electrode, then positioned the garment with the negative electrode on the skin over the patella and the positive return electrode over the anterior distal thigh. The device was turned on between 0 and 12V until a tingling sensation was felt over the night or thigh, and then reducing the amplitude until his sensation disappeared.. Duration 12 weeks. Concurrent medication/care: Stable NSAID and/or analgesic use was maintained 1 month prior to and throughout the study rather than being withdrawn to produce a disease flare. Indirectness: No indirectness (n=19) Intervention 2: Sham electrotherapy. Sham treatment using the same device the same initiation. However, the devices were set to shut off after the amplitude was reduced, and further adjustments required all devices to be restarted.. Duration 12 weeks. Concurrent medication/care: Stable NSAID and/or analgesic use was maintained 1 month prior to and throughout the study rather than being withdrawn to produce a disease flare. Indirectness: No indirectness
Funding	Study funded by industry (Supported by a grant from BioniCare Medical Technologies, Inc. Drs Harrington and Zizic are employees of BioniCare medical Technologies, Inc.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 12 weeks; Group 1: mean -13.2 (SD 22.33); n=39, Group 2: mean -3.1 (SD 15.38); n=19; WOMAC 0-100 Top=High is poor outcome; Comments: Baseline active: 50.6 (14.2). Baseline sham: 44.9 (12.47).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported gender, age, medication requirements, years diagnosed, BMI, use of assistive devices, total knee surgery candidates and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months - Actual outcome: WOMAC function at 12 weeks; Group 1: mean -12 (SD 19.22); n=39, Group 2: mean 1.7 (SD 13.48); n=19; WOMAC function 0-100 Top=High is poor outcome; Comments: Baseline active: 51.9 (15.98). Baseline sham: 44.9 (14.87). Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported gender, age, medication requirements, years diagnosed, BMI, use of assistive devices, total knee surgery candidates and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 3: Mild adverse events at </= 3 months - Actual outcome: Skin rash over the site of electrode placement at 12 weeks; Group 1: 7/39, Group 2: 4/19; Comments: Reported: 17.9% of active patients and 21.1% of placebo patients Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported gender, age, medication requirements, years diagnosed, BMI, use of assistive devices, total knee surgery candidates and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	**Gunaydin 2020[90]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=60 (including kinesio taping group which is not included))
Countries and setting	Conducted in Turkey; Setting: Hacettepe University School of Physiotherapy and Rehabilitation.
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: exercise intervention- 12 weeks, ESWT intervention- 6 weeks. Follow-up at 12 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis made by an orthopaedic surgeon. Classified using K-L grading 1-3.
Stratum	Overall

Subgroup analysis within study	Not applicable
Inclusion criteria	Unilateral or bilateral knee OA diagnosis (grade 1-3 according to K-L criteria); presence of pain for > 1 month; presence of bone densitometry test with the last 6 months; and willingness to participate.
Exclusion criteria	Previous knee operation; receiving medication; being over K-L stage 3; presence of osteoporosis; having perception and coordination disorders; or any systemic disease.
Recruitment/selection of patients	Patients who had been referred to the clinic following diagnosis.
Age, gender and ethnicity	Age - Mean (SD): 58.8 (6.2) years. Gender (M:F): All female. Ethnicity: Not reported
Further population details	1. Age (≤/> 75 years): </=75 years (Age range 49-72). 2. Diagnosis : Diagnosis with imaging (K-L grade 1-3). 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity (baseline VAS during squats): ESWT group: 8.38(3.42), exercise group: 7.84 (2.14) Duration: not reported
Indirectness of population	No indirectness
Interventions	(n=18) Intervention 1: Non-invasive electrotherapy interventions - Extracorporeal shockwave therapy. ESWT intervention was performed once a week for 6 weeks. During the treatment, participants were placed in supine position, and the affected knee was flexed at 90 degrees. Before starting, the intervention area on the tibiofemoral and patellofemoral joints was identified with a pen. The probe was then placed on the painted area after a gel application. An average of 2000 beats at a frequency of 6-8Hz was used per session. During the application, peroneal nerve and vein structures were avoided. Home exercise, prescribed by a physiotherapist for 12 weeks (no further details).. Duration 12 weeks. Concurrent medication/care: Not reported. Indirectness: No indirectness (n=20) Intervention 2: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. Home exercise, prescribed by a physiotherapist for 12 weeks (no further details).. Duration 12 weeks. Concurrent medication/care: Not reported.. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EXTRACORPOREAL SHOCKWAVE THERAPY+ EXERCISE versus EXERCISE ALONE

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: VAS pain doing squats at 12 weeks; Group 1: mean 4.13 (SD 2.36); n=8, Group 2: mean 2.74 (SD 2.16); n=20; VAS 0-10 Top=High is poor outcome; Comments: Baseline values: ESWT group: 8.38 (3.42), exercise group: 7.84 (2.14)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low,

Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 10, Reason: Pain during application of treatment.; Group 2 Number missing: 0, Reason: N/A	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Gundog 2012[91]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=60)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 3 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Clinical (criteria of the American College of Rheumatology) and radiologic (a grade of 2 or 3 on the Kellgren Lawrence scale fro severity of osteoarthritis) osteoarthritis of the knee for at least 6 months duration
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	DeRanging in age from 40 to 80 years, with clinical and radiologic osteoarthritis of the knee for at least a 6 month duration
Exclusion criteria	Had an experience of electrotherapy; received intra-articular injections in the affected joint within the months before the study and/or if they were ascertained or suspected of pregnancy or to be lactating; known or suspected joint infection or a specific condition (i.e. peripheral or central nervous system lesions, neoplasm, diabetes mellitus, osteonecrosis, recent trauma and pacemaker); poor general health status that would interfere with functional assessments during the study
Recruitment/selection of patients	Recruited from the outpatient clinic
Age, gender and ethnicity	Age - Mean (SD): 60.0 (9.1). Gender (M:F): 12:48. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Not stated Duration of symptoms: At least 6 months
Indirectness of population	No indirectness
Interventions	(n=45) Intervention 1: Non-invasive electrotherapy interventions - Interferential therapy. Interferential therapy at different frequencies: 40Hz, 100Hz or 180Hz. This was applied 5 times a week for 3 weeks using a premodulated bipolar method with a carrier frequency of 4 kHz. Each treatment was continued for approximately 20 minutes. Two electrodes (8 x 6cm) were placed laterally to the patella from a combination therapy unit. The people were told that to produce an effect the stimulator must be maintained at a "strong but comfortable level".. Duration 3 weeks. Concurrent

	medication/care: No additional information. Indirectness: No indirectness Comments: The three different dose groups were combined for the analysis due to class effect as agreed in the protocol (n=15) Intervention 2: Sham electrotherapy. Sham interferential therapy with placement of the same pads for the same time, but no electrical stimulation being applied to the probes. Duration 3 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Academic or government funding (Equipment and financial support for the project provided by Ege University)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTERFERENTIAL THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: WOMAC pain at 3 weeks; Group 1: mean 7.2 (SD 2.3); n=45, Group 2: mean 16.1 (SD 1.5); n=15; WOMAC 0-20 Top=High is poor outcome; Comments: Reported 40Hz: 7.2 (1.6). Reported 100Hz: 6.7 (1.2). Reported 180Hz: 7.8 (3.3). Baseline 40Hz: 18.6 (2.6). Baseline 100Hz: 19.3 (2.6). Baseline 180Hz: 19.4 (2.4). Baseline sham: 19.1 (1.8). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, BMI, gender, side, duration and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 2: Physical function at </= 3 months - Actual outcome: WOMAC function at 3 weeks; Group 1: mean 27.5 (SD 7.2); n=45, Group 2: mean 57.8 (SD 6.1); n=15; WOMAC 0-68 Top=High is poor outcome; Comments: Reported 40Hz: 27.2 (5.0). Reported 100Hz: 26.2 (3.5). Reported 180Hz: 29.1 (10.7). Baseline 40Hz: 62.4 (5.5). Baseline 100Hz: 65.7 (7.6). Baseline 180Hz: 67.2 (5.8). Baseline sham: 64.3 (5.9). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, BMI, gender, side, duration and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Gur 2003[92]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=90)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 14 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Osteoarthritis according to the American College of Rheumatology criteria and radiographic evidence of knee osteoarthritis of Kelgren-Lawrence grade 2-4
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with osteoarthritis by clinical and radiographic criteria including uni- or bilateral osteoarthritis of the knee suffering from exercise-induced pain of at least 6 months duration
Exclusion criteria	People with cancer; any acute diseases; uncontrolled diabetes mellitus; untreated hypertension; neurological deficits (motor or sensory); psychotic disorders; dementia; "mental retardation"; other organic mental disorders; people who had received intra- or periarticular injection therapy or physiotherapy during the 6 weeks; people with secondary osteoarthritis due to inflammatory joint diseases and people with routine medical examinations indicated other causes for knee-related pain (e.g. osteoarthritis of the hip, arterial insufficiency, lumbar root compression)
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 59.7 (7.0). Gender (M:F): 18:72. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Radiographic grade 2-4, median grade 3 Duration of symptoms (mean [SD]): 57.0 (45.0) months
Indirectness of population	No indirectness
Interventions	(n=60) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. Laser therapies using a Ga-AS infrared laser, class IIIb laser product, with a wavelength of 904nm, Frank Line IR30, Fysiomed Belgium. This involved either 5 minutes, 3 J total dose and exercise or 3 minutes, 2 J total dose and exercise. In the first group: 5 minute stimulation time, 200 nanosecond maximum pulse duration, 2.5kHz pulse

	frequency, 20W maximum output per pulse, 10mW average power, 1cm² surface, 3J total energy and 30J accumulated dose when applied. In the second group: 3 minute stimulation time, 200 nanosecond maximum pulse duration, 2.8kHz pulse frequency, 20W maximum output per pulse, 11.2mW average power, 1cm² surface, 2J total energy, and 20J accumulated dose. The treatment was applied to the anterolateral portal, which is located approximately 1cm above the lateral joint line and approximately 1cm lateral to the margin of the patellar tendon, and the anteromedial portal. This was completed for 10 treatments.. Duration 14 weeks. Concurrent medication/care: All people received exercise therapy that was continued for 14 weeks and involved isometric quadriceps exercise (straight leg raising). Indirectness: No indirectness Comments: The two different dose groups were combined due to class effect as agreed in the protocol (n=30) Intervention 2: Sham electrotherapy. Placebo laser treatment where the laser emitter was similar to the infrared emitter in appearance but did not emit light. The treatment was applied to the anterolateral portal, which is located approximately 1cm above the lateral joint line and approximately 1cm lateral to the margin of the patellar tendon, and the anteromedial portal. This was completed for 10 treatments.. Duration 14 weeks. Concurrent medication/care: All people received exercise therapy that was continued for 14 weeks and involved isometric quadriceps exercise (straight leg raising). Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: Pain at movement (VAS) at 12 weeks; Group 1: mean 3.69 (SD 1); n=60, Group 2: mean 4.3 (SD 1.38); n=30; VAS 0-10 Top=High is poor outcome; Comments: Reported laser group 1: 3.58 (1.12). Reported laser group 2: 3.80 (0.86). Baseline laser group 1: 7.32 (2.37). Baseline laser group 2: 7.44 (1.38). Baseline sham: 6.74 (1.73). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, BMI, duration of disease, sex, educational level, smoking, sport activity, pain localisation, systemic disease, crepitation, effusion, involved knee, Heberden's nodules, osteopenia, history, radiological grade and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild

	adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Gworys 2012[93]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=125)
Countries and setting	Conducted in Poland; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis of knee osteoarthritis according to the criteria established by the American College of Rheumatology
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with pain of more than 6 weeks' duration and a diagnosis of knee osteoarthritis according to the criteria established by the American College of Rheumatology. Enrollment criteria also included 2nd degree joint injury according to Seyfried on the basis of clinical examination.
Exclusion criteria	Intraarticular corticosteroids, hyaluronic acid or other drugs within the 3 months preceding the study; physical therapy during the 3 months; contraindications for physical therapy
Recruitment/selection of patients	People treated at the Clinical Department of Medical Rehabilitation, 2nd Rehabilitation Department at the Medical University in Lodz, and the Outpatient Rehabilitation Clinic
Age, gender and ethnicity	Age - Mean (SD): 64.0 (11.3). Gender (M:F): Not stated. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Not stated / Unclear 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: 2nd degree joint injury according to Seyfried on the basis of clinical examination Duration of symptoms: Pain for at least 6 weeks
Indirectness of population	No indirectness
Interventions	(n=94) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. Laser therapy sessions performed once a day, 5 days a week over 2 weeks. This included 3 groups: group 1, received one-wave laser irradiation (wave length 810nm, dose 8J/point, surface density of energy 12.7 J/cm², power 400mW, surface density of power 634.9 mW/cm²) in the continuous mode; group 2, received MLS laser irradiation (power 1100mW, frequency 2000Hz, dose 12.4 J/point, energy density 6.21 J/cm²); group 3, received MLS laser irradiation (power 1100mW, frequency 2000Hz, dose

	6.6J/point, energy density 3.28J/cm²). Duration 2 weeks. Concurrent medication/care: No additional ifnromation. Indirectness: No indirectness (n=31) Intervention 2: Sham electrotherapy. Laser therapies without actual irradiation. Duration 2 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: Pain (VAS) at 2 weeks; Group 1: mean 2.3 (SD 1.6); n=94, Group 2: mean 1.5 (SD 1); n=31; VAS 0-10 Top=High is poor outcome; Comments: Reported laser group 1: 2.0 (0.8). Reported laser group 2: 3.2 (1.8). Reported laser group 3: 1.7 (1.5). Baseline laser group 1: 5.4 (1.4). Baseline laser group 2: 5.6 (1.9). Baseline line group 3: 5.5 (2.2). No baseline data for the placebo group. Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age. Reports baseline values for pain for only the laser groups.; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Helianthi 2016[96]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=62)
Countries and setting	Conducted in Indonesia; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 7 weeks (5 weeks of treatment)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with grade 2 and grade 3 knee osteoarthritis based on the Kellgren-Lawrence grading scale, either unilateral or bilateral and who also had average pain intensity of more than 40 on a 100mm visual analogue scale
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People aged more than 60 years old who have been diagnosed with osteoarthritis of the knee
Exclusion criteria	People who had a previous knee replacement surgery; consumed opioids as well as the patients who had a previous corticosteroid intraarticular injection in the last 4 months or those with hyaluronic acid intraarticular injection in the last 6 months or local-oral NSAIDs medication in the last 3 days or topical capsaicin treatment prior to study entry; people who received TENS, ultrasound or laser therapy in the previous 2 weeks or those with conditions of laser treatment contraindication (cancer, infections with high fever, untreated epilepsy, acute solaris dermatitis, increased photoallergic responsiveness, congestive heart failure) as well as those with conditions that would interfere outcome measures (e.g. psychosis, moderate-severe cognitive impairment)
Recruitment/selection of patients	People who visited the Geriatric Outpatient Clinic, Acupuncture Outpatient Clinic and Rheumatology Outpatient Clinic at Cipto Mangunkusumo Hospital, Jakarta, Indonesia
Age, gender and ethnicity	Age - Mean (SD): 69 (5). Gender (M:F): 17:42. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Grade 2-3 (median grade 3) Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=31) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. Laser acupuncture using a single-probe gallium aluminum arsenide laser devices. Output

	power 50mW output power, 25mW/cm² power density, wavelength 785nm. Laser acupuncture was performed at the acupuncture points of ST35 Dubi, ST36 Zusanli, SP9 Yinlingquan, GB34 Yanglingquan and EX-LE-4 Neixiyan. A laserpuncture dose of 4 Joule was carried out for 80 seconds at each point. The treatment was given twice a week as many as 10 sessions.. Duration 5 weeks. Concurrent medication/care: People were allowed to take paracetamol as required for severe pain (with a maximum dose of 4g/day). Indirectness: No indirectness (n=31) Intervention 2: Sham electrotherapy. Sham laser therapy (can see the red light but no active treatment). Duration 5 weeks. Concurrent medication/care: People were allowed to take paracetamol as required for severe pain (with a maximum dose of 4g/day). Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: Visual analogue scale at 7 weeks; Group 1: mean -40.5 (SD 14.8); n=31, Group 2: mean -1.3 (SD 6); n=31; VAS 0-100 Top=High is poor outcome; Comments: Baseline laser: 60.2 (12.2). Baseline sham: 54.1 (10.8). Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported baseline values of age, gender, body mass index, grades of osteoarthritis, paracetamol use and baseline values of outcomes; Group 1 Number missing: 1, Reason: 1 drop out; Group 2 Number missing: 2, Reason: 2 drop out	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Hinman 2014[97]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=282)
Countries and setting	Conducted in Australia; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 12 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Knee pain of longer than 3 months duration, knee pain on most days with average severity of 4 or more out of 10 on a numeric rating scale, and had morning stiffness lasting less than 30 minutes (consistent with a clinical diagnosis of osteoarthritis0
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Fulfilling clinical criteria of osteoarthritis who were aged 50 years or older
Exclusion criteria	History of any systemic arthritic condition; history of knee arthroplasty on the most painful knee; wait listed for any knee surgery for either knee; history of any knee surgery in previous 6 months; any other condition affecting lower limb function (eg trauma, malignancy, neurological condition); history of any knee injection in past 6 months (eg cortisone, hyaluronic acid); current use of oral or injectable anticoagulant medication; use of acupuncture in past 12 months; any bleeding disorder; allergy to light; referral to pain clinic or use of morphine or pethidine within past 6 months; any other medical condition precluding participation in the trial (eg kidney or liver disease, deep vein thrombosis); knee pain subject to compensation claim; unable to give written informed consent
Recruitment/selection of patients	People recruited from the metropolitan Melbourne and regional Victoria via advertisements in the community, media, and medical/physical therapy clinics between February 2010 and December 2011.
Age, gender and ethnicity	Age - Mean (SD): 63.6 (8.4). Gender (M:F): 143:139. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis without imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Not stated Duration of symptoms: <1 year to ≥10 years, median 5-<10 years
Indirectness of population	No indirectness

Interventions	(n=71) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. Laser acupuncture administered to selected points by custom-manufactured Acupak laser machines with the patient supine or sitting over the edge of a treatment couch. Standard class 3B laser devices were used (measured output 10mW and energy output 0.2J/point, with a red light at the probe tip that lit up in active and sham models to maintain blinding. The laser was set to give active or sham treatment dependent on the participant code, which was entered onto the machine.. Duration 12 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=70) Intervention 2: Sham electrotherapy. Sham laser acupuncture. Duration 12 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=71) Intervention 3: No intervention - No treatment. No acupuncture. Duration 12 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=70) Intervention 4: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. Needle acupuncture treatment. Duration 12 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness Comments: This group was not included in the analysis as it did not meet the inclusion criteria in the protocol
Funding	Academic or government funding (Funded by the National Health and Medical Research Council 9project 566783). Drs Hinman and Bennell are both funded in part by Australian Research Council Future Fellowships (FT130100175 and FT0991413, respectively). Dr McCrory is funded in part by a National Health and Medical Research Council Practitioner Fellowship (1026383). Dr Pirotta is funded in part by a National Health and Medical Research Council Career Development Fellowship 910508300. Dr Williamson was funded in part by a National Health and Medical Research Council grant (1004233).)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: SF-12 PCS at 12 weeks; Group 1: mean 39.4 (SD 9.5); n=65, Group 2: mean 40.2 (SD 10.1); n=58; SF-12 PCS 0-100 Top=High is good outcome; Comments: Baseline laser: 37.6 (10.3). Baseline sham: 37.9 (9.6).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover -

Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, height, weight, BMI, symptom duration, unilateral symptoms, medication use, past treatment and baseline values of outcomes; Group 1 Number missing: 13, Reason: 12 declined treatment invitation, 1 other medical problem; Group 2 Number missing: 16, Reason: 9 declined invitation for treatment, 5 not interested, 1 time commitment, 1 could not contact
- Actual outcome: SF-12 MCS at 12 weeks; Group 1: mean 53 (SD 9.9); n=65, Group 2: mean 53.2 (SD 10.4); n=58; SF-12 MCS 0-100 Top=High is good outcome; Comments: Baseline laser: 52.5 (11.1). Baseline sham: 52.4 (9.5).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, height, weight, BMI, symptom duration, unilateral symptoms, medication use, past treatment and baseline values of outcomes; Group 1 Number missing: 13, Reason: 12 declined treatment invitation, 1 other medical problem; Group 2 Number missing: 16, Reason: 9 declined invitation for treatment, 5 not interested, 1 time commitment, 1 could not contact

Protocol outcome 2: Health-related quality of life at > 3 months
- Actual outcome: SF-12 PCS at 1 year; Group 1: mean 38.8 (SD 10.2); n=58, Group 2: mean 38.2 (SD 9.9); n=51; SF-12 PCS 0-100 Top=High is good outcome; Comments: Baseline laser: 37.6 (10.3). Baseline sham: 37.9 (9.6).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, height, weight, BMI, symptom duration, unilateral symptoms, medication use, past treatment and baseline values of outcomes; Group 1 Number missing: 18, Reason: 12 declined treatment invitation, 1 other medical problem, 4 not interested, 1 knee replacement; Group 2 Number missing: 22, Reason: 9 declined invitation for treatment, 11 not interested, 1 time commitment, 1 could not contact
- Actual outcome: SF-12 MCS at 1 year; Group 1: mean 52.1 (SD 9.8); n=58, Group 2: mean 52.8 (SD 9.1); n=51; SF-12 MCS 0-100 Top=High is good outcome; Comments: Baseline laser: 52.5 (11.1). Baseline sham: 52.4 (9.5).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, height, weight, BMI, symptom duration, unilateral symptoms, medication use, past treatment and baseline values of outcomes; Group 1 Number missing: 18, Reason: 12 declined treatment invitation, 1 other medical problem, 4 not interested, 1 knee replacement; Group 2 Number missing: 22, Reason: 9 declined invitation for treatment, 11 not interested, 1 time commitment, 1 could not contact

Protocol outcome 3: Pain at </= 3 months
- Actual outcome: WOMAC pain at 12 weeks; Group 1: mean 6.6 (SD 3.9); n=65, Group 2: mean 6.6 (SD 3.9); n=58; WOMAC 0-20 Top=High is poor outcome; Comments: Baseline laser: 8.3 (3.1). Baseline sham: 8.6 (3.5).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, height, weight, BMI, symptom duration, unilateral symptoms, medication use, past treatment and baseline values of outcomes; Group 1 Number missing: 13, Reason: 12 declined treatment invitation, 1 other medical problem; Group 2 Number missing: 16, Reason: 9 declined invitation for treatment, 5 not interested, 1 time commitment, 1 could not contact

Protocol outcome 4: Pain at > 3 months
- Actual outcome: WOMAC pain at 1 year; Group 1: mean 7.1 (SD 4.1); n=58, Group 2: mean 6.9 (SD 4); n=51; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline laser: 8.3 (3.1). Baseline sham: 8.6 (3.5).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover -

Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, height, weight, BMI, symptom duration, unilateral symptoms, medication use, past treatment and baseline values of outcomes; Group 1 Number missing: 18, Reason: 12 declined treatment invitation, 1 other medical problem, 4 not interested, 1 knee replacement; Group 2 Number missing: 22, Reason: 9 declined invitation for treatment, 11 not interested, 1 time commitment, 1 could not contact

Protocol outcome 5: Physical function at </= 3 months
- Actual outcome: WOMAC function at 12 weeks; Group 1: mean 21.9 (SD 12.3); n=65, Group 2: mean 21.7 (SD 12); n=58; WOMAC 0-68 Top=High is poor outcome; Comments: Baseline laser: 27.0 (11.3). Baseline sham: 27.5 (12.4).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, height, weight, BMI, symptom duration, unilateral symptoms, medication use, past treatment and baseline values of outcomes; Group 1 Number missing: 13, Reason: 12 declined treatment invitation, 1 other medical problem; Group 2 Number missing: 16, Reason: 9 declined invitation for treatment, 5 not interested, 1 time commitment, 1 could not contact

Protocol outcome 6: Physical function at > 3 months
- Actual outcome: WOMAC function at 1 year; Group 1: mean 22.6 (SD 13.1); n=58, Group 2: mean 21.6 (SD 13.6); n=51; WOMAC function 0-68 Top=High is poor outcome; Comments: Baseline laser: 27.0 (11.3). Baseline sham: 27.5 (12.4).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, height, weight, BMI, symptom duration, unilateral symptoms, medication use, past treatment and baseline values of outcomes; Group 1 Number missing: 18, Reason: 12 declined treatment invitation, 1 other medical problem, 4 not interested, 1 knee replacement; Group 2 Number missing: 22, Reason: 9 declined invitation for treatment, 11 not interested, 1 time commitment, 1 could not contact

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus NO TREATMENT

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: SF-12 PCS at 12 weeks; Group 1: mean 39.4 (SD 9.5); n=65, Group 2: mean 39.5 (SD 10.7); n=69; SF-12 PCS 0-100 Top=High is good outcome; Comments: Baseline laser: 37.6 (10.3). Baseline no treatment: 39.2 (9.0).
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, height, weight, BMI, symptom duration, unilateral symptoms, medication use, past treatment and baseline values of outcomes; Group 1 Number missing: 13, Reason: 12 declined treatment invitation, 1 other medical problem; Group 2 Number missing: 2, Reason: 2 not interested
- Actual outcome: SF-12 MCS at 12 weeks; Group 1: mean 53 (SD 9.9); n=65, Group 2: mean 55.8 (SD 9.1); n=69; SF-12 MCS 0-100 Top=High is good outcome; Comments: Baseline laser: 52.5 (11.1). Baseline no treatment: 55.6 (10.2).
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, height, weight, BMI, symptom duration, unilateral symptoms, medication use, past treatment and baseline values of outcomes; Group 1 Number missing: 13, Reason: 12 declined treatment invitation, 1 other medical problem; Group 2 Number missing: 2, Reason: 2 not interested

Protocol outcome 2: Health-related quality of life at > 3 months
- Actual outcome: SF-12 PCS at 1 year; Group 1: mean 38.8 (SD 10.2); n=58, Group 2: mean 38.9 (SD 11.2); n=62; SF-12 PCS 0-100 Top=High is good outcome; Comments: Baseline laser: 37.6 (10.3). Baseline no treatment: 39.2 (9.0).
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, height, weight, BMI, symptom duration, unilateral symptoms, medication use, past treatment and baseline values of outcomes; Group 1 Number missing: 18, Reason: 12 declined treatment invitation, 1 other medical problem, 4 not interested, 1 knee replacement; Group 2 Number missing: 9, Reason: 6 not interested, 2 family illness, 1 other medical problem
- Actual outcome: SF-12 MCS at 1 year; Group 1: mean 52.1 (SD 9.8); n=58, Group 2: mean 54.4 (SD 10.2); n=62; SF-12 MCS 0-100 Top=High is good outcome; Comments: Baseline laser: 52.5 (11.1). Baseline no treatment: 55.6 (10.2).
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, height, weight, BMI, symptom duration, unilateral symptoms, medication use, past treatment and baseline values of outcomes; Group 1 Number missing: 18, Reason: 12 declined treatment invitation, 1 other medical problem, 4 not interested, 1 knee replacement; Group 2 Number missing: 9, Reason: 6 not interested, 2 family illness, 1 other medical problem

Protocol outcome 3: Pain at </= 3 months
- Actual outcome: WOMAC pain at 12 weeks; Group 1: mean 6.6 (SD 3.9); n=65, Group 2: mean 7.3 (SD 3.9); n=69; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline laser: 8.3 (3.1). Baseline no treatment: 7.8 (3.4).
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, height, weight, BMI, symptom duration, unilateral symptoms, medication use, past treatment and baseline values of outcomes; Group 1 Number missing: 13, Reason: 12 declined treatment invitation, 1 other medical problem; Group 2 Number missing: 2, Reason: 2 not interested

Protocol outcome 4: Pain at > 3 months
- Actual outcome: WOMAC pain at 1 year; Group 1: mean 7.1 (SD 4.1); n=58, Group 2: mean 7.4 (SD 4.1); n=62; WOMAC 0-20 Top=High is poor outcome; Comments: Baseline laser: 8.3 (3.1). Baseline no treatment: 7.8 (3.4).
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, height, weight, BMI, symptom duration, unilateral symptoms, medication use, past treatment and baseline values of outcomes; Group 1 Number missing: 18, Reason: 12 declined treatment invitation, 1 other medical problem, 4 not interested, 1 knee replacement; Group 2 Number missing: 9, Reason: 6 not interested, 2 family illness, 1 other medical problem

Protocol outcome 5: Physical function at </= 3 months
- Actual outcome: WOMAC function at 12 weeks; Group 1: mean 21.9 (SD 12.3); n=65, Group 2: mean 21.7 (SD 12); n=58; WOMAC 0-68 Top=High is poor outcome; Comments: Baseline laser: 27.0 (11.3). Baseline no treatment: 26.1 (12.4).
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, height, weight, BMI,

symptom duration, unilateral symptoms, medication use, past treatment and baseline values of outcomes; Group 1 Number missing: 13, Reason: 12 declined treatment invitation, 1 other medical problem; Group 2 Number missing: 2, Reason: 2 not interested Protocol outcome 6: Physical function at > 3 months - Actual outcome: WOMAC function at 1 year; Group 1: mean 22.6 (SD 13.1); n=58, Group 2: mean 21.6 (SD 13.6); n=51; WOMAC 0-68 Top=High is poor outcome; Comments: Baseline laser: 27.0 (11.3). Baseline no treatment: 26.1 (12.4). Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, height, weight, BMI, symptom duration, unilateral symptoms, medication use, past treatment and baseline values of outcomes; Group 1 Number missing: 18, Reason: 12 declined treatment invitation, 1 other medical problem, 4 not interested, 1 knee replacement; Group 2 Number missing: 9, Reason: 6 not interested, 2 family illness, 1 other medical problem	
Protocol outcomes not reported by the study	Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Hsieh 2012[100]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=73)
Countries and setting	Conducted in Taiwan; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 2 weeks of treatment, 2 additional weeks of follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Combined clinical and radiographic criteria of knee osteoarthritis, as established by the American college of Rheumatology
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People who fulfilled the combined clinical and radiographic criteria of knee osteoarthritis; with Kellgren Lawrence scores of 2 or greater
Exclusion criteria	People with a history of a previous knee operation with an implant; people who were pregnant or planning to become pregnant; those who had a self-reported history of malignancy, vertigo or stroke
Recruitment/selection of patients	People recruited from the clinic of the department of physical medicine and rehabilitation at Shin Kong Wu Ho-Su Memorial Hospital in Taiwan
Age, gender and ethnicity	Age - Mean (SD): 61.2 (10.7). Gender (M:F): 10:62. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : High morbidity score (People with comorbidity: 39. People without comorbidity: 33.). 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence scores of 2 or greater in both knees Duration of symptoms: Not stated.
Indirectness of population	No indirectness
Interventions	(n=37) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. Short-term monochromatic infrared energy therapy with an Anodyne Therapy Professional infrared Therapy System (model 480). Delivered a radiant power at 6.24W through 8 flexible therapy pads, each containing 60 supraluminous gallium-aluminum arsenide diodes that emitted an 890nm wavelength of light energy. The pads were placed on the anterior, posterior, medial and lateral surfaces of the knee. The pads were held in place with neoprene straps supplied by the manufacturer.All people received 40 minutes of treatment, with the power on for the treatment group.

	This was achieved 3 times a week for a total of 6 sessions spread over 2 weeks, participants in the group received 2.08 J/cm²/min.. Duration 2 weeks of treatment (2 more weeks of follow up). Concurrent medication/care: No additional information. Indirectness: No indirectness (n=35) Intervention 2: Sham electrotherapy. Sham laser treatment with the same laser but switched off during therapy. Duration 2 weeks of treatment (2 more weeks of follow up). Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: KOOS quality of life at 4 weeks; Group 1: mean 61.3 (SD 13.3); n=37, Group 2: mean 61.4 (SD 14.7); n=35; KOOS quality of life 0-100 Top=High is good outcome; Comments: Baseline laser: 50.8 (19.1). Baseline placebo: 55.4 (18.3).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported gender, age, BMI, married status, educational level, working status, comorbidity, smoking, drinking, Kellgren Lawrence score, baseline values of outcomes; Group 1 Number missing: 4, Reason: 1 did not received the allocated intervention (due to lack of personal time), 3 lost to follow up (due to lack of personal time); Group 2 Number missing: 2, Reason: 1 lack of personal time, 1 pain aggravation

Protocol outcome 2: Pain at </= 3 months
- Actual outcome: KOOS pain at 4 weeks; Group 1: mean 79.2 (SD 12); n=37, Group 2: mean 77.5 (SD 14); n=35; KOOS pain 0-100 Top=High is good outcome; Comments: Baseline laser: 74.5 (13.7). Baseline placebo: 75.4 (16.4).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported gender, age, BMI, married status, educational level, working status, comorbidity, smoking, drinking, Kellgren Lawrence score, baseline values of outcomes; Group 1 Number missing: 4, Reason: 1 did not received the allocated intervention (due to lack of personal time), 3 lost to follow up (due to lack of personal time); Group 2 Number missing: 2, Reason: 1 lack of personal time, 1 pain aggravation

Protocol outcome 3: Physical function at </= 3 months
- Actual outcome: KOOS function in daily living at 4 weeks; Group 1: mean 78.9 (SD 15.5); n=37, Group 2: mean 76.5 (SD 16.1); n=35; KOOS function in daily living 0-100 Top=High is good outcome; Comments: Baseline laser: 74.7 (17.3). Baseline placebo: 75.4 (18.0).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported gender, age, BMI, married status, educational level, working status, comorbidity, smoking, drinking, Kellgren Lawrence score, baseline values of outcomes; Group 1 Number missing: 4, Reason: 1 did not received the allocated intervention (due to lack of personal time), 3 lost to follow up (due to lack of personal time); Group 2 Number missing: 2, Reason: 1 lack

of personal time, 1 pain aggravation	
Protocol outcomes not reported by the study	Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Huang 2005[101]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=120)
Countries and setting	Conducted in Taiwan; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 8 weeks (1 year total follow up)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Bilateral moderate knee osteoarthritis with periarticular soft tissue pain, as identified by painful sensations during palpation or passive stretching of the arthritic knee under orthopedic examination. The locations of soft tissue pain were confirmed by the findings of musculoskeletal ultrasound images.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with bilateral moderate knee osteoarthritis with periarticular soft tissue pain, as identified by painful sensations during palpation or passive stretching of the arthritis knee.
Exclusion criteria	No additional information
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 62.0 (8.4). Gender (M:F): 23:97. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging (Ultrasonography). 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Altman grade 2 Duration of symptoms: 6 months - 11 years.
Indirectness of population	No indirectness
Interventions	(n=60) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. Two groups: isokinetic exercise and continuous ultrasound therapy and isokinetic exercise and pulsed ultrasound. Given 3 times weekly for 8 weeks. Ultrasound treatment was given according to the locations of tendinopathy, ethesopathy, Baker's cyst formation or bursitis indicated by the real time 5 to 12MHz high-resolution linear scanner, followed by tender point findings on orthopedic examination. The continuous ultrasound included a duty cycle of 100%, with frequency of 1MHz and a spatial and temporal peak intensity of 1.5W/cm². The US probe was applied for 5 minutes to each

	treated region (a total treated area of approximately 25cm²). The pulsed sonication included a frequency of 1MHz and a spatial and temporal peak intensity of 2.5W/cm², and pulsed at a duty cycle of 25%. The duration applied to each region was the same as the continuous sonication. The intensity was adjusted to the level at which the person felt a warm sensation or mild sting.. Duration 8 weeks. Concurrent medication/care: All groups received 20 minutes of hot packs and 5 minutes of passive ROM exercise on an electric stationary bike (20 ycles/min) of both knees before undergoing muscle strengthening exercises.. Indirectness: No indirectness Comments: The groups were combined due to class effect as agreed in the protocol (n=30) Intervention 2: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. Isokinetic muscle strengthening exercises 3 times weekly for 8 weeks. The isokinetic exercise included quadriceps and hamstrings stretching with 1-5 sets during the first through fifth sessions and 6 sets for the remaining 6th through 24th sessions. Each set included 5 repetitions at different angular velocities.. Duration 8 weeks. Concurrent medication/care: All groups received 20 minutes of hot packs and 5 minutes of passive ROM exercise on an electric stationary bike (20 cycles/min) of both knees before undergoing muscle strengthening exercises.. Indirectness: No indirectness (n=30) Intervention 3: No intervention - No treatment. No treatment (no exercise or ultrasound). Duration 8 weeks. Concurrent medication/care: All groups received 20 minutes of hot packs and 5 minutes of passive ROM exercise on an electric stationary bike (20 ycles/min) of both knees before undergoing muscle strengthening exercises.. Indirectness: No indirectness Comments: This group was not included in the analysis as it was not comparable to the intervention group as agreed in the protocol
Funding	Academic or government funding (Supported by the National Science Council of Taiwan (grant no. NSC-92-2314-B-037-067))

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: Pain (VAS) at 8 weeks; Group 1: mean 1.6 (SD 1.5); n=60, Group 2: mean 2.4 (SD 1.8); n=30; VAS 0-10 Top=High is poor outcome;
Comments: Reported continuous ultrasound: 1.2 (1.4). Reported pulsed ultrasound: 1.9 (1.6). Baseline continuous ultrasound: 4.9 (1.5). Baseline pulsed ultrasound: 5.2 (1.7). Baseline no treatment: 5.0 (1.3).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 2: Pain at > 3 months - Actual outcome: Pain (VAS) at 1 year; Group 1: mean 3.1 (SD 1.6); n=60, Group 2: mean 2.2 (SD 1.8); n=30; VAS 0-10 Top=High is poor outcome; Comments: Reported continuous ultrasound: 3.5 (1.7). Reported pulsed ultrasound: 2.6 (1.4). Baseline continuous ultrasound: 4.9 (1.5). Baseline pulsed ultrasound: 5.2 (1.7). Baseline no treatment: 5.0 (1.3). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Huang 2005[102]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=140)
Countries and setting	Conducted in Taiwan; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 8 weeks of treatment (1 year in total)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with bilateral moderate knee osteoarthritis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with bilateral knee osteoarthritis (Altman Grade 2)
Exclusion criteria	No additional information
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 65.0 (6.4). Gender (M:F): 27:113. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Not stated / Unclear 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Altman grade 2 Duration of symptoms: 5 months - 12 years
Indirectness of population	No indirectness
Interventions	(n=35) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. Isokinetic exercise and pulse ultrasound. Isokinetic exercise included a muscle strengthening exercise program 3 times a week for 8 weeks at a variety of angles with five repetitions of concentric contractions. The ultrasound treatment was used in locations of tendopathy, enthesopathy or cystitis indicated by the real-time 5-12 mHz high-resolution linear scanner followed by tender point findings made during orthopedic examination. The most common periarticular soft tissue lesions included anserine bursitis, medial collateral enthestis, popliteal tendonitis, Baker's cyst, and supra- and infrapatellar bursitis. Pulse sonication was used with a frequency of 1MHz and a spatial and temporal peak intensity of 2.5 W/cm², and pulsed at a duty cycle of 25%. Sonication was performed 3 times a week for 8 weeks. The ultrasound probe was applied for 5 minutes to each treated region over the medial collateral ligament, anserine bursa, and the popliteal fossa tender points , a total treated area of around 25cm². The intensity was adjusted to the level at which the person experienced a

	warm sensation or a mild sting.. Duration 8 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=35) Intervention 2: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. Isokinetic exercise and pulse ultrasound. Isokinetic exercise included a muscle strengthening exercise program 3 times a week for 8 weeks at a variety of angles with five repetitions of concentric contractions.. Duration 8 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=35) Intervention 3: No intervention - No treatment. No interventions. Duration 8 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness Comments: This group was not included in the analysis as it was not comparable to the intervention as agreed in the protocol (n=35) Intervention 4: No intervention - No treatment. Hyaluronic acid injections, exercise and ultrasound treatment. Duration 8 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness Comments: This group was not included in the analysis as it did not fulfill the inclusion criteria in the protocol
Funding	Academic or government funding (Supported by a project grant from the National Science Council of Taiwan)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: Pain (VAS) at 8 weeks; Group 1: mean 2.5 (SD 1.9); n=35, Group 2: mean 1.2 (SD 1.6); n=35; VAS 0-10 Top=High is poor outcome; Comments: Baseline ultrasound: 5.5 (1.7). Baseline no treatment: 5.3 (1.5).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Pain at > 3 months
- Actual outcome: Pain (VAS) at 1 year; Group 1: mean 2.6 (SD 1.5); n=35, Group 2: mean 3.9 (SD 1.4); n=35; VAS 0-10 Top=High is poor outcome; Comments: Baseline ultrasound: 5.5 (1.7). Baseline no treatment: 5.3 (1.5).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Inal 2016[107]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=93)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 6 weeks (2 weeks of intervention, 4 weeks additional follow up)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Symptomatic knee osteoarthritis according to the American College of Rheumatology criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with symptomatic osteoarthritis of the knee with grade 2 or above osteoarthritic changes according to Kellgren-Lawrence radiologic assessment; pain for at least 6 months
Exclusion criteria	People who underwent surgery to any joints of lower extremities; used non-steroidal anti-inflammatory drugs and chondroprotective agents in the last month; had received extremities; used non-steroidal anti-inflammatory drugs and chondroprotective agents in the last month; had received TENS in the previous 6 months and had cardiac pacemaker; complainted linked to lower extremities such as radiculopathy or pain on ankle; uncontrolled co-morbid chronic disease such as diabetes mellitus and hypertension; a poor general health status; definite/suspected pregnancy; dementia or cognitive impairment; neurological disorders such as multiple sclerosis, Parkinson's and Alzherimer's diseases; major trauma in last 6 months and injection in the last 3 months
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Other: Mean (SE): Placebo = 64.6 (1.88), 4Hz TENS = 64.4 (1.70), 100Hz TENS = 64.1 (0.99). Gender (M:F): 0:93. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Radiographic grade 2-4, median grade 3 Duration of symptoms (median [range]): Placebo = 48 (24-120) months, 4Hz TENS = 48 (16.5-120), 100Hz TENS = 30 (12-75)
Indirectness of population	No indirectness

Interventions	(n=60) Intervention 1: Non-invasive electrotherapy interventions - Transcutaneous electrical nerve stimulation (TENS). TENS over 10 sessions (five sessions per week). One channel of TENS with two rubber electrodes (each 5x9cm²) was connected to both medially above the knees and laterally below the knees, whereas the second channel with similar two rubber electrodes was connected laterally above the knees and medially below the knees. People remained in a supine position with both knees at full extension while electrodes were placed around the painful areas after the skin was cleaned. The intensity of the current was adjusted at a strong but comfortable and tolerable level which was supported before without concurrent muscle contraction for each person in the active group. This was achieved at two doses, 4Hz and 100Hz.. Duration 2 weeks (4 additional weeks of follow up). Concurrent medication/care: All people had physical therapy in the inpatient clinic and were educated primarily about the harmful movements and conditions for her knees. This included hot pack, therapeutic ultrasonography, TENS and exercise programs. Hot packs were applied during 20 minutes to both knees of the people. Therapeutic ultrasound was performed separately to both knees during 5 minutes with a stimulation of 1.5W/cm². Exercise programs consisted of three sessions of range of motion, quadriceps isometric and isotonic exercises in a day with 20 repetition of each exercise in each session. After ten sessions of physical therapy in the hospital the people were discharged with a home exercise program.. Indirectness: No indirectness Comments: The two groups were combined due to class effect as agreed in the protocol (n=30) Intervention 2: Sham electrotherapy. Sham TENS. Duration 2 weeks (4 additional weeks of follow up). Concurrent medication/care: All people had physical therapy in the inpatient clinic and were educated primarily about the harmful movements and conditions for her knees. This included hot pack, therapeutic ultrasonography, TENS and exercise programs. Hot packs were applied during 20 minutes to both knees of the people. Therapeutic ultrasound was performed separately to both knees during 5 minutes with a stimulation of 1.5W/cm². Exercise programs consisted of three sessions of range of motion, quadriceps isometric and isotonic exercises in a day with 20 repetition of each exercise in each session. After ten sessions of physical therapy in the hospital the people were discharged with a home exercise program.. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) versus SHAM ELECTROTHERAPY	

Protocol outcome 1: Pain at </= 3 months - Actual outcome: WOMAC pain at 6 weeks; Group 1: mean 6.5 (SD 4.8); n=60, Group 2: mean 7.1 (SD 4.7); n=30; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reports final values and standard error. Reported 4Hz: 6.70 (0.86). Reported 100Hz: 6.27 (0.90). Reported sham: 7.10 (0.85). Baseline 4Hz: 10.17 (0.52). Baseline 100Hz: 10.70 (0.66). Placebo: 10.77 (0.61). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, BMI, duration of symptoms, radiologic grade and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 2: Physical function at </= 3 months - Actual outcome: WOMAC function at 6 weeks; Group 1: mean 24.8 (SD 15.6); n=60, Group 2: mean 25.7 (SD 14.1); n=30; WOMAC function 0-68 Top=High is poor outcome; Comments: Reports final values and standard error. Reported 4Hz: 25.07 (2.85). Reported 100Hz: 24.43 (2.83). Reported sham: 25.67 (2.57). Baseline 4Hz: 37.33 (1.78). Baseline 100Hz: 36.87 (1.77). Placebo: 38.27 (1.75). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, BMI, duration of symptoms, radiologic grade and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Jia 2016[115]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=106)
Countries and setting	Conducted in China; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 10 days of treatment, 12 additional weeks of follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Knee osteoarthritis fulfilling the American College of Rheumatology classification criteria, Kellgren and Lawrence grade 2-3 with knee pain and limitation on most days within the past 6 months
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Age no less than 40 years; knee osteoarthritis fulfilling the American College of Rheumatology classification criteria, Kellgren and Lawrence class rating of 2-3, knee pain and limitation on most days within the past 6 months
Exclusion criteria	Rheumatoid arthritis; gouty arthritis; infectious arthritis; a history of knee joint replacement on the study knee; current or past (within 6 months) oral or intra-articular corticosteroid use; physiotherapy; acupuncture treatment; the use of exercises specifically for the knee within the past 6 months; a medical condition that precludes safe exercise (such as uncontrolled hypertension, a heart condition, haematological diseases coagulopathy, gastrointestinal ulcers, or a haemorrhage); a history of taking NSAIDs or symptomatic slow-acting drugs for osteoarthritis (diacerein, hyaluronic acid) within the previous 30 days, or the inability to complete the study
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 62.4 (10.1). Gender (M:F): 30:76. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Radiographic grade 2-3 Duration of symptoms (mean [SD]): 62.4 (10.1) months
Indirectness of population	No indirectness
Interventions	(n=53) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. FLIPUS for 20 minutes once daily for a total treatment duration of 10 days. The ultrasound device was place on the person while in a supine position with the knee angled 90 degrees at the flexion position. Low intensity mode was used so people would not feel

	heat or any sensation. The four probes were close to the surface skin of the ST 35 acupoint (located in the depression of the patellar ligament when the knee is flexed) and interior and lateral knee joint spaces respectively. The cartilage of lateral and medial femoral condyle was the tissue being targeted. The model CZG200 ultrasound therapeutic device for arthritis used had an ultrasonic transducer diameter of 25mm, a radius of curvature of 28mm, a frequency of 0.6MHz, a pulse repetition frequency of 300Hz, a spatial and temporal average intensity of 120mW/cm², and a duty cycle of 20%. The ellipsoid-shaped acoustic focus was 0.25mm in diameter and 0.54mm in length, measured at the full width at half-maximum of the acoustic intensity.. Duration 10 days. Concurrent medication/care: All people received diclofenac sodium (oral sustained release, 75mg) once daily for the 10 day period. Indirectness: No indirectness (n=53) Intervention 2: Sham electrotherapy. Sham ultrasound (no energy output) for 10 days. Duration 10 days. Concurrent medication/care: All people received diclofenac sodium (oral sustained release, 75mg) once daily for the 10 day period. Indirectness: No indirectness
Funding	Academic or government funding (Financial support provided by the National Basic Research Program 973 of China (Grant No. 2012 CB722402 and Grant No. 2011 CB707900), the National Natural Science Foundation of China (Grant No. 81127901, 30830040, 11274404, 11574039, 31000435 and 30970827), and the Medical Scientific Research Projects Foundation of ChongQing (Grant No. 2012-2-064))

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus SHAM ELECTROTHERAPY

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: SF-36 physical function at 13 weeks; Group 1: mean 26.9 (SD 13.32); n=49, Group 2: mean 15.4 (SD 12.32); n=48; SF-36 physical function 0-100 Top=High is good outcome; Comments: Baseline ultrasound: 54.30 (12.12). Baseline sham: 57.60 (14.75).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, age, BMI, duration of symptoms, blood pressure, glucose, Kellgren and Lawrence class rating and baseline values of outcomes; Group 1 Number missing: 4, Reason: 1 lost contact, 3 violated study protocol; Group 2 Number missing: 5, Reason: 1 lost contact, 2 violated study protocol, 2 refused treatment
- Actual outcome: SF-36 bodily pain at 13 weeks; Group 1: mean 37.01 (SD 14.44); n=49, Group 2: mean 20.76 (SD 9.49); n=48; SF-36 bodily pain 0-100 Top=High is good outcome; Comments: Baseline ultrasound: 31.30 (13.03). Baseline sham: 34.46 (13.11).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, age, BMI, duration of symptoms, blood pressure, glucose, Kellgren and Lawrence class rating and baseline values of outcomes; Group 1 Number missing: 4, Reason: 1 lost contact, 3 violated study protocol; Group 2 Number missing: 5, Reason: 1 lost contact, 2 violated study protocol, 2 refused treatment

- Actual outcome: SF-36 role physical at 13 weeks; Group 1: mean 13 (SD 16.24); n=49, Group 2: mean 12.33 (SD 17.69); n=48; SF-36 role physical 0-100 Top=High is poor outcome; Comments: Baseline ultrasound: 38.50 (29.11). Baseline sham: 42.90 (29.90).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, age, BMI, duration of symptoms, blood pressure, glucose, Kellgren and Lawrence class rating and baseline values of outcomes; Group 1 Number missing: 4, Reason: 1 lost contact, 3 violated study protocol; Group 2 Number missing: 5, Reason: 1 lost contact, 2 violated study protocol, 2 refused treatment
- Actual outcome: SF-36 vitality at 13 weeks; Group 1: mean 21.62 (SD 12.35); n=49, Group 2: mean 15.9 (SD 9.41); n=48; SF-36 vitality 0-100 Top=High is good outcome; Comments: Baseline ultrasound: 44.00 (15.12). Baseline sham: 40.80 (11.44).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, age, BMI, duration of symptoms, blood pressure, glucose, Kellgren and Lawrence class rating and baseline values of outcomes; Group 1 Number missing: 4, Reason: 1 lost contact, 3 violated study protocol; Group 2 Number missing: 5, Reason: 1 lost contact, 2 violated study protocol, 2 refused treatment
- Actual outcome: SF-36 general health at 13 weeks; Group 1: mean 16.58 (SD 9.29); n=49, Group 2: mean 2.46 (SD 5.68); n=48; SF-36 general health 0-100 Top=High is good outcome; Comments: Baseline ultrasound: 40.64 (13.58). Baseline sham: 43.14 (17.12).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, age, BMI, duration of symptoms, blood pressure, glucose, Kellgren and Lawrence class rating and baseline values of outcomes; Group 1 Number missing: 4, Reason: 1 lost contact, 3 violated study protocol; Group 2 Number missing: 5, Reason: 1 lost contact, 2 violated study protocol, 2 refused treatment
- Actual outcome: SF-36 mental health at 13 weeks; Group 1: mean 23.64 (SD 12.42); n=49, Group 2: mean 18.66 (SD 7.55); n=48; SF-36 mental health 0-100 Top=High is good outcome; Comments: Baseline ultrasound: 42.64 (13.51). Baseline sham: 41.36 (10.74).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, age, BMI, duration of symptoms, blood pressure, glucose, Kellgren and Lawrence class rating and baseline values of outcomes; Group 1 Number missing: 4, Reason: 1 lost contact, 3 violated study protocol; Group 2 Number missing: 5, Reason: 1 lost contact, 2 violated study protocol, 2 refused treatment
- Actual outcome: SF-36 role emotional at 13 weeks; Group 1: mean 14.53 (SD 12.13); n=49, Group 2: mean 14.88 (SD 25.03); n=48; SF-36 role emotional 0-100 Top=High is good outcome; Comments: Baseline ultrasound: 48.67 (22.14). Baseline sham: 43.33 (13.88).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, age, BMI, duration of symptoms, blood pressure, glucose, Kellgren and Lawrence class rating and baseline values of outcomes; Group 1 Number missing: 4, Reason: 1 lost contact, 3 violated study protocol; Group 2 Number missing: 5, Reason: 1 lost contact, 2 violated study protocol, 2 refused treatment
- Actual outcome: SF-36 social functioning at 13 weeks; Group 1: mean 26.25 (SD 17.34); n=49, Group 2: mean 19.5 (SD 15.19); n=48; SF-36 social functioning 0-100 Top=High is good outcome; Comments: Baseline ultrasound: 54.75 (14.70). Baseline sham: 51.75 (13.83).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, age, BMI, duration of symptoms, blood pressure, glucose, Kellgren and Lawrence class rating and baseline values of outcomes; Group 1 Number missing: 4, Reason: 1 lost contact, 3 violated study protocol; Group 2 Number missing: 5, Reason: 1 lost contact, 2 violated study protocol, 2 refused treatment

Protocol outcome 2: Pain at </= 3 months

- Actual outcome: VAS at 13 weeks; Group 1: mean -5.44 (SD 0.84); n=49, Group 2: mean -4.48 (SD 0.84); n=48; VAS 0-10 Top=High is poor outcome; Comments: Baseline ultrasound: 6.98 (1.06). Baseline sham: 6.76 (1.02). Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, age, BMI, duration of symptoms, blood pressure, glucose, Kellgren and Lawrence class rating and baseline values of outcomes; Group 1 Number missing: 4, Reason: 1 lost contact, 3 violated study protocol; Group 2 Number missing: 5, Reason: 1 lost contact, 2 violated study protocol, 2 refused treatment	
Protocol outcomes not reported by the study	Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	**NCT03705039 trial: Karakas 2020[118]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=96)
Countries and setting	Conducted in Turkey; Setting: Dokuz Eylul University, Department of Physical Medicine and Rehabilitation.
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 8 week intervention, 4 week follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR diagnostic criteria, plus stage 1-3 K-L stage.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnosis of knee OA according to ACR criteria; grade ≤3 according to K-L staging, and both gender groups to be between 45-75 years of age.
Exclusion criteria	Systemic inflammatory arthritis, taking oral steroids in the last 3 months, intra-articular corticosteroid injection for knee in the last 6 months, presence of neurological deficit in the lower extremity, history of knee surgery, presence of central or peripheral nervous system disease,and patients whose therapeutic ultrasound administrations are contraindicated (large and severe skin wounds, open wounds at risk of infection, pregnancy, coexistence of malignancy).
Recruitment/selection of patients	not reported

Age, gender and ethnicity	Age - Mean (SD): US group: 59.10 (7.45), sham group: 60.75 (7.46) years. Gender (M:F): 17M/ 79F. Ethnicity: not reported
Further population details	1. Age (≤/> 75 years): </=75 years (Age range 47-75 years). 2. Diagnosis : Diagnosis with imaging (ACR plus K-L criteria). 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity (K-L grade 2): US group: 29, sham group: 24 Severity (K-L grade 3): US group: 11, sham group: 12 Duration: not reported
Indirectness of population	No indirectness
Interventions	(n=48) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. The pulsed ultrasound group received a total of 24 sessions of pulsed ultrasound treatment (1 MHz, 1w/cm², 1:4 ratio, 10 minutes) 3 sessions a week for 8 weeks. The pulsed therapeutic ultrasound (Enraf Nonius Sonopuls 492 device) was administered by a researcher while patients were at supine position with their knees at flexion in order to cover the knee joint, medial and lateral joint spacing, and suprapatellar regions. the duration of the ultrasound was estimated for each patient using Gray's formula. Total treatment time= planned local exposure time x tissue area/ effective radiating area. For this study the average local exposure time was planned to be one minute, and the effective radiating area of the transducer head was 5cm². For a patient with an area of knee pain of 50cm² for example the required total treatment time was 1 minute x (50cm²/ 5cm²)= 10 minutes.. Duration 8 weeks. Concurrent medication/care: Both groups were given a standard home exercise programme consisting of knee joint range of motion and isometric strengthening. The home exercise programme was given to each patient before starting the treatment. In addition, when they came to the treatment, whether they exercise or not was constantly checked. In both groups, patients were only allowed to take paracetamol for pain. The use of any other analgesics was avoided during the treatment and until the end of the 4 weeks following the completion of the US therapy.. Indirectness: No indirectness (n=48) Intervention 2: Sham electrotherapy. Sham ultrasound (no further details) given as per the active treatment group.. Duration 8 weeks. Concurrent medication/care: Both groups were given a standard home exercise programme consisting of knee joint range of motion and isometric strengthening. The home exercise programme was given to each patient before starting the treatment. In addition, when they came to the treatment, whether they exercise or not was constantly checked. In both groups, patients were only allowed to take paracetamol for pain. The use of any other analgesics was avoided during the treatment and until the end of the 4 weeks following the completion of the US therapy.. Indirectness: No indirectness
Funding	Academic or government funding (The study was financed by the Scientific and Technological Research Council of Turkey (TUBATAK) as the TUBITAK 3001 R&D Project (project Np: 216S913))

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED ULTRASOUND versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain subscale. at 12 weeks; Group 1: mean 5.26 (SD 3.94); n=39, Group 2: mean 5.92 (SD 3.26); n=36; WOMAC pain subscale 0-20 Top=High is poor outcome; Comments: Baseline values: US group: 8.92 (3.64), sham group: 8.25 (3.12)
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low,

Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9, Reason: unable to contact (3), with own request (6); Group 2 Number missing: 12, Reason: unable to contact (6), with own request (4), severe knee pain (2) Protocol outcome 2: Physical function at </= 3 months - Actual outcome: WOMAC function subscale. at 12 weeks; Group 1: mean 18.92 (SD 13.79); n=39, Group 2: mean 21.39 (SD 10.1); n=36; WOMAC-physical function subscale 0-68 Top=High is poor outcome; Comments: Baseline values: US group: 32.13(14.29), sham group: 30.31(10.16) Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9, Reason: unable to contact (3), with own request (6); Group 2 Number missing: 12, Reason: unable to contact (6), with own request (4), severe knee pain (2)	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Kheshie 2014[120]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=53)
Countries and setting	Conducted in Saudi Arabia; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 6 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Painful knee osteoarthritis for at least 6 months with degenerative osteoarthritic knee of grade 2-3 or less based on radiographic diagnosis in the Kellgren and Lawrence grading of osteoarthritis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with painful knee osteoarthritis for at least 6 months with degenerative osteoarthritic knee of grade 2-3 or less based on radiographic diagnosis in the Kellgren and Lawrence grading of osteoarthritis; had no limitation of range of motion except for minimum tightness in the knee joint; did not engage in any high joint loading exercises such as hiking or tennis playing and had not undergone any specific treatments 3 months before entering the study; had a minimum score of 25 on the WOMAC total score; had a knee pain of at least 4 on the visual analog scale in the previous 3 months
Exclusion criteria	Any other musculoskeletal problems associated with the knee joint, such as fracture, tendon or ligament tears, meniscus injury, rheumatoid arthritis, or knee surgery; musculoskeletal problems associated with the hip or ankle/foot joints; had central or peripheral neuropathy; or had received physical therapy and/or intra-articular corticosteroid or hyaluronic acid injections during the last 6 months
Recruitment/selection of patients	People seen in the physical therapy department of Umm Al-Qura University, Saudi Arabia
Age, gender and ethnicity	Age - Mean (SD): 54.6 (8.49). Gender (M:F): 53:0. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Radiographic grade 2-3, median grade 2 Duration of symptoms: At least 3 months
Indirectness of population	No indirectness

Interventions	(n=38) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. High intensity and low-level laser therapy. High intensity laser therapy using a pulsed Nd:YAG laser, produced by HIRO 3 device. Applied to the knee flexed at 30 degrees. The scanning was performed transversely and longitudinally in the anterior, medial and lateral aspects of the knee joint with emphasis on the application on the joint line between the tibial and femoral epicondyles. The total energy delivered to the person during one session was 1250J through three phases of treatment. The initial phase was performed with fast manual scanning with a total of 500J. In the initial phase, the laser fluency was set to two successive subphases of 710 and 810mJ/cm² for a total of 500J. In the intermediate phase, the handpiece was applied on the joint line just proximal to the medial and lateral tibial condyles with 25j, a fluency of 610mJ/cm², and a time of 14s for each point and a total of 250J in this phase. The final phase was the same as the initial phase except that scanning was slow manual scanning. The application time for all three phases was approximately 15min with the total energy delivered during one session of 1250J. This was delivered in 2 sessions per week for 6 weeks. Low-level laser therapy was delivered by a gallium-arsenide diode laser (BTL-5000 laser) infrared probes with a wavelength of 830nm, out put power of 800mW, average energy density of 50J/cm², frequency of 1kHz, and duty cycle of 80%. All participants attended the physical therapy department two times per week for 6 weeks. The cluster laser was in direct contact and perpendicular to the affected knee with a time of application of 32 min and 33s per session and a total energy of 1250J.. Duration 6 weeks. Concurrent medication/care: All groups received an exercise program consisting of active range of motion exercises, muscle strengthening, and flexibility exercises. These were completed in a supervised form and at home.. Indirectness: No indirectness Comments: The two groups were combined due to class effect as agreed in the protocol (n=15) Intervention 2: Sham electrotherapy. Sham laser therapy twice a week for 6 weeks. Duration 6 weeks. Concurrent medication/care: All groups received an exercise program consisting of active range of motion exercises, muscle strengthening, and flexibility exercises. These were completed in a supervised form and at home.. Indirectness: No indirectness
Funding	Academic or government funding (This research received a grant from the Institute of Scientific Research and rEvival of Islamic Heritage at Umm Al-Qura university, Makkah, Saudi Arabia)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 6 weeks; Group 1: mean 3.92 (SD 1.39); n=36, Group 2: mean 6.26 (SD 1.22); n=12; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported high intensity: 3.15 (1.136). Reported low intensity: 4.77 (1.11). Baseline high intensity: 9.70 (1.41). Baseline low intensity: 10.055 (1.86). Baseline sham: 9.80 (1.82).
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, weight, height, BMI, Kelgren Lawrence stage and baseline values of outcomes; Group 1 Number missing: 2, Reason: 2 withdrew from group 1 and 3 from group 3 due to exercise incompliance and infrequent scheduled treatment sessions; Group 2 Number missing: 3, Reason: 2 withdrew from group 1 and 3 from group 3 due to exercise incompliance and infrequent scheduled treatment sessions

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function at 6 weeks; Group 1: mean 15.3 (SD 2.48); n=38, Group 2: mean 20.6 (SD 2.44); n=15; WOMAC function 0-68 Top=High is poor outcome; Comments: Reported high intensity: 13.90 (1.86). Reported low intensity: 16.88 (2.11). Baseline high intensity: 31.70 (3.74). Baseline low intensity: 30.44 (3.66). Baseline sham: 31.00 (3.42).
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, weight, height, BMI, Kelgren Lawrence stage and baseline values of outcomes; Group 1 Number missing: 2, Reason: 2 withdrew from group 1 and 3 from group 3 due to exercise incompliance and infrequent scheduled treatment sessions; Group 2 Number missing: 3, Reason: 2 withdrew from group 1 and 3 from group 3 due to exercise incompliance and infrequent scheduled treatment sessions

Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	**Kim 2019[121]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=40)
Countries and setting	Conducted in South Korea; Setting: Home-based self-therapy.

Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 8 week treatment period, approximately 24 day follow-up.
Method of assessment of guideline condition	Unclear method of assessment/diagnosis: ? K-L grade I to IV by standing posteroanterior X-ray in 15 degree knee flexion were eligible.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients aged >18 years with knee pain. All participants who were K-L grade I to IV by standing posteroanterior X-ray in 15 degree knee flexion were eligible.
Exclusion criteria	Any patient with a history of knee surgery within the last 6 months, history of steroid injection in the lower extremity within the last month, knee joint infection, inflammatory joint disease, acute tendon or ligament injury of the knee, dementia or cognitive impairment, neurological disorders such as central nerve system disorder, lumbosacral radiculopathy or polyneuropathy and hypesthesia in the lower extremity, and pregnant women.
Recruitment/selection of patients	Recruited through a note posted on the bulletin board of the hospital.
Age, gender and ethnicity	Age - Mean (SD): 57.6 (8.26). Gender (M:F): 32F/ 8M. Ethnicity: Not reported
Further population details	1. Age (≤/> 75 years): Systematic review: mixed (aged 46-85 years). 2. Diagnosis : Diagnosis with imaging (K-L grade I to IV by standing posteroanterior X-ray in 15 degree knee flexion were eligible.). 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity (WOMAC pain at baseline): combination group: 8.63 (3.09) TENS group: 7.53 (3.67) Duration of pain (months): combination group: 64.84(62.70) TENS group: 62.74(65.58)
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Non-invasive electrotherapy interventions - Combination therapy (e.g. ultrasound and interferential therapy). LIPUS combined with TENS therapy. Performed using CARESTAR (GENEMEDI CO, Ltd, South Korea). CARESTAR consisted of two 2.8 diameter applicators and gave LIPUS energy and TENS in 1s shifts. Therefore, 50%of the stimulation was offered by LIPUS and the remaining 50% was provided by TENS. The LIPUS signal is transmitted at a frequency of 1MHz, with an intensity of 0.1 W/cm². The effective radiating area was 3.3cm². The duty cycle of pulsed ultrasonic waves was 40%. The TENS setting was in a conventional mode, with a frequency of 80Hz and a pulse duration of 50-100μs. The intensity of TENS current was set to produce a strong tingling sensation, but without pain. The participant was placed in a sitting position, with the affected knee flexed at 90 degrees to enhance ultrasonic energy penetration into the joint space. A nondrug coupling gel was applied. The participant was taught to allocate the two applicators medial and lateral to the involved knee by fixing with an elastic band. A clinical research co-ordinator educated participants on how to manipulate the TENS machine or a stimulator using LIPUS combined with TENS. Each participant took a device home and administered home-based self-therapy. Both groups

	underwent a 20 minute self-therapy per session, which was performed 3 or <3 sessions per day and > 10 sessions per week for 8 weeks. They completed a self-therapy checklist daily. A clinical research co-ordinator contacted the patients by telephone once a week and visited at home once a month to monitor the home-based self-therapy.. Duration 8 weeks. Concurrent medication/care: Participants were only allowed to take their pain medication which was started at least 2 months before the screening. They were not allowed to change the dose or type of pain medication or start any other types of treatment for knee OA during the trial. In addition, participants were requested not to change their physical exercise level.. Indirectness: No indirectness (n=20) Intervention 2: Non-invasive electrotherapy interventions - Transcutaneous electrical nerve stimulation (TENS). TENS alone. A commercially available TENS machine (Chil-Sung, Co, Ltd, South Korea) was used for stimulation. The TENS setting was in a conventional mode, with a frequency of 100Hz and a pulse duration of 50-100μs. The participant was placed in a sitting position with the affected knee fled at 90 degrees. Two 5x5 cm electrodes were placed above the patella, and 2 were placed below. The intensity of the stimulation was set to low intensity to stimulate large diameter, low threshold non-noxious afferent fibres (A-beta). Thus, the stimulation intensity was set to produce a strong tingling sensation, but without pain. A clinical research co-ordinator educated participants on how to manipulate the TENS machine or a stimulator using LIPUS combined with TENS. Each participant took a device home and administered home-based self-therapy. Both groups underwent a 20 minute self-therapy per session, which was performed 3 or <3 sessions per day and > 10 sessions per week for 8 weeks. They completed a self-therapy checklist daily. A clinical research co-ordinator contacted the patients by telephone once a week and visited at home once a month to monitor the home-based self-therapy.. Duration 8 weeks. Concurrent medication/care: Participants were only allowed to take their pain medication which was started at least 2 months before the screening. They were not allowed to change the dose or type of pain medication or start any other types of treatment for knee OA during the trial. In addition, participants were requested not to change their physical exercise level.. Indirectness: No indirectness
Funding	Academic or government funding (Supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HI15C1529), and supported by research funds of Chonbuk National University in 2017.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINATION THERAPY (US + TENS) versus TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS)

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: SF-36 global score at 21±3 days after treatment; Group 1: mean 67.8 (SD 2.53); n=19, Group 2: mean 67.34 (SD 4.18); n=19; Comments: Data reported are SE, not SD
Baseline values: combination group: 59.11 (16.59), TENS group: 58.25(17.08)
Risk of bias: All domain - Low, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: Single blind (assessor) only; Group 1 Number missing: 1, Reason: history of steroid injection in to the affected knee/ initiation of NSAIDs.; Group 2 Number missing: 1, Reason: history of steroid injection in to the

	affected knee/ initiation of NSAIDs. Protocol outcome 2: Pain at </= 3 months - Actual outcome: WOMAC pain subscale at 21±3 days after treatment; Group 1: mean 5.32 (SD 0.71); n=19, Group 2: mean 4.26 (SD 0.86); n=19; WOMAC- pain subscale 0-20 Top=High is poor outcome; Comments: Data reported are SE, not SD Baseline values: combination group: 8.63 (3.09), TENS group:7.53 (3.67) Risk of bias: All domain - Low, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: Single blind (assessor) only; Group 1 Number missing: 1, Reason: history of steroid injection in to the affected knee/ initiation of NSAIDs.; Group 2 Number missing: 1, Reason: history of steroid injection in to the affected knee/ initiation of NSAIDs. Protocol outcome 3: Physical function at </= 3 months - Actual outcome: WOMAC physical function subscale at 21±3 days after treatment; Group 1: mean 15.84 (SD 2.31); n=19, Group 2: mean 10.79 (SD 2.31); n=19; WOMAC physical function subscale 0-68 Top=High is poor outcome; Comments: Data reported are SE, not SD Baseline values: combination group: 25.05(11.20), TENS group: 20.89(11.79) Risk of bias: All domain - Low, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: Single blind (assessor) only; Group 1 Number missing: 1, Reason: history of steroid injection in to the affected knee/ initiation of NSAIDs.; Group 2 Number missing: 1, Reason: history of steroid injection in to the affected knee/ initiation of NSAIDs. Protocol outcome 4: Mild adverse events at </= 3 months - Actual outcome: Adverse effects at 21±3 days after treatment; Group 1: 0/20, Group 2: 0/20; Comments: Narrative statement ‘adverse affects from the treatment were not observed’ Risk of bias: All domain - Low, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: Single blind (assessor) only; Group 1 Number missing: 1, Reason: history of steroid injection in to the affected knee/ initiation of NSAIDs.; Group 2 Number missing: 1, Reason: history of steroid injection in to the affected knee/ initiation of NSAIDs. Protocol outcome 5: Moderate/major adverse events at </= 3 months - Actual outcome: Adverse effects at 21±3 days after treatment; Group 1: 0/20, Group 2: 0/20; Comments: Narrative statement ‘adverse affects from the treatment were not observed’ Risk of bias: All domain - Low, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Blinding details: Single blind (assessor) only; Group 1 Number missing: 1, Reason: history of steroid injection in to the affected knee/ initiation of NSAIDs.; Group 2 Number missing: 1, Reason: history of steroid injection in to the affected knee/ initiation of NSAIDs.
Protocol outcomes not reported by the study	Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at > 3 months

Study	NCT03952221 trial: Kiraly 2021[124]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=71)
Countries and setting	Conducted in Hungary; Setting: Conducted at the Department of Rheumatology in Petz Aladar County Teaching Hospital and at the Musculoskeletal Rehabilitation Department in Zsigmondy Vilmos Harkany Spa Hospital.
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 14 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: clinically and radiologically moderate hip OA(K-L II-III stage) as defined by ACR
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	1) Hungarian Caucasian Patients > 50 years of age with clinically and radiologically moderate hip OA(K-L II-III stage) as defined by ACR; 2) chronic hip pain for at least 8 weeks prior to the study; 3) pain intensity ≥50mm on the VAS of 100mm; and 4) no physiotherapy or local injections (i.e. no steroids or hyaluronic acid) administered in the region of the hip joints or into the joint itself within 3 months before starting the study.
Exclusion criteria	1) acute or subacute hip pain for less than 8 weeks; 2) local (intraarticular or periarticular) injection (corticosteroid or hyaluronic acid); 3) physiotherapy within 3 months prior to the study; 4) significant laboratory signs of inflammation; and 5) infections, ever, osteomyelitis, severe osteoporosis, preegnancy, untreated hypertension, heart failure, malignancy, epilepsy, pacemaker or an intracardiac device.
Recruitment/selection of patients	Inpatients admitted to the Rheumatology and Rehabilitation Departments for hospital care.
Age, gender and ethnicity	Age - Other: Mean 65 years. Gender (M:F): 14/57. Ethnicity: All Caucasian
Further population details	1. Age (≤/> 75 years): Not stated / Unclear 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : High morbidity score (continuous US group: 10/21, pulsed US group: 13/17, combination group: 6/15, placebo group: 12/18). 4. Site of osteoarthritis: Hip
Extra comments	Severity (resting VAS pain at baseline): continuous US group: 64.38 (12.45), pulsed US group: 63.88 (14.47), combination group: 61.33 (17.78), placebo group: 62.94 (9.37) Duration of symptoms: at least 8 weeks prior to the start of the study

Indirectness of population	No indirectness
Interventions	(n=38) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. Participants received continuous ultrasound therapy (UST) with moving head in three fields: 1) inguinal; 2) gluteal; and 3) trochanteric for 3 minutes per field, altogether for 9 minutes every working day for 2 weeks, on a total of 10 occasions (calibrated BTL-4825S Premium device, head size: 5cm, 3 MHz frequency, 1.5W/cm2 intensity), or pulsed UST (1.5 W/cm2 intensity, 3 MHz frequency, 50% duty cycle). Participants in each group received conventional treatment (i.e. physical exercise, massage and balneotherapy) every working day for two weeks, on a total of 10 occasions. Exercises included standardised hip exercises. Swedish massage techniques were used during the massage therapy, and the balneotherapy was performed in thermal water at 34 degrees C. Duration 2 weeks. Concurrent medication/care: Participants were permitted to take analgesics or anti-rheumatic drugs during the study-these medications were recorded on their documents. They were not permitted to receive any additional therapy during the 3 months follow-up period. (n=15) Intervention 2: Non-invasive electrotherapy interventions - Combination therapy (e.g. ultrasound and interferential therapy). Participants received combined UST and TENS therapy for 10 minutes per day (continuous US: 0.5 W/cm2 intensity, 3MHs carrier frequency; TENS: 100 Hz frequency, 100μs impulse, constant frequency). Duration 2 weeks. Concurrent medication/care: Participants were permitted to take analgesics or anti-rheumatic drugs during the study-these medications were recorded on their documents. They were not permitted to receive any additional therapy during the 3 months follow-up period. Indirectness: No indirectness (n=18) Intervention 3: Sham electrotherapy. Participants received sham UST (the device was switched off). Duration 2 weeks. Concurrent medication/care: Participants were permitted to take analgesics or anti-rheumatic drugs during the study-these medications were recorded on their documents. They were not permitted to receive any additional therapy during the 3 months follow-up period. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CONTINUOUS OR PULSED ULTRASOUND versus SHAM ULTRASOUND

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: SF-36 pain subscale at 14 weeks; Group 1: mean 46.251 (SD 26.202); n=38, Group 2: mean 47.15 (SD 20.02); n=18; SF-36 pain subscale 0-100 Top=High is good outcome; Comments:
Values for continuous and pulsed ultrasound are averages. Value for continuous US group: 41.67 (25.68), pulsed US group: 51.91 (25.73)
Baseline values: placebo group: 35.56 (17.05), continuous US group: 34.05 (14.57), pulsed ultrasound group: 32.65 (17.75)

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1, Reason: lack of compliance; Group 2 Number missing: 1, Reason: lack of compliance
- Actual outcome: SF-36 general health subscale at 14 weeks; Group 1: mean 42.75 (SD 19.462); n=38, Group 2: mean 43.89 (SD 17.62); n=18; SF-36 general health subscale 0-100 Top=High is good outcome; Comments: Values for continuous and pulsed ultrasound are averages. Value for continuous US group: 41.43(17.4), pulsed US group: 44.38(21.63)
Baseline values: placebo group: 33.33(12.25), continuous US group: 38.81(16.42), pulsed ultrasound group: 36.47(18.44)

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1, Reason: lack of compliance; Group 2 Number missing: 1, Reason: lack of compliance

Protocol outcome 2: Pain at </= 3 months
- Actual outcome: VAS resting pain at 14 weeks; Group 1: mean 38.445 (SD 28.485); n=38, Group 2: mean 40.22 (SD 20.88); n=18; VAS 0-100 Top=High is poor outcome; Comments: Values for continuous and pulsed ultrasound are averages. Value for continuous US group: 41.76 (26.41), pulsed US group: 34.35(30.36)
Baseline values: placebo group: 62.94(9.37), continuous US group: 64.38(12.45), pulsed ultrasound group: 63.88(14.47)

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1, Reason: lack of compliance; Group 2 Number missing: 1, Reason: lack of compliance

Protocol outcome 3: Mild adverse events at </= 3 months
- Actual outcome: Adverse events at 14 weeks; Group 1: 0/38, Group 2: 0/18; Comments: Narrative statement 'we did not observe any adverse events attributed to the non- pharmacological interventions in the study'.
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1, Reason: lack of compliance; Group 2 Number missing: 1, Reason: lack of compliance

Protocol outcome 4: Moderate/major adverse events at </= 3 months
- Actual outcome: Adverse events at 14 weeks; Group 1: 0/38, Group 2: 0/18; Comments: Narrative statement 'we did not observe any adverse events attributed to the non- pharmacological interventions in the study'.
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1, Reason: lack of compliance; Group 2 Number missing: 1, Reason: lack of compliance

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINATION THERAPY (ULTRASOUND AND TENS) versus CONTINUOUS OR PULSED ULTRASOUND

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: SF-36 pain subscale at 14 weeks; Group 1: mean 48 (SD 23.07); n=15, Group 2: mean 46.251 (SD 26.202); n=38; SF-36 pain subscale 0-100 Top=High is good outcome; Comments: Values for continuous and pulsed ultrasound are averages. Value for continuous US group: 41.67 (25.68), pulsed US group: 51.91 (25.73)
Baseline values: combination group: 30.5 (17.58), continuous US group: 34.05 (14.57), pulsed ultrasound group: 32.65 (17.75)
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: N/A; Group 2 Number missing: 1, Reason: lack of compliance
- Actual outcome: SF-36 general health subscale at 14 weeks; Group 1: mean 51.63 (SD 18.2); n=15, Group 2: mean 42.75 (SD 19.462); n=38; SF-36 general health subscale 0-100 Top=High is good outcome; Comments: Values for continuous and pulsed ultrasound are averages. Value for continuous US group: 41.43(17.4), pulsed US group: 44.38 (21.63)
Baseline values: combination group: 36.33 (18.27), continuous US group: 38.81(16.42), pulsed ultrasound group: 36.47 (18.44)
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: N/A; Group 2 Number missing: 1, Reason: lack of compliance

Protocol outcome 2: Pain at </= 3 months
- Actual outcome: VAS resting pain at 14 weeks; Group 1: mean 31.13 (SD 22.26); n=15, Group 2: mean 38.445 (SD 28.485); n=38; VAS 0-100 Top=High is poor outcome; Comments: Values for continuous and pulsed ultrasound are averages. Value for continuous US group: 41.76(26.41), pulsed US group: 34.35(30.36)
Baseline values: combination group: 64.38 (12.45), continuous US group: 63.88(14.47), pulsed ultrasound group: 61.33(17.78)
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: N/A; Group 2 Number missing: 1, Reason: lack of compliance

Protocol outcome 3: Mild adverse events at </= 3 months
- Actual outcome: Adverse events at 14 weeks; Group 1: 0/15, Group 2: 0/38; Comments: Narrative statement 'we did not observe any adverse events attributed to the non- pharmacological interventions in the study'.
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: N/A; Group 2 Number missing: 1, Reason: lack of compliance

Protocol outcome 4: Moderate/major adverse events at </= 3 months
- Actual outcome: Adverse events at 14 weeks; Group 1: 0/15, Group 2: 0/38; Comments: Narrative statement 'we did not observe any adverse events attributed to the non- pharmacological interventions in the study'.

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: N/A; Group 2 Number missing: 1, Reason: lack of compliance

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINATION THERAPY (ULTRASOUND AND TENS) versus SHAM ULTRASOUND

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: SF-36 pain subscale at 14 weeks; Group 1: mean 48 (SD 23.07); n=15, Group 2: mean 47.15 (SD 20.02); n=18; VAS pain subscale 0-100 Top=High is good outcome; Comments:
Baseline values: combination group: 30.5 (17.58), placebo group: 35.56 (17.05)

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: N/A; Group 2 Number missing: 1, Reason: lack of compliance
- Actual outcome: SF-36 general health subscale at 14 weeks; Group 1: mean 51.63 (SD 18.2); n=15,
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: N/A; Group 2 Number missing: 1, Reason: lack of compliance

Protocol outcome 2: Pain at </= 3 months
- Actual outcome: VAS resting pain at 14 weeks; Group 1: mean 31.13 (SD 22.26); n=15, Group 2: mean 40.22 (SD 20.88); n=18; VAS 0-100 Top=High is poor outcome; Comments: Baseline values: combination group: 61.33 (17.78), placebo group: 62.94 (9.37)
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: N/A; Group 2 Number missing: 1, Reason: lack of compliance

Protocol outcome 3: Mild adverse events at </= 3 months
- Actual outcome: Adverse events at 14 weeks; Group 1: 0/15, Group 2: 0/18; Comments: Narrative statement 'we did not observe any adverse events attributed to the non- pharmacological interventions in the study'.
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: N/A; Group 2 Number missing: 1, Reason: lack of compliance

Protocol outcome 4: Moderate/major adverse events at </= 3 months

- Actual outcome: Adverse events at 14 weeks; Group 1: 0/15, Group 2: 0/18; Comments: Narrative statement 'we did not observe any adverse events attributed to the non- pharmacological interventions in the study'. Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: N/A; Group 2 Number missing: 1, Reason: lack of compliance	
Protocol outcomes not reported by the study	Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at > 3 months

Study	Koybasi 2010[126]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=45)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 2 weeks of treatment, additional follow up for 3 months in total
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Hip pain for more than 3 months and having Kellgren Lawrence scores of 2-3 on radiologic evaluation. Diagnosis based on the American College of Rheumatology criteria, verified through history and physical examination.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Presence of hip pain for more than 3 months (not due to secondary causes including trauma, congenital hip dislocation, malalignments, metabolic bone diseases, or endocrine dysfunction) and having Kellgren-Lawrence scores of 2-3 on radiologic evaluation
Exclusion criteria	People with low back pain; dysfunction of the knee or ankle/foot; local or generalized polyarthritis; neurologic abnormality; any contraindication for physical therapy; lower limb arthroplasty; who were on any previous physiotherapy program or received intra-articular hip injections in the preceding year
Recruitment/selection of patients	People were self-referred to the Physical Medicine and Rehabilitation outpatient clinic who fulfilled the diagnostic criteria of the American College of Rheumatology
Age, gender and ethnicity	Age - Mean (SD): 65.3 (6.7). Gender (M:F): 12:33. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Hip
Extra comments	Severity: Kellgren Lawrence grade 2-3, median grade 2 Duration of symptoms (mean [SD]): 2.5 (1.7) years
Indirectness of population	No indirectness
Interventions	(n=15) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. Ultrasound and conventional physical therapy (exercise and hot pack treatment). Ultrasound was applied with the following parameters: frequency 1mHz, continuous mode, intensity 1W/cm², and head size 5cm². The hip joint was treated from the

	anterior, posterior, and lateral fields, 5 minutes for each field. The treatment area was around 70-80cm² to the affected hip. Treatment was applied give times weekly for two weeks.. Duration 2 weeks. Concurrent medication/care: Hot packs were applied on the hip joint for 20 minutes before the therapies. In all groups, the people performed strengthening exercises for the hip muscles and lengthening exercises for the ligaments around the hip joint, for a duration of 20 minutes, directed by an experienced physiotherapist. People were instructed to complete exercise three times a week, with ten repetitions for each exercise (strengthening exercises).. Indirectness: No indirectness (n=15) Intervention 2: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. No ultrasound. Duration 2 weeks. Concurrent medication/care: Hot packs were applied on the hip joint for 20 minutes before the therapies. In all groups, the people performed strengthening exercises for the hip muscles and lengthening exercises for the ligaments around the hip joint, for a duration of 20 minutes, directed by an experienced physiotherapist. People were instructed to complete exercise three times a week, with ten repetitions for each exercise (strengthening exercises).. Indirectness: No indirectness (n=15) Intervention 3: Sham electrotherapy. Sham ultrasound (applicator disconnected) in 5 sessions/week for 2 weeks. Duration 2 weeks. Concurrent medication/care: Hot packs were applied on the hip joint for 20 minutes before the therapies. In all groups, the people performed strengthening exercises for the hip muscles and lengthening exercises for the ligaments around the hip joint, for a duration of 20 minutes, directed by an experienced physiotherapist. People were instructed to complete exercise three times a week, with ten repetitions for each exercise (strengthening exercises).. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: SF-36 physical component at 3 months; Group 1: mean 40.9 (SD 6.6); n=15, Group 2: mean 40.9 (SD 5.1); n=15; SF-36 physical component 0-100 Top=High is good outcome; Comments: Baseline ultrasound: 36.4 (7.1). Baseline no treatment: 37.7 (5.4).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI, symptom duration, involved side, Kellgren Lawrence grade and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

- Actual outcome: SF-36 mental component at 3 months; Group 1: mean 41.4 (SD 4.2); n=15, Group 2: mean 39.3 (SD 4.8); n=15; SF-36 mental component 0-100 Top=High is good outcome; Comments: Baseline ultrasound: 39.4 (7.0). Baseline no treatment: 39.2 (7.1). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI, symptom duration, involved side, Kellgren Lawrence grade and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 2: Pain at </= 3 months - Actual outcome: Pain on activity (VAS) at 3 months; Group 1: mean 47.8 (SD 18); n=15, Group 2: mean 74.3 (SD 13.6); n=15; Pain on activity (VAS) 0-100 Top=High is poor outcome; Comments: Baseline ultrasound: 72.5 (12.5). Baseline no treatment: 75.6 (13.0). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI, symptom duration, involved side, Kellgren Lawrence grade and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0 RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus SHAM ELECTROTHERAPY Protocol outcome 1: Health-related quality of life at </= 3 months - Actual outcome: SF-36 physical component at 3 months; Group 1: mean 40.9 (SD 6.6); n=15, Group 2: mean 39.2 (SD 6.4); n=15; SF-36 physical component 0-100 Top=High is good outcome; Comments: Baseline ultrasound: 36.4 (7.1). Baseline sham: 38.2 (7.0). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI, symptom duration, involved side, Kellgren Lawrence grade and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0 - Actual outcome: SF-36 mental component at 3 months; Group 1: mean 41.4 (SD 4.2); n=15, Group 2: mean 40.8 (SD 7.3); n=15; SF-36 mental component 0-100 Top=High is good outcome; Comments: Baseline ultrasound: 39.4 (7.0). Baseline sham: 40.7 (7.1). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI, symptom duration, involved side, Kellgren Lawrence grade and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 2: Pain at </= 3 months - Actual outcome: Pain on activity (VAS) at 3 months; Group 1: mean 47.8 (SD 18); n=15, Group 2: mean 73.6 (SD 14.6); n=15; Pain on activity (VAS) 0-100 Top=High is poor outcome; Comments: Baseline ultrasound: 72.5 (12.5). Baseline sham: 75.3 (10.6). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI, symptom duration, involved side, Kellgren Lawrence grade and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse

	events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Laufer 2014[131]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=50)
Countries and setting	Conducted in Israel; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 6 weeks of treatment, 12 weeks postintervention follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Knee osteoarthritis at grade 2 or higher, according to the Kellgren and Lawrence classification
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with knee osteoarthritis at grade 2 or higher, according to the Kellgren and Lawrence classification; age 50 years or older; knee pain for at least 3 months; ability to ambulate independently for at least 10m
Exclusion criteria	Pacemaker; presence of a medical condition that could affect functional performance; knee joint injection in the previous 6 months
Recruitment/selection of patients	People attending an outpatient physical therapy clinic
Age, gender and ethnicity	Age - Mean (SD): 68.9 (7.7). Gender (M:F): 8:42. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence radiographic grade 2 or higher Duration of symptoms (mean [SD]): 4.7 (6.1) years
Indirectness of population	No indirectness
Interventions	(n=25) Intervention 1: Non-invasive electrotherapy interventions - Neuromuscular electrical stimulation. Neuromuscular electrical stimulation delivered to the quadriceps femoris muscle of the involved leg given ten contractions at the maximal tolerated intensity for a total of 12 sessions. Duration 6 weeks. Concurrent medication/care: An exercise program was completed with quadriceps muscle strengthening exercise. Indirectness: No indirectness (n=25) Intervention 2: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. No additional treatment. Duration 6 weeks. Concurrent medication/care: An exercise program was completed with quadriceps muscle strengthening exercise. Indirectness: No indirectness

Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NEUROMUSCULAR ELECTRICAL STIMULATION versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT Protocol outcome 1: Pain at </= 3 months - Actual outcome: VAS at 6 weeks; Group 1: mean 3.3 (SD 1.3); n=25, Group 2: mean 5 (SD 2.4); n=25; VAS 0-10 Top=High is poor outcome; Comments: Reports means and 95% confidence intervals. Reported NMES: 3.3 (2.4-3.4). Reported no treatment: 5 (4.1-6). Baseline NMES: 7.4 (6.5-8.4). Baseline no treatment: 7.5 (6.5-8.4). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported gender, age, heght, weight, BMI, osteoarthritis duration and baseline values of outcomes; Group 1 Number missing: 5, Reason: Did not receive allocated intervention (5) - 1 no tolerance to electrical stimulation, 3 non-compliance, 1 pneumonia; Group 2 Number missing: 8, Reason: Did not receive allocated intervention (8) - 7 non-compliance, 1 pneumonia Protocol outcome 2: Pain at > 3 months - Actual outcome: VAS at 18 weeks; Group 1: mean 3.4 (SD 2.3); n=23, Group 2: mean 5.3 (SD 2.3); n=21; VAS 0-10 Top=High is poor outcome; Comments: Reports means and 95% confidence intervals. Reported NMES: 3.4 (2.4-4.3). Reported no treatment: 5.3 (4.3-6.3). Baseline NMES: 7.4 (6.5-8.4). Baseline no treatment: 7.5 (6.5-8.4). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported gender, age, heght, weight, BMI, osteoarthritis duration and baseline values of outcomes; Group 1 Number missing: 9, Reason: Did not receive allocated intervention (5) - 1 no tolerance to electrical stimulation, 3 non-compliance, 1 pneumonia. 4 lost to follow up.; Group 2 Number missing: 10, Reason: Did not receive allocated intervention (8) - 7 non-compliance, 1 pneumonia. 2 lost to follow up.	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Law 2004[132]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=48)
Countries and setting	Conducted in Hong Kong (China); Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Osteoarthritis of the knee with at least grade 2 changes on their x-rays
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with at least grade 2 osteoarthritis changes in their x-rays, competent enough to complete the VAS, OA should be the only cause of their present knee pain
Exclusion criteria	People who had received prior knee surgery; had received intra-articular corticosteroids within 4 weeks of the study; who had any chronic or uncontrolled co-morbid diseases; people with a cardiac pacemaker; people who had received any TENS 1 month prior to the study
Recruitment/selection of patients	Recruited from a local care home
Age, gender and ethnicity	Age - Mean (SD): 82.5 (6.3). Gender (M:F): 1:47. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): > 75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Osteoarthritis grade 2 radiographic changes Duration of symptoms (mean [SD]): 8.7 (9.7) years
Indirectness of population	No indirectness
Interventions	(n=38) Intervention 1: Non-invasive electrotherapy interventions - Transcutaneous electrical nerve stimulation (TENS). TENS used for stimulation with the stimulation duration set to 40 minutes. The parameters that were fixed by the manufacturer included: for a frequency of 2Hz, the pulse width was fixed at 576microseconds. For the frequency of 100Hz, the pulse width was set at 200microseconds. For the alternating frequencies of 2Hz and 100Hz, 2 Hz was delivered for 3 seconds with a pulse width of 576 microseconds, followed by 100Hz with the pulse width at 200 microseconds for 2.5 seconds. Two pairs of rubber electrodes (4.5x3.8cm²) placed over the acupuncture points of the knees. The points used were ST35, LE4, SP9 and GB34. The intensity of the current was set at a comfortable level as determined by the

	subjects, and ranged from 25mA to 35mA. During stimulation, the subjects experienced mild paraesthesia and mild twitched. The current was turned up if the person accommodated to the current 5 minutes into the stimulation. People were told they may or may not feel a tingling sensation during the stimulation.. Duration 2 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness Comments: The three groups were combined due to class effect as agreed in the protocol (n=10) Intervention 2: Sham electrotherapy. Sham TENS, using a device where the electrical circuit was disconnected. People were told they may or may not feel a tingling sensation during the stimulation. The person administering treatment increased the settings after 5 minutes to imitate adjustment for accommodation.. Duration 2 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: VAS at 2 weeks; Group 1: mean 1.4 (SD 1.8); n=38, Group 2: mean 4.4 (SD 3); n=10; VAS 0-10 Top=High is poor outcome; Comments: Reported TENS2: 1.6 (1.8). Reported TENS100: 0.9 (1.0). Reported TENS2/100: 1.6 (2.2). Baseline TENS2: 6.6 (2.0). Baseline TENS100: 5.2 (1.8). Baseline TENS2/100: 5.4 (2.2). Baseline sham: 5.8 (3.0). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Comments - Randomisation by drawing lots out of an envelope; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, body weight, height, BMI, history of knee pain, x-ray grading, baseline VAS score and baseline MMSI score; Group 1 Number missing: -, Reason: Overall 2 people withdrew, 1 due to medical reason, 1 due to the subject having moved out of the complex; Group 2 Number missing: -, Reason: Overall 2 people withdrew, 1 due to medical reason, 1 due to the subject having moved out of the complex	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Loyola-sanchez 2012[142]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=27)
Countries and setting	Conducted in Canada; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 2 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People who fulfilled the American College of Rheumatology clinical and radiological diagnostic criteria for knee osteoarthritis and presented with OARSI atlas classification grades 1 or 2 tibiofemoral compartment joint space narrowing
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Adults 45 years of age or older who fulfilled the American College of Rheumatology clinical and radiological diagnostic criteria for knee osteoarthritis, and presented with OARSI atlas classification grades 1 or 2 tibiofemoral compartment joint space narrowing. All people were fluent in English.
Exclusion criteria	Secondary causes of arthritis (metabolic or inflammatory); a surgical intervention or intraarticular injection in the affected knee in the previous 6 months; any contraindication to MRI or radiograph; experienced an injury to the affected knee during the study
Recruitment/selection of patients	People were recruited from 2 rheumatology clinics
Age, gender and ethnicity	Age - Mean (SD): 61.9 (10.5). Gender (M:F): 6:21. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: OARSI atlas grade 1-2, median grade 2 Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=14) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. Ultrasound interventions administered using a 1MHz ultrasound device with a sound-head area of 5cm², effective radiating area of 3.5 and 5cm², a beam nonuniformity ratio of 5:1, and a therapeutic dose of approximately 112.5J/cm². That is, pulsed ultrasound was delivered for 9.5 minutes with a peak intensity of 1W/cm² at a 20% duty cycle, to achieve a spatial average temporal average intensity of 0.2W/cm². This

	was delivered as 24 sessions with 3 sessions per week. Duration 8 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=13) Intervention 2: Sham electrotherapy. Sham ultrasound administered using an identical device but without a sound-head crystal.. Duration 8 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Academic or government funding (Supported in part by a Natural Sciences and Engineering Research Council Discovery Grant (no. 311896); Consejo Nacional de Ciencia y Tecnologia of Mexico scholarship (no. 209621); and McMaster University School of Graduate Studies International Excellence Award)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 8 weeks; Group 1: mean 6.92 (SD 3.96); n=12, Group 2: mean 5.62 (SD 4.33); n=13; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline active: 7.67 (2.42). Baseline sham: 5.92 (4.23).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, weight, height, BMI, OARSI-medial JSN, bilateral involvement and baseline values of outcomes; Group 1 Number missing: 3, Reason: 2 lost to follow up - not able to make contact with them, 1 discontinued intervention (work-related problems); Group 2 Number missing: 1, Reason: 1 discontinued intervention (family problems)

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function at 8 weeks; Group 1: mean 23.92 (SD 11.3); n=12, Group 2: mean 20.38 (SD 13); n=13; WOMAC function 0-68 Top=High is poor outcome; Comments: Baseline active: 28.83 (7.97). Baseline sham: 23.54 (14.13).
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, weight, height, BMI, OARSI-medial JSN, bilateral involvement and baseline values of outcomes; Group 1 Number missing: 3, Reason: 2 lost to follow up - not able to make contact with them, 1 discontinued intervention (work-related problems); Group 2 Number missing: 1, Reason: 1 discontinued intervention (family problems)

Protocol outcome 3: Mild adverse events at </= 3 months
- Actual outcome: Electric shock/stinging sensations at 8 weeks; Group 1: 2/14, Group 2: 2/13
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, weight, height, BMI, OARSI-medial JSN, bilateral involvement and baseline values of outcomes; Group 1 Number missing: 3, Reason: 2 lost to follow up - not able to make contact with them, 1 discontinued intervention (work-related problems); Group 2 Number missing: 1, Reason: 1 discontinued intervention (family problems)

Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3

	months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Madani 2014[146]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=20)
Countries and setting	Conducted in Iran; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 8 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with limited mandibular movements, and suffered from arthralgia and crepitation, especially in the late afternoon or evening, based on the Research Diagnostic Criteria for Temporomandibular Disorders and confirmed through cone beam-computed tomography images taken from the TMJs
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with limited mandibular movements, and suffered from arthralgia and crepitation, especially in the late afternoon or evening, fulfilling on the Research Diagnostic Criteria for Temporomandibular Disorders and confirmed through cone beam-computed tomography images taken from the TMJs.
Exclusion criteria	People with temporomandibular disorders resulting from muscular or disc displacement (with or without reduction) disorders; those having any systemic disease affecting the TMJs; people with psychiatric disorders and those undergoing any other form of therapy during the study period (such as analgesic or anti-inflammatory drugs, or occlusal splints)
Recruitment/selection of patients	People attending the Department of Prosthodontics of Mashhad Dental School, Mashhad University of Medical Sciences, Mashhad, Iran.
Age, gender and ethnicity	Age - Range: 35-60 years. Gender (M:F): 1:19. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: TMJ
Extra comments	Severity: Not stated Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=10) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. Active laser therapy with a low-level laser emitting a pulsed infrared beam of 810nm wavelength. The laser was applied in contact mode with a peak power of

	approximately 80W, 50mW average power at a pulse repetition rate of 1500Hz, pulse length of 1 microseconds, 6J per point, 3.4 J/cm², and spot size 1.76 cm², for 2 minutes per point. Painful muscles diagnosed at the first examination were irradiated, in addition to four points around the TMJs (posterior, anterior and superior of the mandibular condyles, and inside the external auditory duct). The total dose applied in each session varied between 27.2 and 60.8 J/cm², depending on the number of painful areas. The people attended therapy three times a week for 4 weeks.. Duration 4 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=10) Intervention 2: Sham electrotherapy. The same treatment protocol without laser irradiation. Duration 4 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Academic or government funding (The authors would like to thank the vice-chancellor for research of Mashhad University of Medical Sciences for the financial support of this project (grant no. 89342).)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: VAS at 8 weeks; Group 1: mean 1.5 (SD 2.3); n=10, Group 2: mean 1.6 (SD 2.2); n=10; VAS 0-10 Top=High is poor outcome; Comments: Reported pain for each of the muscle regions which were combined for this outcome. Laser: Reported origin of masseter: 1.32 (1.59). Reported body of masseter: 1.50 (2.12). Reported insertion of masseter: 1.50 (2.59). Reported anterior temporalis: 1.40 (2.66). Reported middle temporalis: 1.27 (1.90). Reported posterior temporalis: 0.70 (1.75). Reported insertion of internal pterygoid: 2.75 (2.50). Sham: Reported origin of masseter: 0.90 (1.66). Reported body of masseter: 1.87 (1.78). Reported insertion of masseter: 1.42 (1.82). Reported anterior temporalis: 1.30 (1.98). Reported middle temporalis: 0.80 (1.02). Reported posterior temporalis: 1.27 (1.62). Reported insertion of internal pterygoid: 3.55 (3.41). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports the baseline values for outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Mahler 2019[148]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=55)
Countries and setting	Conducted in Netherlands; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: American College of Rheumatology knee osteoarthritis criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with knee osteoarthritis; age at least 50 years; a NRS score of at least 5/10 in the index knee; insufficient response to both analgesics and exercise therapy
Exclusion criteria	Treatment by a physical therapist in the previous 6 months; NRS pain score >2/10 in the contralateral knee or hips; corticosteroids in the previous 4 weeks; fibromyalgia; Kellgren and LAwrence score >3.
Recruitment/selection of patients	Recruited from two centers in Nijmegen, the Netherlands
Age, gender and ethnicity	Age - Mean (SD): 65 (10). Gender (M:F): 27:28. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Low morbidity score (38 people had less than or equal to 1 comorbidity). 4. Site of osteoarthritis: Knee
Extra comments	Severity: The majority had a Kellgren Lawrence score of at least 2 Duration of symptoms: The majority had symptoms for less than or equal to 5 years.
Indirectness of population	No indirectness
Interventions	(n=27) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. Laser therapy consisting of a total dose of 6 Gray, applied in six fractions of 1 Gray, delivered every other weekday over 2 weeks. Duration 2 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=28) Intervention 2: Sham electrotherapy. Sham laser delivering 0 Gray. Duration 2 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Academic or government funding (The study costs were jointly covered by Sint Maartenskliniek and Radboud University Medical Center)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: SF-36 physical component scale at 3 months; Group 1: mean 0.1 (SD 7); n=27, Group 2: mean 2.4 (SD 6.9); n=28; SF-36 physical component scale 0-50 Top=High is good outcome; Comments: Baseline laser: 39 (7). Baseline sham: 39 (8).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI, duration of symptoms, Kellgren Lawrence grade, comorbidities, inflammatory signs, MRI, serum inflammatory markers and baseline values of outcomes; Group 1 Number missing: 1, Reason: 1 prematurely discontinued treatment; Group 2 Number missing: 0
- Actual outcome: SF-36 mental component scale at 3 months; Group 1: mean 0.9 (SD 8.4); n=27, Group 2: mean -4.2 (SD 10); n=28; SF-36 mental component scale 0-50 Top=High is good outcome; Comments: Baseline laser: 53 (10). Baseline sham: 52 (10).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI, duration of symptoms, Kellgren Lawrence grade, comorbidities, inflammatory signs, MRI, serum inflammatory markers and baseline values of outcomes; Group 1 Number missing: 1, Reason: 1 prematurely discontinued treatment; Group 2 Number missing: 0

Protocol outcome 2: Pain at </= 3 months
- Actual outcome: WOMAC pain at 3 months; Group 1: mean 8 (SD 13); n=27, Group 2: mean 11 (SD 14); n=28; WOMAC pain 0-100 Top=High is good outcome; Comments: Baseline laser: 59 (14). Baseline sham: 61 (17).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI, duration of symptoms, Kellgren Lawrence grade, comorbidities, inflammatory signs, MRI, serum inflammatory markers and baseline values of outcomes; Group 1 Number missing: 1, Reason: 1 prematurely discontinued treatment; Group 2 Number missing: 0

Protocol outcome 3: Physical function at </= 3 months
- Actual outcome: WOMAC function at 3 months; Group 1: mean 9.7 (SD 8); n=27, Group 2: mean 6.3 (SD 14); n=28; WOMAC function 0-100 Top=High is good outcome; Comments: Baseline laser: 60 (17). Baseline sham: 62 (19).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI, duration of symptoms, Kellgren Lawrence grade, comorbidities, inflammatory signs, MRI, serum inflammatory markers and baseline values of outcomes; Group 1 Number missing: 1, Reason: 1 prematurely discontinued treatment; Group 2 Number missing: 0

Protocol outcome 4: Mild adverse events at </= 3 months
- Actual outcome: Collapse, severe knee pain, cold sensations in the lower index leg, fatigue at 3 months; Group 1: 7/27, Group 2: 5/28; Comments: LDRT: 1 collapse, 6 fatigue. Sham: 1 severe knee pain, 1 cold sensations in the lower index leg, 3 fatigue
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI, duration of symptoms, Kellgren

Lawrence grade, comorbidities, inflammatory signs, MRI, serum inflammatory markers and baseline values of outcomes; Group 1 Number missing: 1, Reason: 1 prematurely discontinued treatment; Group 2 Number missing: 0 Protocol outcome 5: Moderate/major adverse events at </= 3 months - Actual outcome: Colon carcinoma at 3 months; Group 1: 0/27, Group 2: 2/28 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, BMI, duration of symptoms, Kellgren Lawrence grade, comorbidities, inflammatory signs, MRI, serum inflammatory markers and baseline values of outcomes; Group 1 Number missing: 1, Reason: 1 prematurely discontinued treatment; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at > 3 months

Study	Marquina 2012[150]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=126)
Countries and setting	Conducted in USA; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 4 weeks (and an additional 4 weeks of follow up)
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: People with chronic knee pain
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People, 21 years of age or older, with chronic knee pain
Exclusion criteria	Pregnancy; pacemakers; benign or malignant tumours; any subject currently undergoing any systemic medical or surgical treatment or physical therapy for the knee joint
Recruitment/selection of patients	People were recruited from three private clinics in the cities of Richmond and Charlottesville, Virginia
Age, gender and ethnicity	Age - Range: 25-80. Gender (M:F): 78:48. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years (Realistically a mix). 2. Diagnosis : Not stated / Unclear 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Not stated Duration of symptoms: Not stated
Indirectness of population	Serious indirectness: Doesn't define that it is for people with osteoarthritis
Interventions	(n=53) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. Laser treatment using a Theralase TLC-1000 therapeutic laser systems, a class 3B medical laser system. The system has a dual wavelength, TLC-900 multiple diode laser cluster probe that consists of a cluster of five 905nm super-pulsed near-infrared laser diodes (50,000mW peak power, up to 100mW average power, 200ns pulse width, up to 10,000 Hz frequency) and four 660nm visible red laser diodes (25 mW average power). It was used in direct contact to the tissues. The probe was positioned for 1 minute over each of seven specific locations around the knee joint of the subject encompassing three locations on the lateral aspect of the knee, three locations on the medial aspect of the knee and one location on the posterior aspect of the knee at the midline of the popliteal fossa, and both inferior and superior to the midline of the popliteal fossa. The therapeutic laser system was set to an average power of 60mW

	with a treatment time of 60s per location to produce a dose or energy density of 3.6J/cm² at the skin surface per 905nm laser diode. The total optical output of the laser probe was therefore 5x60mW @905 nm + 4x25 mW @ 660nm = 400mW for 60s or 24J/cm² per location. Treatments were delivered as 12 treatments, 3 treatments per week over 4 weeks. The intervals were not allowed to be >3 days.. Duration 4 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=48) Intervention 2: Sham electrotherapy. Sham laser with no NIR optical output and 660nm 1mW light emitting diodes were used instead of 660nm visible red laser diodes.. Duration 4 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Study funded by industry (This clinical trial was funded by Theralase Inc., Ontario, Canada)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: Pain (VAS) at 8 weeks; Group 1: mean 2.8 (SD 2.4); n=53, Group 2: mean 4.6 (SD 2.6); n=48; VAS 0-10 Top=High is poor outcome; Comments: Baseline laser: 6.32 (1.43). Baseline sham: 6.61 (1.45). Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, and baseline values of outcome; Group 1 Number missing: -, Reason: Provides total only: 13 drop outs, 2 discrepant files, 6 lost to follow up (almost 20% attrition overall); Group 2 Number missing: -, Reason: Provides total only: 13 drop outs, 2 discrepant files, 6 lost to follow up (almost 20% attrition overall)	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Mascarin 2012[151]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in Brazil; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 12 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with knee osteoarthritis according to the American College of Rheumatology criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with knee osteoarthritis; female gender, a minimum of 45 years old; free from any other lower limb disease (except bilateral knee osteoarthritis); able to perform physical exercise; not currently receiving physical therapy treatments for the knee osteoarthritis condition; medication compliance (all people were taking glucocorticoids at the time of study); diagnosis of bilateral knee osteoarthritis according to the American College of Rheumatology criteria
Exclusion criteria	Any rheumatic disease (with the exception of bilateral knee osteoarthritis); unilateral knee osteoarthritis; neurological disorders; cognitive limitations or history of cardiovascular, pulmonary or endocrinology disease
Recruitment/selection of patients	People recruited from a Rheumatology clinic
Age, gender and ethnicity	Age - Mean (SD): 62.1 (7.6). Gender (M:F): 0:40. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Not stated / Unclear 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Not stated Duration of symptoms (mean [SD]): 5.2 (5.5) years
Indirectness of population	No indirectness
Interventions	(n=12) Intervention 1: Non-invasive electrotherapy interventions - Transcutaneous electrical nerve stimulation (TENS). TENS delivered by a transcutaneous electrical stimulator with two channels and four square, self-adhesive percutaneous electrodes measuring 5 x 5cm. The TENS were applied using a frequency of 100Hz, pulse width of 50 microseconds, intensity (MA) set at the individual subject's sensorial threshold, modulation up to 50% of variation frequency, quadratic biphasic symmetrical pulse and a length of application of 20 minutes. The participants were stimulated in dorsal

	decubitus, adequately positioned with a roll under their knees. The percutaneous electrodes for the electrical stimulation were placed on the anterior medial and lateral portions of the knee. Delivered as 12 week (24 sessions).. Duration 12 weeks. Concurrent medication/care: Kinesthetic exercise including stretching and isometric exercises for the entire lower limb conducted in supervised 20 minute sessions. Indirectness: No indirectness (n=12) Intervention 2: Non-invasive electrotherapy interventions - Ultrasound. The ultrasound protocol consisted of continuous ultrasonic waves of 1MHz frequency of 0.8W/cm power, applied with a 5cm diameter applicator. The people were placed in a supine position, and an acoustic gel that did not contain any pharmacologically active substance was applied. Ultrasound was then applied to the medial and lateral parts of the knee in circular movements with the probe at right angles to ensure maximum absorption of the energy. Each session lasted 3-4 minutes, depending on the knee size due to oedema. This was delivered as 24 sessions over 12 weeks.. Duration 12 weeks. Concurrent medication/care: Kinesthetic exercise including stretching and isometric exercises for the entire lower limb conducted in supervised 20 minute sessions. Indirectness: No indirectness (n=16) Intervention 3: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. No electrotherapy treatment. Duration 12 weeks. Concurrent medication/care: Kinesthetic exercise including stretching and isometric exercises for the entire lower limb conducted in supervised 20 minute sessions. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) versus ULTRASOUND

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 8 weeks; Group 1: mean 3.3 (SD 2.9); n=12, Group 2: mean 6.2 (SD 4.2); n=12; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline TENS: 10.7 (3.0). Baseline ultrasound: 10.1 (3.8).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, mass, years diagnosed with osteoarthritis and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC physical function at 8 weeks; Group 1: mean 10.1 (SD 8.3); n=12, Group 2: mean 20.6 (SD 9.8); n=12; WOMAC physical function

0-68 Top=High is poor outcome; Comments: Baseline TENS: 31.8 (9.2). Baseline ultrasound: 38.3 (9.1).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, mass, years diagnosed with osteoarthritis and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 8 weeks; Group 1: mean 3.3 (SD 2.9); n=12, Group 2: mean 2 (SD 2.3); n=16; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline TENS: 10.7 (3.0). Baseline no treatment: 8.9 (4.4).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, mass, years diagnosed with osteoarthritis and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC physical function at 8 weeks; Group 1: mean 10.1 (SD 8.3); n=12, Group 2: mean 4.6 (SD 5.9); n=16; WOMAC physical function 0-68 Top=High is poor outcome; Comments: Baseline TENS: 31.8 (9.2). Baseline no treatment: 25.6 (13.6).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, mass, years diagnosed with osteoarthritis and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 8 weeks; Group 1: mean 6.2 (SD 4.2); n=12, Group 2: mean 2 (SD 2.3); n=16; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline ultrasound: 10.1 (3.8). Baseline no treatment: 8.9 (4.4).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, mass, years diagnosed with osteoarthritis and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC physical function at 8 weeks; Group 1: mean 20.6 (SD 9.8); n=12, Group 2: mean 4.6 (SD 5.9); n=16; WOMAC physical function 0-68 Top=High is poor outcome; Comments: Baseline ultrasound: 38.3 (9.1). Baseline no treatment: 25.6 (13.6).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, mass, years diagnosed with osteoarthritis and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Melo mde 2015[152] (Melo 2019[153])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=45)
Countries and setting	Conducted in Brazil; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 12 weeks (4 week control period followed by 8 weeks of intervention)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Grade 2 or 3 knee osteoarthritis diagnosed by a traumatology-orthopaedic physician according to the criteria proposed by Kellgren and Lawrence
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Grade 2 or 3 knee osteoarthritis; age between 63 and 75 years; female gender; and one or more episodes of knee pain in the past 6 months
Exclusion criteria	Body mass index higher than 40kg/m²; hip, ankle or toe osteoarthritis diagnosis; the use of crutches for locomotion; participation in a strength-training programme or physiotherapy treatment for knee osteoarthritis in the past 6 months; neurological or cognitive disorders; rheumatoid arthritis; electronic implants; previous or upcoming surgery (within three months); or any cardiorespiratory, neuromuscular or metabolic disease that could represent an absolute contraindication or a contraindication to the performance of maximum strength tests
Recruitment/selection of patients	People were recruited via advertisements in disclosure media
Age, gender and ethnicity	Age - Mean (SD): 68.8 (5.1). Gender (M:F): 0:45. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren-Lawrence grade 2-3 Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=15) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. Low level laser therapy programme. During the first four intervention weeks, laser therapy was administered for 30 seconds per point, with a dose of 6J per point (totalling 36J), to optimise the laser's analgesic and the anti-inflammatory effects. In the remaining four weeks, the treatment focused on cartilage regeneration, for which an approximately 30% lower energy dose was used, i.e. 20 seconds per point,

	resulting in a dose of 4J per point (totalling 24J).. Duration 8 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=15) Intervention 2: Non-invasive electrotherapy interventions - Neuromuscular electrical stimulation. Neuromuscular electrical stimulation sessions twice a week, at 48 hour intervas, over an eight week period, with a progressive increase in the intensity and volume. Electrical stimulation as administered with portable, constant-voltage electrical stimulation equipment. All sessions were performed at the same time of the day with participants seated on a conventional chair, knees flexed to 90 degrees and the treated lower-limb strapped to the chair with a band. During electrical stimulation, two electrodes (5cm x 13cm) were placed anteriorly on the participants' thighs. The proximal electrode was positioned over the quadriceps motor point, and the distal electrode was placed perpendicular to the longitudinal thigh axis just above the patellar border.. Duration 8 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=15) Intervention 3: Non-invasive electrotherapy interventions - Combination therapy (e.g. ultrasound and interferential therapy). Laser and neuromuscular electrical stimulation (combination of the same protocols stated for the previous groups). Duration 8 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	No funding (This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus NEUROMUSCULAR ELECTRICAL STIMULATION

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: Pain 6-minute walking test at 12 weeks; Group 1: mean 1.6 (SD 0.8); n=15, Group 2: mean 0.9 (SD 0.5); n=15; VAS 0-10 Top=High is poor outcome; Comments: Baseline laser: 2.3 (1.1). Baseline NMES: 3.5 (1.9).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, mass, thigh length, blood pressure, BMI, Kellgren Lawrence grade and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINATION THERAPY (E.G. ULTRASOUND AND INTERFERENTIAL THERAPY) versus LASER THERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: Pain 6-minute walking test at 12 weeks; Group 1: mean 1.2 (SD 0.9); n=14, Group 2: mean 1.6 (SD 0.8); n=15; VAS 0-10 Top=High is poor outcome; Comments: Baseline combination: 3.3 (1.8). Baseline laser: 2.3 (1.1).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, mass, thigh length, blood pressure, BMI, Kellgren Lawrence grade and baseline values of outcomes; Group 1 Number missing: 1, Reason: 1 dropped out due to personal reasons; Group 2 Number missing: 0

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINATION THERAPY (E.G. ULTRASOUND AND INTERFERENTIAL THERAPY) versus NEUROMUSCULAR ELECTRICAL STIMULATION

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: Pain 6-minute walking test at 12 weeks; Group 1: mean 1.2 (SD 0.9); n=14, Group 2: mean 0.9 (SD 0.5); n=15; VAS 0-10 Top=High is poor outcome; Comments: Baseline combination: 3.3 (1.8). Baseline NMES: 3.5 (1.9).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, mass, thigh length, blood pressure, BMI, Kellgren Lawrence grade and baseline values of outcomes; Group 1 Number missing: 1, Reason: 1 dropped out due to personal reasons; Group 2 Number missing: 0

Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Mizusaki imoto 2013[154]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=100)
Countries and setting	Conducted in Brazil; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 8 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Knee osteoarthritis based on the American College of Rheumatology criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Age 50 to 75 years; osteoarthritis grade 2 or greater according to the radiographic classification of osteoarthritis proposed by Kellgren and Lawrence, and diagnosis of knee osteoarthritis based on the American College of Rheumatology criteria
Exclusion criteria	use of a pacemaker; unstable heart conditions; participation in another physical activity program; inability to exercise on a stationary bicycle ergometer; inability to walk; previous hip or knee arthroplasty; diagnosis of fibromyalgia, epilepsy and skin tumor or lesions at the NMES application site
Recruitment/selection of patients	People were referred from the Rheumatology Department
Age, gender and ethnicity	Age - Mean (SD): 61.1 (6.8). Gender (M:F): 14:86. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 2-4, median grade 2 Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=50) Intervention 1: Non-invasive electrotherapy interventions - Neuromuscular electrical stimulation. Neuromuscular electrical stimulation applied using an electrical stimulator with two 7.5 x 13cm self-adhesive electrodes placed over the region of the quadriceps muscle (rectus femoris and vastus medialis). NMES parameters were as follows: pulsed current, biphasic, asymmetrical, rectangular waveform, frequency 50Hz, pulse duration 250 microseconds. contraction time 10s, rest time 30s every 20 minutes, current intensity was the maximum tolerated by each person. Duration 8 weeks. Concurrent medication/care: Exercise including 10 minutes on a stationary bicycle, stretching of hamstring muscles (3 repetitions of 30 seconds) with the aid of

	an elastic band, and loaded quadriceps strengthening exercises combined with NmES. Performed in a sitting position with the knee and hip flexed to 90 degrees, people contracted their quadriceps at each NMES stimulus. Paracetamol was prescribed for pain, and diacerein and chloroquine for osteoarthritis control. (n=50) Intervention 2: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. No electrotherapy intervention. Duration 8 weeks. Concurrent medication/care: Exercise including 10 minutes on a stationary bicycle, stretching of hamstring muscles (3 repetitions of 30 seconds) with the aid of an elastic band, and loaded quadriceps strengthening exercises combined with NmES. Performed in a sitting position with the knee and hip flexed to 90 degrees, people contracted their quadriceps at each NMES stimulus. Paracetamol was prescribed for pain, and diacerein and chloroquine for osteoarthritis control.. Indirectness: No indirectness
Funding	Academic or government funding (This study was supported by Fundacao de Apolo a Pesquisa do Estado de Sao Paulo (FAPESP))

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NEUROMUSCULAR ELECTRICAL STIMULATION versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 8 weeks; Group 1: mean -2.97 (SD 4.51); n=50, Group 2: mean -3.87 (SD 4.15); n=50; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported change score and 95% confidence intervals. Reported NMES: -2.97 (-4.22 to -1.72). Reported no treatment: -3.87 (-5.02 to -2.72). Baseline NMES: 8.72 (4.20). Baseline no treatment: 9.34 (2.47).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, treated leg, BMI, Kellgren Lawrence grade and baseline values of outcomes; Group 1 Number missing: 6, Reason: 5 lost to follow up (noncompliance), 1 discontinued (hypertension peak); Group 2 Number missing: 7, Reason: 3 knee pain, 1 death in family, 2 found a new job, 1 found a treatment close to home

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function at 8 weeks; Group 1: mean -8.02 (SD 12); n=50, Group 2: mean -10.95 (SD 14.1); n=50; WOMAC function 0-68 Top=High is poor outcome; Comments: Reported change score and 95% confidence intervals. Reported NMES: -8.02 (-11.34 to -4.69). Reported no treatment: -10.95 (-14.84 to -7.05). Baseline NMES: 28.54 (13.96). Baseline no treatment: 35.15 (11.88).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, treated leg, BMI, Kellgren Lawrence grade and baseline values of outcomes; Group 1 Number missing: 6, Reason: 5 lost to follow up (noncompliance), 1 discontinued (hypertension peak); Group 2 Number missing: 7, Reason: 3 knee pain, 1 death in family, 2 found a new job, 1 found a treatment close to home

Protocol outcome 3: Mild adverse events at </= 3 months - Actual outcome: Blood pressure spike at 8 weeks; Group 1: 1/50, Group 2: 0/50 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, treated leg, BMI, Kellgren Lawrence grade and baseline values of outcomes; Group 1 Number missing: 6, Reason: 5 lost to follow up (noncompliance), 1 discontinued (hypertension peak); Group 2 Number missing: 7, Reason: 3 knee pain, 1 death in family, 2 found a new job, 1 found a treatment close to home	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Moffett 1996[155]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=92)
Countries and setting	Conducted in United Kingdom; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 3 weeks of treatment, 12 weeks follow up in total
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with osteoarthritis of the hip or knee with radiological changes
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Radiological changes in the hip or knee reported as degenerative or osteoarthritic; pain predominantly emanating from the one joint; ability to walk 50m
Exclusion criteria	Previous arthroplasty on joint to be treated; surgery to this joint in past 6 months; physiotherapy for joint over the past 6 months; documented contra-indications to PSW (e.g. pacemaker, pregnancy); serious obesity as defined by Quetellet's Index, which would make it difficult to position the applicator close to the hip joint
Recruitment/selection of patients	People referred from the outpatient clinics of the Nuffield Orthopaedic Centre
Age, gender and ethnicity	Age - Mean (SD): 63.5 (9.9). Gender (M:F): 34:58. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Other (Knee or hip).
Extra comments	Severity: Not stated Duration of symptoms (mean [SD]): 92.1 (124.4) months
Indirectness of population	No indirectness
Interventions	(n=30) Intervention 1: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. Pulsed short wave machine Ultramed 11S 601 with a drum applicator, called a 'Circuplode' containing a coil, providing the PEMF. Nine session of treatment provided over a 3 week period, each application lasting for 15 minutes.. Duration 3 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=30) Intervention 2: Sham electrotherapy. Sham electrotherapy using the same machine (machine was altered to have a dial with 10 positions, half of the numbers did not work while half worked - people were assigned numbers randomly). Duration 3

	weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=30) Intervention 3: No intervention - No treatment. No treatment. Duration 3 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Academic or government funding (The Arthritis and Rheumatism Council are acknowledged for funding this study)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: NRS at 12 weeks; Group 1: mean 35.92 (SD 32.84); n=30, Group 2: mean 53.86 (SD 29.36); n=30; NRS 0-10 Top=High is poor outcome; Comments: Baseline values not reported Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, duration of history, pain diary reports and GHQ. Does not report baseline values for NRS.; Group 1 Number missing: 4, Reason: No information given; Group 2 Number missing: 8, Reason: No information given Protocol outcome 2: Psychological distress at </= 3 months - Actual outcome: GHQ at 12 weeks; Group 1: mean 30.27 (SD 15.8); n=30, Group 2: mean 26.79 (SD 13.58); n=30; GHQ 0-90 Top=High is poor outcome; Comments: Baseline pulsed SWT: 29.34 (12.78). Baseline placebo: 25.72 (9.38). Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, duration of history, pain diary reports and GHQ. Does not report baseline values for NRS.; Group 1 Number missing: 4, Reason: No information given; Group 2 Number missing: 8, Reason: No information given RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus NO TREATMENT Protocol outcome 1: Psychological distress at </= 3 months - Actual outcome: GHQ at 12 weeks; Group 1: mean 30.27 (SD 15.8); n=30, Group 2: mean 32 (SD 14.18); n=30; GHQ 0-90 Top=High is poor outcome; Comments: Baseline pulsed SWT: 29.34 (12.78). Baseline placebo: 28.24 (10.75). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, duration of history, pain diary reports and GHQ. Does not report baseline values for NRS.; Group 1 Number missing: 4, Reason: No information given; Group 2 Number missing: 3, Reason: No information given	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months;

	Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Nelson 2013[160]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=34)
Countries and setting	Conducted in USA; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 6 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with knee pain and an imaging study confirming articular cartilage loss
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with knee pain for at least 3 months with an imaging study that confirmed articular cartilage loss, an initial VAS score of at least 4 and at least 2 hours of daily standing activity in a physical occupation
Exclusion criteria	People with rheumatoid arthritis, gout and pregnancy; people with cortisone injections, surgery, or an effective viscosupplementation series within the past 6 months; people with implanted electronic devices; people receiving health related benefits or with third party claims
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 57.1 (2.9). Gender (M:F): 10:24. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade (mean [SD]): 2.8 (0.3) Duration of symptoms: At least 3 months
Indirectness of population	No indirectness
Interventions	(n=15) Intervention 1: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. Pulsed electromagnetic field therapy consisting of a 7ms burst of 6.8mHz sinusoidal waves repeating at 1 burst/s delivering a peak induced electric field of 34+/-8 V/m in the knee from the portable battery operated device, was used twice daily for 15 minutes. The device was light weight and people could easily position the coil directly over the knee, even over clothing. Once manually activated, treatment was automatically applied for 15 minutes. manual activation was required for each treatment.. Duration 6 weeks. Concurrent medication/care: Standard care could include unrestricted NSAID use. Standard care was allowed throughout.. Indirectness:

	No indirectness (n=19) Intervention 2: Sham electrotherapy. Sham devices otherwise being used in the same way. Duration 6 weeks. Concurrent medication/care: Standard care could include unrestricted NSAID use. Standard care was allowed throughout.. Indirectness: No indirectness
Funding	Equipment / drugs provided by industry (The authors gratefully acknowledge partial support of this work by the Department of Orthopaedic Surgery, Henry Ford Hospital, Detroit Michigan, and Ivivi Health Sciences, LLC, San Francisco, CA, who manufacturer the PEMF devices utilized in this study)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: VAS at 6 weeks; Group 1: mean 4.19 (SD 0.71); n=15, Group 2: mean 6.11 (SD 0.54); n=19; VAS 0-10 Top=High is poor outcome; Comments: Baseline active: 6.85 (0.33). Baseline sham: 7.18 (0.31). Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, BMI, Kellgren Lawrence grade and baseline value of the outcome; Group 1 Number missing: 3, Reason: 3 withdrew (perceived no benefit); Group 2 Number missing: 7, Reason: 7 withdrew (perceived no benefit)	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Ozgonenel 2009[166]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=67)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Clinical and radiological criteria defined by the American College of Rheumatology for knee osteoarthritis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People newly diagnosed with osteoarthritis of the knee; aged 45-65 years; knee pain and limitation on most days of the past 6 months; Kellgren Lawrence scores of 2-3 on radiological evaluation
Exclusion criteria	Any systemic illness or abnormal laboratory test result; any contraindication for physical therapy; any knee operation. lower limb arthroplasty or had been on any physiotherapy program before or receive intra-articular knee injections or ultrasound therapy in the preceding year
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 54.9 (7.6). Gender (M:F): 13:54. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 2-3, median grade 3 Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=34) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. Ultrasound applied using an aqueous gel as a coupling medium in circular movements with the probe at right angles. The treatment area was 25cm² and extended to both patellofemoral and tibiofemoral borders of the target knee on both the lateral and medial margins, avoiding the patella. Continuous ultrasonic waves with 1mHz frequency and 1 watt/cm² power were applied with a 4cm diameter applicator for 5 min in each session. This was completed once a day for 10 days.. Duration 10 days. Concurrent medication/care: No additional information. Indirectness: No indirectness

	(n=33) Intervention 2: Sham electrotherapy. Sham ultrasound (applicator disconnected from the back of the working machine) applied to the target knee in the same manner using the same acoustic gel for 5 minutes per session. Duration 10 days. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 10 days; Group 1: mean 6.9 (SD 3.6); n=34, Group 2: mean 8.4 (SD 4.2); n=33; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline ultrasound: 10.4 (3.0). Baseline placebo: 9.4 (3.6).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, weight, sex, target knee, severity on x-ray and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: 2 dropped out due to increased pain

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function at 10 days; Group 1: mean 23.6 (SD 11.6); n=34, Group 2: mean 27.1 (SD 14); n=33; WOMAC function 0-68 Top=High is poor outcome; Comments: Baseline ultrasound: 33.4 (11.2). Baseline placebo: 30.6 (11.4).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, weight, sex, target knee, severity on x-ray and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: 2 dropped out due to increased pain

Protocol outcome 3: Mild adverse events at </= 3 months
- Actual outcome: Increased pain at 10 days; Group 1: 0/34, Group 2: 2/33
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, weight, sex, target knee, severity on x-ray and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Ozgonenel 2018[167]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=33)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 4 weeks (2 weeks of intervention)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Clinical and radiological criteria defined by the American College of Rheumatology for knee osteoarthritis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	45-65 years old; if they had knee pain and limitation on most days of the past 6 months; if the Kellgren-Lawrence scores were III on radiological evaluation
Exclusion criteria	Any systemic illness or abnormal laboratory test result; any contraindication for physical therapy; history of a knee operation, including lower limb arthroplasty; if they had been on any physiotherapy program before; if they had received intra-articular knee injections of ultrasound therapy in the preceding year
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 54.8 (14.8). Gender (M:F): 15:18. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 3 Duration of symptoms: At least 6 months
Indirectness of population	No indirectness
Interventions	(n=15) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. Ultrasound therapy delivered using an aqueous gel as a coupling medium in circular movements with the probe at right angles. The treatment area was 25 cm² and extended to both patellofemoral and tibiofemoral borders of the target knee on both the lateral and medial margins, avoiding the patella. Continuous ultrasonic waves with 1MHz frequency and 1W/cm² power were applied with a 4cm diameter applicator for 5 minutes in each session.. Duration 2 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=18) Intervention 2: Sham electrotherapy. Sham ultrasound (an applicator

	disconnected from the back to working ultrasound machine) applied to the target knee in the same manner, using the same acoustic gel, 5 minutes per session.. Duration 2 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: VAS at 4 weeks; Group 1: mean 5.93 (SD 0.8); n=15, Group 2: mean 5.89 (SD 0.68); n=18; VAS 0-10 Top=High is poor outcome; Comments: Baseline ultrasound: 7.53 (0.92). Baseline sham: 7.28 (1.18). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, target knee, age, bmI, and baseline values of outcomes; Group 1 Number missing: -; Group 2 Number missing: -	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Ozguclu 2010[168]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis of knee osteoarthritis according to the American College of Rheumatology
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 45-75 years; diagnosis of knee osteoarthritis; radiological alterations in the knee joint according to the Kellgren-Lawrence criteria grade 2 and above; an average pain intensity of 40 or more on a 100mm visual analog scale in the last 1 week
Exclusion criteria	Pain in the knee due to inflammatory, malignant or autoimmune disease or other reasons for pain in the knee such as serious varus or valgus defective position; knee surgery or arthroscopy of the affected knee in the past year; chondroprotective or intra-articular injection in the past 4 months; systemic corticosteroid or physiotherapy in the past 1 month; if they were unable to understand the questionnaire
Recruitment/selection of patients	People recruited from the outpatient clinic at the Department of Physical Medicine and Rehabilitation, Hacettepe University Hospital in Ankara
Age, gender and ethnicity	Age - Mean (SD): 61.3 (7.8). Gender (M:F): 11:29. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 2 and above Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. Pulsed electromagnetic therapy using two pairs of solenoid applicators. The applicators were held at the sides of the knee by a velcro band. PEMF was applied at a frequency of 50Hz, 30-G intensity, 90s interval and 30 minute durations in each session. 5 sessions weekly for 2 weeks.. Duration 2 weeks. Concurrent medication/care: In each session 20 minutes hot pack and 5 minutes of therapeutic ultrasound were given. People were taught terminal isometric knee exercise to

	complete at home as required (three times a day, 30 repeats each). People were allowed to take paracetamol for knee pain if necessary. Other pain treatments (including NSAIDs) were not allowed.. Indirectness: No indirectness (n=20) Intervention 2: Sham electrotherapy. Same as the standard therapy but the device had an intensity of near zero.. Duration 2 weeks. Concurrent medication/care: In each session 20 minutes hot pack and 5 minutes of therapeutic ultrasound were given. People were taught terminal isometric knee exercise to complete at home as required (three times a day, 30 repeats each). People were allowed to take paracetamol for knee pain if necessary. Other pain treatments (including NSAIDs) were not allowed.. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: WOMAC pain at 2 weeks; MD; -0.15 (SE: 1.26) WOMAC pain 0-20 Top=High is poor outcome, Comments: Calculated from reported final values. Reported PEMF (n=20): 5.30. Reported sham: 5.45 (n=20). P value = 0.906. Baseline PEMF: 9.95 (3.42). Baseline sham: 9.5 (3.5).; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, weight, height, Kellgren Lawrence score, duration of symptoms, and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 2: Physical function at </= 3 months - Actual outcome: WOMAC disability at 2 weeks; MD; -1.05 (SE: 4.3) WOMAC disability 0-68 Top=High is poor outcome, Comments: Calculated from final values and p-value. Reported PEMF: 19.05 (n=20). Reported sham: 20.10 (n=20). P-value = 0.809. Baseline PEMF: 32.75 (9.3). Baseline sham: 34.2 (12.1).; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, weight, height, Kellgren Lawrence score, duration of symptoms, and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Palmer 2014[169]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=224)
Countries and setting	Conducted in United Kingdom; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 6 weeks of intervention (24 weeks follow up in total)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Knee osteoarthritis confirmed by the American College of Rheumatology clinical criteria (including knee pain accompanied by at least 3 out of 6 signs and symptoms [age >50 years, stiffness <30 minutes, crepitus, body tenderness, bony enlargement and no palpable warmth)
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Age at least 18 years old with knee osteoarthritis confirmed by American College of Rheumatology clinical criteria
Exclusion criteria	Comorbidities preventing participation in the knee group; contraindications to TENS; previous TENS experience
Recruitment/selection of patients	People referred to physiotherapy at University Hospital Bristol with confirmed or suspected knee osteoarthritis
Age, gender and ethnicity	Age - Mean (SD): 61.4 (10.5). Gender (M:F): 83:141. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Not stated / Unclear 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Not stated Duration of symptoms: 4.0 (8.7) years
Indirectness of population	No indirectness
Interventions	(n=73) Intervention 1: Non-invasive electrotherapy interventions - Transcutaneous electrical nerve stimulation (TENS). TENS given over 6 weeks (initially with support from instructors, then self-administered). People were taught to position 4 electrodes around the knee joint: 2 on the medial and 2 on the lateral aspect on either side of the joint line (such that each of the 2 electrical circuits diagonally crossed the knee). The devices were set to a continuous mode (program A: 110Hz, 50 microseconds). All electrical pulses were asymmetric and biphasic. People were advised to use the device as much as needed.. Duration 6 weeks. Concurrent medication/care: All people received a knee exercise and education program. This was a 6 week program

	involving a group of up to 12 people attending for 1 hour (30 minutes of education and 30 minutes of group exercise) on 6 consecutive weeks. The education program aimed to enhance people's ability to self-manage their condition. The education program included information on setting personal objectives, pacing, managing flares, diet, medical management of osteoarthritis, local community exercise opportunities and long-term exercise adherence. The exercise component included a 5 minute warm up followed by a circuit of exercises aimed at improving lower extremity strength, proprioception and function. Each exercise had specific ideas for progression that people advanced as able to over the 6 weeks. All people were taught home exercises during the second session and advised to perform them daily. These included step ups, sit to stand, balancing on one leg, and heel to toe walking. This was supported by a booklet containing written advice on the topics covered in the education session, details of the home exercises and tools to aid goal setting.. Indirectness: No indirectness (n=74) Intervention 2: Sham electrotherapy. Sham TENS (same device type but set to release no current). Duration 6 weeks. Concurrent medication/care: All people received a knee exercise and education program. This was a 6 week program involving a group of up to 12 people attending for 1 hour (30 minutes of education and 30 minutes of group exercise) on 6 consecutive weeks. The education program aimed to enhance people's ability to self-manage their condition. The education program included information on setting personal objectives, pacing, managing flares, diet, medical management of osteoarthritis, local community exercise opportunities and long-term exercise adherence. The exercise component included a 5 minute warm up followed by a circuit of exercises aimed at improving lower extremity strength, proprioception and function. Each exercise had specific ideas for progression that people advanced as able to over the 6 weeks. All people were taught home exercises during the second session and advised to perform them daily. These included step ups, sit to stand, balancing on one leg, and heel to toe walking. This was supported by a booklet containing written advice on the topics covered in the education session, details of the home exercises and tools to aid goal setting.. Indirectness: No indirectness (n=77) Intervention 3: No intervention - No treatment. No TENS. Duration 6 weeks. Concurrent medication/care: All people received a knee exercise and education program. This was a 6 week program involving a group of up to 12 people attending for 1 hour (30 minutes of education and 30 minutes of group exercise) on 6 consecutive weeks. The education program aimed to enhance people's ability to self-

	manage their condition. The education program included information on setting personal objectives, pacing, managing flares, diet, medical management of osteoarthritis, local community exercise opportunities and long-term exercise adherence. The exercise component included a 5 minute warm up followed by a circuit of exercises aimed at improving lower extremity strength, proprioception and function. Each exercise had specific ideas for progression that people advanced as able to over the 6 weeks. All people were taught home exercises during the second session and advised to perform them daily. These included step ups, sit to stand, balancing on one leg, and heel to toe walking. This was supported by a booklet containing written advice on the topics covered in the education session, details of the home exercises and tools to aid goal setting.. Indirectness: No indirectness Comments: This group was not included in the analysis as the intervention given was identified as a treatment package and so will be compared in a separate review.
Funding	Academic or government funding (Supported by grants from the Physiotherapy Research Foundation (part of the Chartered Society of PHysiotherapy Charitable Trust) and Above & Beyond Charities)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 12 weeks; Group 1: mean 7 (SD 7.8); n=73, Group 2: mean 7 (SD 7); n=74; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline TENS: 9.0 (6.0). Baseline sham: 9.0 (5.0).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, study knee, age, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 15, Reason: At 24 weeks: 15 lost to follow up. 7 no reason, 3 work and family commitments, 1 other medical problem, 1 difficulty attending, 1 died, 2 other reasons; Group 2 Number missing: 13, Reason: At 24 weeks: 13 lost to follow up. 5 no reason, 3 rwork and family committments, 2 knee surgery, 1 other medical problem, 1 difficulty attending, 1 other reason

Protocol outcome 2: Pain at > 3 months
- Actual outcome: WOMAC pain at 24 weeks; Group 1: mean 7 (SD 8); n=73, Group 2: mean 6 (SD 8); n=74; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline TENS: 9.0 (6.0). Baseline sham: 9.0 (5.0).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, study knee, age, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 15, Reason: At 24 weeks: 15 lost to follow up. 7 no reason, 3 work and family commitments, 1 other medical problem, 1 difficulty attending, 1 died, 2 other reasons; Group 2 Number missing: 13, Reason: At 24 weeks: 13 lost to follow up. 5 no reason, 3 rwork and family committments, 2 knee surgery, 1 other medical problem, 1 difficulty attending, 1 other reason

Protocol outcome 3: Physical function at </= 3 months - Actual outcome: WOMAC function at 12 weeks; Group 1: mean 25.3 (SD 14.1); n=73, Group 2: mean 25.7 (SD 14.1); n=74; WOMAC function 0-68 Top=High is poor outcome; Comments: Baseline TENS: 29.3 (14.0). Baseline sham: 28.8 (13.0). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, study knee, age, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 15, Reason: At 24 weeks: 15 lost to follow up. 7 no reason, 3 work and family commitments, 1 other medical problem, 1 difficulty attending, 1 died, 2 other reasons; Group 2 Number missing: 13, Reason: At 24 weeks: 13 lost to follow up. 5 no reason, 3 rwork and family committments, 2 knee surgery, 1 other medical problem, 1 difficulty attending, 1 other reason Protocol outcome 4: Physical function at > 3 months - Actual outcome: WOMAC function at 24 weeks; Group 1: mean 25.8 (SD 13.8); n=73, Group 2: mean 25.3 (SD 15); n=74; WOMAC function 0-68 Top=High is poor outcome; Comments: Baseline TENS: 29.3 (14.0). Baseline sham: 28.8 (13.0). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, study knee, age, BMI, pain duration and baseline values of outcomes; Group 1 Number missing: 15, Reason: At 24 weeks: 15 lost to follow up. 7 no reason, 3 work and family commitments, 1 other medical problem, 1 difficulty attending, 1 died, 2 other reasons; Group 2 Number missing: 13, Reason: At 24 weeks: 13 lost to follow up. 5 no reason, 3 rwork and family committments, 2 knee surgery, 1 other medical problem, 1 difficulty attending, 1 other reason	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Palmieri-smith 2010[170]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=30)
Countries and setting	Conducted in USA; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 4 weeks of intervention, 16 weeks total of follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Knee osteoarthritis with radiographic evidence, defined as a score of at least 2 on the Kellgren and Lawrence scale
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Women with osteoarthritis of the knee with radiographic evidence
Exclusion criteria	Had previously undergone a total knee arthroplasty or tibial osteotomy; had diagnosed arthritis of the hip, ankle or foot; had a body mass index of at least 40; used an assistive device while ambulating; had a disease of the central or peripheral nervous system; had any cardiac pathology; reported a previous ligamentous knee injury; had previously undergone NMES therapy for osteoarthritis; currently undergoing physical therapy for any lower-extremity orthopedic condition; taking COX-2 inhibitors; receiving corticosteroid or hyaluronic acid injections
Recruitment/selection of patients	Recruited from the osteoarthritis registry at the University of Michigan
Age, gender and ethnicity	Age - Mean (SD): 57.4 (2.9). Gender (M:F): 0:30. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 2-3, majority grade 2 Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=16) Intervention 1: Non-invasive electrotherapy interventions - Neuromuscular electrical stimulation. Neuromuscular electrical stimulation 3 times per week over 4 weeks. Each session consisted of 10 electrically induced contractions of the quadriceps musculature. This was delivered to one limb only. During each session the person was seated in a chair with their leg positioned in 90 degrees of flexion and fixed to a pad that was attached to a load cell. Self-adhesive electrodes (2.75 x 5 inches [6.98 x 12.7 cm]) were positioned proximally over the rectus femoris muscle and distally over the vastus medialis muscle. Quadriceps muscle contractions were

	elicited using a commercial electrical stimulating unit delivering a 2500Hz alternating current, modulated at 50 bursts per second, with aramp-up time of 2 seconds. the electrical current was set for a sequence of 10 seconds on (which includes the 2 second ramp up time) and 50 seconds off. Current intensity was set at each woman's maximum tolerance, although a target intensity of at least 35% on the participant's daily knee extension maximum voluntary isometric contraction was encouraged.. Duration 4 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=14) Intervention 2: No intervention - No treatment. No intervention (seen as the standard of care). Duration 4 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Academic or government funding (This study was supported by a grant from the Michigan Chapter of the Arthritis Foundation to Dr Palmieri-Smith)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NEUROMUSCULAR ELECTRICAL STIMULATION versus NO TREATMENT

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 5 weeks; Group 1: mean -0.53 (SD 3.74); n=16, Group 2: mean 0 (SD 2.21); n=14; WOMAC pain 5-25 Top=High is poor outcome; Comments: Reports mean change scores and 95% confidence intervals. Reported NMES: -0.53 (-2.37 to 1.30). Reported control: 0.00 (-1.16 to 1.16). Baseline NMES: 7.6 (2.7). Baseline sham: 8.9 (4.3).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, mass, BMI, quadriceps muscle parameters , baseline values of outcomes, Kellgren and Lawrence scale score, bilateral knee osteoarthritis and symptomatic osteoarthritis; Group 1 Number missing: 1, Reason: 1 discontinued; Group 2 Number missing: 2, Reason: 1 lost to follow up, 1 unable to report

Protocol outcome 2: Pain at > 3 months
- Actual outcome: WOMAC pain at 16 weeks; Group 1: mean -0.54 (SD 2.63); n=16, Group 2: mean 1.4 (SD 3.17); n=14; WOMAC pain 5-25 Top=High is poor outcome; Comments: Reports mean change scores and 95% confidence intervals. Reported NMES: -0.54 (-1.83 to 0.75). Reported control: 1.4 (-0.26 to 3.06). Baseline NMES: 7.6 (2.7). Baseline sham: 8.9 (4.3).
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, mass, BMI, quadriceps muscle parameters , baseline values of outcomes, Kellgren and Lawrence scale score, bilateral knee osteoarthritis and symptomatic osteoarthritis; Group 1 Number missing: 4, Reason: 1 discontinued, 3 lost to follow up; Group 2 Number missing: 4, Reason: 4 lost to follow up

Protocol outcome 3: Physical function at </= 3 months
- Actual outcome: WOMAC disability at 5 weeks; Group 1: mean -4.86 (SD 13.1); n=16, Group 2: mean 0 (SD 9.5); n=14; WOMAC disability 17-85 Top=High is poor outcome; Comments: Reports mean change scores and 95% confidence intervals. Reported NMES: -4.86 (-11.29 to 1.56). Reported control: 0.00 (-

5.00 to 5.00). Baseline NMES: 27.1 (12.1). Baseline sham: 28.8 (15.3). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, mass, BMI, quadriceps muscle parameters , baseline values of outcomes, Kellgren and Lawrence scale score, bilateral knee osteoarthritis and symptomatic osteoarthritis; Group 1 Number missing: 1, Reason: 1 discontinued; Group 2 Number missing: 2, Reason: 1 lost to follow up, 1 unable to report Protocol outcome 4: Physical function at > 3 months - Actual outcome: WOMAC disability at 16 weeks; Group 1: mean -4.92 (SD 12.2); n=16, Group 2: mean 5 (SD 8.4); n=14; WOMAC disability 17-85 Top=High is poor outcome; Comments: Reports mean change scores and 95% confidence intervals. Reported NMES: -4.92 (-10.89 to 1.05). Reported control: 5.0 (0.59 to 9.41). Baseline NMES: 27.1 (12.1). Baseline sham: 28.8 (15.3). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, mass, BMI, quadriceps muscle parameters , baseline values of outcomes, Kellgren and Lawrence scale score, bilateral knee osteoarthritis and symptomatic osteoarthritis; Group 1 Number missing: 4, Reason: 1 discontinued, 3 lost to follow up; Group 2 Number missing: 4, Reason: 4 lost to follow up	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Pietrosimone 2011[178] (Pietrosimone 2010[176])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=36)
Countries and setting	Conducted in USA; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with a clinical diagnosis of tibiofemoral osteoarthritis with a quadriceps CAR of less than 0.90 and a Kellgren Lawrence score between 1-4
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with a clinical diagnosis of tibiofemoral osteoarthritis with a quadriceps CAR of less than 0.90 and a Kellgren Lawrence score between 1-4
Exclusion criteria	People with a diagnosed heart condition limiting exercise; altered sensation over the anterior knee region; lower body surgery or knee trauma
Recruitment/selection of patients	People referred from participating orthopaedic surgeons in the University Health System
Age, gender and ethnicity	Age - Other: Not stated. Gender (M:F): 15:21. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): Not stated / Unclear 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence score 1-4, median grade 3
Indirectness of population	No indirectness
Interventions	(n=12) Intervention 1: Non-invasive electrotherapy interventions - Transcutaneous electrical nerve stimulation (TENS). TENS using 4 separate 2x2 inch self-adhesive electrodes. They were applied on the medial and lateral superior, as well as the medial and lateral inferior borders of the patella. 2 TENS currents were crossed to encompass the most surface area under stimulation. People were instructed to wear the units during all therapeutic exercise sessions and at least 8 hours a day. The stimulators were set to deliver a continuous TENS biphasic pulsatile current at 150Hz, with a phase duration of 150 microseconds. People were allowed to increase and decrease the amplitude between 1 and 60mA to achieve a strong, comfortable sensory stimulation intensity that was not strong enough to elicit muscle contraction.. Duration 4 weeks. Concurrent medication/care: Therapeutic exercise was available to

	all participants including quadriceps strengthening lower extremity exercises 3 times a week for 4 weeks, for a total of 12 sessions.. Indirectness: No indirectness (n=12) Intervention 2: Sham electrotherapy. Sham TENS, the same as the standard TENS unit but would stop producing an effect after 30 seconds of stimulation.. Duration 4 weeks. Concurrent medication/care: Therapeutic exercise was available to all participants including quadriceps strengthening lower extremity exercises 3 times a week for 4 weeks, for a total of 12 sessions.. Indirectness: No indirectness (n=12) Intervention 3: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. No TENS intervention. Duration 4 weeks. Concurrent medication/care: Therapeutic exercise was available to all participants including quadriceps strengthening lower extremity exercises 3 times a week for 4 weeks, for a total of 12 sessions.. Indirectness: No indirectness
Funding	Equipment / drugs provided by industry (the authors would like to thank the Orthopaedic Section of the American Physical Therapy Association and the National Athletic Trainers Association Research and Education Foundation for funding this study, as well as EMPI inc for providing the stimulator units)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 4 weeks; Group 1: mean 10 (SD 3); n=12, Group 2: mean 12.3 (SD 3.9); n=12; WOMAC pain 5-25 Top=High is poor outcome; Comments: Reported final values and 95% confidence intervals. Reported TENS: 10.0 (8.3-11.7). Reported sham: 12.3 (10.1-14.5). Baseline TENS: 14.7 (11.4-18.1). Baseline sham: 15.0 (11.7-18.6).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, weight, height, BMI, Kellgren Lawrence score, previous history of knee injury or surgery, physical therapy for knee and TENs and baseline values of outcomes; Group 1 Number missing: 2, Reason: 2 drop outs (muscle soreness and unrelated illness); Group 2 Number missing: 2, Reason: 2 drop outs (muscle soreness and knee joint pain during exercise)

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function at 4 weeks; Group 1: mean 22.5 (SD 5.1); n=12, Group 2: mean 31.1 (SD 8.7); n=12; WOMAC function 17-85 Top=High is poor outcome; Comments: Reported final values and 95% confidence intervals. Reported TENS: 22.5 (19.6-25.4). Reported sham: 31.1 (26.2-36.0). Baseline TENS: 37.6 (30.0-45.6). Baseline sham: 40.2 (31.7-48.7).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, weight, height, BMI, Kellgren Lawrence score, previous history of knee injury or surgery, physical therapy for knee and TENs and baseline values of outcomes; Group 1 Number missing: 2, Reason: 2

drop outs (muscle soreness and unrelated illness); Group 2 Number missing: 2, Reason: 2 drop outs (muscle soreness and knee joint pain during exercise) Protocol outcome 3: Mild adverse events at </= 3 months - Actual outcome: Adverse events at 4 weeks; Group 1: 0/12, Group 2: 0/12 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, weight, height, BMI, Kellgren Lawrence score, previous history of knee injury or surgery, physical therapy for knee and TENs and baseline values of outcomes; Group 1 Number missing: 2, Reason: 2 drop outs (muscle soreness and unrelated illness); Group 2 Number missing: 2, Reason: 2 drop outs (muscle soreness and knee joint pain during exercise) RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT Protocol outcome 1: Pain at </= 3 months - Actual outcome: WOMAC pain at 4 weeks; Group 1: mean 10 (SD 3); n=12, Group 2: mean 11.8 (SD 4.8); n=12; WOMAC pain 5-25 Top=High is poor outcome; Comments: Reported final values and 95% confidence intervals. Reported TENS: 10.0 (8.3-11.7). Reported no treatment: 11.8 (8.9-14.3). Baseline TENS: 14.7 (11.4-18.1). Baseline no treatment: 14.3 (11.0-17.0). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, weight, height, BMI, Kellgren Lawrence score, previous history of knee injury or surgery, physical therapy for knee and TENs and baseline values of outcomes; Group 1 Number missing: 2, Reason: 2 drop outs (muscle soreness and unrelated illness); Group 2 Number missing: 1, Reason: 1 drop out (moved away during intervention) Protocol outcome 2: Physical function at </= 3 months - Actual outcome: WOMAC function at 4 weeks; Group 1: mean 22.5 (SD 5.1); n=12, Group 2: mean 24.9 (SD 7.1); n=12; WOMAC function 17-85 Top=High is poor outcome; Comments: Reported final values and 95% confidence intervals. Reported TENS: 22.5 (19.6-25.4). Reported no treatment: 24.9 (20.9-28.9). Baseline TENS: 37.6 (30.0-45.6). Baseline no treatment: 34.2 (27.3-41.0). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, weight, height, BMI, Kellgren Lawrence score, previous history of knee injury or surgery, physical therapy for knee and TENs and baseline values of outcomes; Group 1 Number missing: 2, Reason: 2 drop outs (muscle soreness and unrelated illness); Group 2 Number missing: 1, Reason: 1 drop out (moved away during intervention) Protocol outcome 3: Mild adverse events at </= 3 months - Actual outcome: Adverse events at 4 weeks; Group 1: 0/12, Group 2: 0/12 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported sex, weight, height, BMI, Kellgren Lawrence score, previous history of knee injury or surgery, physical therapy for knee and TENs and baseline values of outcomes; Group 1 Number missing: 2, Reason: 2 drop outs (muscle soreness and unrelated illness); Group 2 Number missing: 1, Reason: 1 drop out (moved away during intervention)	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress

	at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	**NCT02634814 trial: Pietrosimone 2020[175]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=90)
Countries and setting	Conducted in USA; Setting: Physical therapy clinic.
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 8 weeks
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Age 40-70 years, with a WOMAC function score >30% (out of 100 points, indicating most dysfunction), and radiographic evidence of tibiofemoral OA(2-4 on the Kellgran-Lawrencescale). Quadriceps voluntary activation failure was defined as a central activation ratio <92, which is less than the upper 95% confidence interval of age-matched individuals without KOA.
Exclusion criteria	Those with a cardiovascular condition restricting exercise, a neurodegenerative condition or neural sensory dysfunction over the knee, cancer or a BMI>35kg:m². Anyone with a traumatic knee injury within the previous 6 months, a history of total hip, knee or ankle arthroplasty on either extremity, or any orthopaedic surgery12 months before testing. Anyone with rheumatoid or psoriatic arthritis was also excluded.
Recruitment/selection of patients	Recruited from orthopaedic, rheumatology and physical medicine and rehabilitation clinics within the University of North Carolina Health System using recriutment letters and electronic mail.
Age, gender and ethnicity	Age - Mean (SD): TENS group: 60.8 (7.3) sham TENS group: 62.5 (7.7), exercise group:63 (7.4). Gender (M:F): Male: 39, female: 51. Ethnicity: Not reported
Further population details	1. Age (≤/> 75 years): </=75 years (Age 40-70 years). 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren-Lawrence grade 2: TENS group: 9, sham: 7, exercise: 9

	Kellgren-Lawrence grade 3: TENS group: 18, sham: 17, exercise: 14 Kellgren-Lawrence grade 4: TENS group: 5, sham: 5, exercise: 6 Duration: not reported
Indirectness of population	No indirectness
Interventions	(n=32) Intervention 1: Non-invasive electrotherapy interventions - Transcutaneous electrical nerve stimulation (TENS). Identical TENS units (EMPI, Inc, St Paul, MN) and four separate self-adhesive electrodes (Re-ply reusable electrodes; Uni-Patch, Wabasha, MN) were used to deliver the TENS or sham TENS interventions. Each participant was instructed on how to properly apply the electrodes on the knee joint and operate the TENS unit. Electrodes were applied on the medial and lateral superior and inferior borders of the patella in both groups. Electrodes were positioned close to the patella and away from the quadriceps and musculature of the anterior leg. Participants were instructed to utilise the TENS or sham TENS units during all TE sessions and during activities of daily living. The stimulator units in the active TENS+TE group were set to deliver a continuous TENS biphasic pulsatile current at 150Hz, with a phase duration of 150µs. Participants could adjust the amplitude between 1 and 60mA and were instructed to adjust the amplitude to a strong, manageable sensory stimulation intensity that was not strong enough to elicit muscle contraction. The TENS+TE participants were instructed to maintain this sensation throughout each treatment session by adjusting intensity as needed. The participants in the sham TENS+TE group received the same stimulators with active indicator lights and were instructed to increase and maintain an arbitrary intensity level of 4. The sham TENS units provided a low-level sensory stimulation for 30s and then were programmed to automatically decrease the electrical current over approx. 10s until no electricity was emitted. Participants in the sham tENS+TE group were told 'the current may be felt at first but that they would quickly accommodate and may not feel the stimulus'. All participants were provided with a standardised instruction manual specific to each device, as well as the phone number of an unblinded investigator to call with any questions regarding the device. Participants were asked to self-report the number of hours that the device was used og, whereas an investigator also documented the device-recorded hours each week. Investigators met the participants at the clinic weekly to record usage data from the TENS devices, answer any device-related questions, and provide new electrodes or batteries if necessary.. Duration 4 weeks. Concurrent medication/care: 10 sessions of therapeutic exercise (TE) over a 28 day period, which was directed by a licensed physical therapist at a single clinic. Visits were scheduled to include at least one session per week but not to exceed three sessions over a single week. The physical therapists reviewed medical history and conducted an initial exam on each participant before initiating the standardised TE regimen to determine any potential needs for exercise protocol modification or contraindication. The primary goal of the TE programme was to increase lower extremity strength while secondarily addressing range of motion restrictions, as well as impaired balance. Lower extremity strengthening incorporated both open and closed chain exercises which were individually progressed for each participant using the daily adjusted progressive resistive exercise system. Procedural reliability of the intervention was maximised by 1) training sessions for the physical therapist to ensure all exercises are taught and progressed in the same manner, 2) conducting random patient chart reviews to determine all exercises were performed, and 3) evaluating the delivery of TE on a subset of patients at random time points using a rubric.. Indirectness: No indirectness (n=29) Intervention 2: Sham electrotherapy. Identical TENS units (EMPI, Inc, St Paul, MN) and four separate self-adhesive electrodes (Re-ply reusable electrodes; Uni-Patch, Wabasha, MN) were used to deliver the TENS or sham TENS

	interventions. Each participant was instructed on how to properly apply the electrodes on the knee joint and operate the TENS unit. Electrodes were applied on the medial and lateral superior and inferior borders of the patella in both groups. Electrodes were positioned close to the patella and away from the quadriceps and musculature of the anterior leg. Participants were instructed to utilise the TENS or sham TENS units during all TE sessions and during activities of daily living. The stimulator units in the active TENS+TE group were set to deliver a continuous TENS biphasic pulsatile current at 150Hz, with a phase duration of 150µs. Participants could adjust the amplitude between 1 and 60mA and were instructed to adjust the amplitude to a strong, manageable sensory stimulation intensity that was not strong enough to elicit muscle contraction. The TENS+TE participants were instructed to maintain this sensation throughout each treatment session by adjusting intensity as needed. The participants in the sham TENS+TE group received the same stimulators with active indicator lights and were instructed to increase and maintain an arbitrary intensity level of 4. The sham TENS units provided a low-level sensory stimulation for 30s and then were programmed to automatically decrease the electrical current over approx. 10s until no electricity was emitted. Participants in the sham tENS+TE group were told 'the current may be felt at first but that they would quickly accommodate and may not feel the stimulus'. All participants were provided with a standardised instruction manual specific to each device, as well as the phone number of an unblinded investigator to call with any questions regarding the device. Participants were asked to self-report the number of hours that the device was used og, whereas an investigator also documented the device-recorded hours each week. Investigators met the participants at the clinic weekly to record usage data from the TENS devices, answer any device-related questions, and provide new electrodes or batteries if necessary.. Duration 4 weeks. Concurrent medication/care: 10 sessions of therapeutic exercise (TE) over a 28 day period, which was directed by a licensed physical therapist at a single clinic. Visits were scheduled to include at least one session per week but not to exceed three sessions over a single week. The physical therapists reviewed medical history and conducted an initial exam on each participant before initiating the standardised TE regimen to determine any potential needs for exercise protocol modification or contraindication. The primary goal of the TE programme was to increase lower extremity strength while secondarily addressing range of motion restrictions, as well as impaired balance. Lower extremity strengthening incorporated both open and closed chain exercises which were individually progressed for each participant using the daily adjusted progressive resistive exercise system. Procedural reliability of the intervention was maximised by 1) training sessions for the physical therapist to ensure all exercises are taught and progressed in the same manner, 2) conducting random patient chart reviews to determine all exercises were performed, and 3) evaluating the delivery of TE on a subset of patients at random time points using a rubric.. Indirectness: No indirectness (n=29) Intervention 3: No intervention - Additional treatment when compared to electrotherapy plus additional treatment. 10 sessions of therapeutic exercise (TE) over a 28 day period, which was directed by a licensed physical therapist at a single clinic. Visits were scheduled to include at least one session per week but not to exceed three sessions over a single week. The physical therapists reviewed medical history and conducted an initial exam on each participant before initiating the standardised TE regimen to determine any potential needs for exercise protocol modification or contraindication. The primary goal of the TE programme was to increase lower extremity strength while secondarily addressing range of motion restrictions, as well as impaired balance. Lower extremity strengthening incorporated both open and closed chain exercises which were individually progressed for each participant using the daily adjusted progressive resistive exercise system. Procedural reliability of the intervention was maximised by 1) training sessions for the physical therapist to ensure all

	exercises are taught and progressed in the same manner, 2) conducting random patient chart reviews to determine all exercises were performed, and 3) evaluating the delivery of TE on a subset of patients at random time points using a rubric.. Duration 4 weeks. Concurrent medication/care: Not reported. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC- pain subscale at 8 weeks; Group 1: mean 29.3 (SD 21.6); n=30, Group 2: mean 26.5 (SD 15.2); n=29; WOMAC- pain subscale 0-100 Top=High is poor outcome; Comments: Baseline values: TENS group: 43.8 (20.0), sham group: 42.7 (21.6), exercise group: 40.2 (15.4)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: gallbladder surgery (1), did not have time (1); Group 2 Number missing: 7, Reason: did not have time (4), kidney stone (1), unrelated fall (1), automobile accident (1)

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC- physical function subscale at 8 weeks; Group 1: mean 30.3 (SD 17.5); n=30, Group 2: mean 30.2 (SD 17); n=22; WOMAC- physical function subscale 0-100 Top=High is poor outcome; Comments: Baseline values: TENS group: 49.6 (16.4), sham group: 45.7 (12.1), exercise group: 48.7 (12.4)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: gallbladder surgery (1), did not have time (1); Group 2 Number missing: 7, Reason: did not have time (4), kidney stone (1), unrelated fall (1), automobile accident (1)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) versus ADDITIONAL TREATMENT WHEN COMPARED TO ELECTROTHERAPY PLUS ADDITIONAL TREATMENT

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC- pain subscale at 8 weeks; Group 1: mean 29.3 (SD 21.6); n=30, Group 2: mean 30.3 (SD 17.9); n=29; WOMAC- pain subscale 0-100 Top=High is poor outcome; Comments: Baseline values: TENS group: 43.8 (20.0), sham group: 42.7 (21.6), exercise group: 40.2 (15.4)
Risk of bias: All domain - Low, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: gallbladder surgery (1), did not have time (1); Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC- physical function subscale at 8 weeks; Group 1: mean 30.3 (SD 17.5); n=30, Group 2: mean 31.9 (SD 14.4); n=29; WOMAC- physical function subscale 0-100 Top=High is poor outcome; Comments: Baseline values: TENS group: 49.6 (16.4), sham group: 45.7 (12.1), exercise group: 48.7 (12.4)
Risk of bias: All domain - Low, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover -

Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: gallbladder surgery (1), did not have time (1); Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Pipitone 2001[179]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=69)
Countries and setting	Conducted in United Kingdom; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 6 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Radiographic evidence and symptoms of osteoarthritis (incompletely relieved by conventional treatments) as judged by the criteria of the American College of Rheumatology
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with osteoarthritis by symptomatic and radiographic evidence
Exclusion criteria	Pregnancy or lack of contraception use in women of childbearing age; use of pacemaker, insulin pump, or of any implanted electrical device; inflammatory joint disease; periarticular PAget's disease; uncontrolled or untreated gout; pseudogout; avascular necrosis and osteonecrosis; Charcot's arthropathy; acromegaly; clinically overt hypothyroidism or hyperthyroidism; haemochromatosis; Wilson's disease; ochronosis; osteopetrosis; Marfan's syndrome; Ehlers-Danlos syndrome; terminal illnesses/malignancies (except for in situ carcinoma and basal cell carcinoma); pain referred to the knee in the absence of local symptoms and signs; intra-articular glucocorticoid injection within one month of study entry; inability to understand/fill out the questionnaires, or to write
Recruitment/selection of patients	People referred to the Rheumatology Department of King's College Hospital
Age, gender and ethnicity	Age - Mean (range): 63.0 (40-84). Gender (M:F): 50:19. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years (Realistically a mix). 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Not stated Duration of symptoms (mean [range]): 72 (5.5-372) months
Indirectness of population	No indirectness
Interventions	(n=34) Intervention 1: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. Unipolar magnetic devices generating pulsed treatment. Pulses were selectable at three base frequencies (3Hz, 7.8Hz and 20Hz). They have a rise time of 1 microseconds, a decay time of 10 microseconds, a low magnetic output (<0.5

	gauss) and a range of activity of up to 30cm around the unit. People were instructed to use the devices at 7.8 Hz in the morning and afternoon and 3Hz in the evening. The device requires no wires or electrodes and only need to be held close to the area to be treated. A velcro band was used to hold the device in place.. Duration 6 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=35) Intervention 2: Sham electrotherapy. Sham electrotherapy using the same device but with a 9V battery, which forced it to switch off automatically after a 10 minute period. . Duration 6 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Study funded by industry (This study was supported by an educational grant from Snowden Healthcare)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: EuroQoL at 6 weeks; Group 1: mean 0.59 (SD 1.01); n=34, Group 2: mean 0.2 (SD 1.36); n=35; EQ-5D 0-100 Top=High is good outcome; Comments: Reported mean change and 95% confidence intervals. Reported active: 0.59 (0.25, 0.93). Reported sham: 0.20 (-0.25, 0.65).
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, disease duration, and baseline values of outcomes; Group 1 Number missing: 5, Reason: 39 were allocated at first.; Group 2 Number missing: 1, Reason: 36 were allocated at first.

Protocol outcome 2: Pain at </= 3 months
- Actual outcome: WOMAC pain at 6 weeks; Group 1: mean 0.88 (SD 2.62); n=34, Group 2: mean 0.49 (SD 3.83); n=35; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported mean change and 95% confidence intervals. Reported active: 0.88 (0.06, 1.82). Reported sham: 0.49 (-0.78, 1.76).
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, disease duration, and baseline values of outcomes; Group 1 Number missing: 5, Reason: 39 were allocated at first.; Group 2 Number missing: 1, Reason: 36 were allocated at first.

Protocol outcome 3: Physical function at </= 3 months
- Actual outcome: WOMAC disability at 6 weeks; Group 1: mean 3.62 (SD 9); n=34, Group 2: mean 0.26 (SD 10.7); n=35; WOMAC disability 0-68 Top=High is poor outcome; Comments: Reported mean change and 95% confidence intervals. Reported active: 3.62 (0.64, 6.69). Reported sham: 0.26 (-3.29, 3.80).
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, disease duration, and baseline values of outcomes; Group 1 Number missing: 5, Reason: 39 were allocated at first.; Group 2 Number missing: 1, Reason: 36 were allocated at first.

Protocol outcome 4: Mild adverse events at </= 3 months
- Actual outcome: Adverse events at 6 weeks; Group 1: 2/34, Group 2: 4/35; Comments: PSWT: Increased pain in one person, pain and numbness int he foot

and poor sleep quality in the other. Placebo: Pain in knee (2), paraesthesia of the right foot and exacerbation of pre-existent diverticulitis (1), tenderness in the sternoclavicular joint associated with local swelling, diagnosed as Tietze's syndrome (1) Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, sex, disease duration, and baseline values of outcomes; Group 1 Number missing: 5, Reason: 39 were allocated at first.; Group 2 Number missing: 1, Reason: 36 were allocated at first.	
Protocol outcomes not reported by the study	Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Sangtong 2019[190]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=148)
Countries and setting	Conducted in Thailand; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with symptomatic knee osteoarthritis fulfilling the American College of Rheumatology criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with symptomatic knee osteoarthritis: diagnosed according to the American College of Rheumatology; aged 50-85 years; numerical rating scale for knee pain of at least 5 out of 10; ability to walk
Exclusion criteria	Medical problems that influence pain scores of knee functions, including rheumatoid arthritis, gouty arthritis of the knee, chronic back pain or tendinitis of the knee; knee arthroplasty; cardiac pacemaker; history of receiving ultrasound therapy; history of intra-articular injection within the past 6 months; contraindications to ibuprofen
Recruitment/selection of patients	People attending the outpatient clinic of the Department of Rehabilitation Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand
Age, gender and ethnicity	Age - Mean (SD): 63.0 (7.8). Gender (M:F): 13:135. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Not stated / Unclear 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Not stated Duration of symptoms (median [range]): 12-24 (1-240)
Indirectness of population	No indirectness
Interventions	(n=74) Intervention 1: Non-invasive electrotherapy interventions - Combination therapy (e.g. ultrasound and interferential therapy). Ultrasound and TENS. People received therapeutic ultrasound (frequency 1MHz, power 1W/cm²) for 10 minutes during each weekday over a two-week period for a total of 10 days. The ultrasound probe was positioned around the medial aspect of the symptomatic knee or around the point of maximal tenderness using a stroking technique. People received ultrasound combined with transcutaneous electrical nerve stimulation (symmetrical biphasic waveform, frequency 32-50Hz, pulse width 80 microseconds) for the same

	amount of time and the same number of days. This single machine (ultrasound combined with TENS) delivers both types of therapy simultaneously for 10 minutes. The TENS electrode was placed over the quadriceps muscle at approximately 10cm above the tibio-femoral joint line. The anode and cathode electrodes were positioned medially and laterally, respectively. 10 sessions within 2 weeks.. Duration 2 weeks. Concurrent medication/care: People were asked to not accept pain medication or physical therapy from other clinics or hospitals for the duration of the study. People in both groups received informational brochures specific to knee osteoarthritis, including risk factors for osteoarthritis and how to properly use the affected knee during activities of daily living. Examples of provided information included reducing body weight, avoidance of knee flexion position >90 degrees, avoidance of unnecessary stair use and emphasis of the importance of knee strengthening exercises. People who were taking NSAIDs were asked to discontinue them one week before entering the study. People with intolerable pain were prescribed ibuprofen 1200mg/day as rescue medication for pain.. Indirectness: No indirectness (n=74) Intervention 2: Non-invasive electrotherapy interventions - Ultrasound. People received therapeutic ultrasound (frequency 1MHz, power 1W/cm²) for 10 minutes during each weekday over a two-week period for a total of 10 days. The ultrasound probe was positioned around the medial aspect of the symptomatic knee or around the point of maximal tenderness using a stroking technique. 10 sessions within 2 weeks.. Duration 2 weeks. Concurrent medication/care: People were asked to not accept pain medication or physical therapy from other clinics or hospitals for the duration of the study. People in both groups received informational brochures specific to knee osteoarthritis, including risk factors for osteoarthritis and how to properly use the affected knee during activities of daily living. Examples of provided information included reducing body weight, avoidance of knee flexion position >90 degrees, avoidance of unnecessary stair use and emphasis of the importance of knee strengthening exercises. People who were taking NSAIDs were asked to discontinue them one week before entering the study. People with intolerable pain were prescribed ibuprofen 1200mg/day as rescue medication for pain.. Indirectness: No indirectness
Funding	Academic or government funding (Funded by a grant from the Faculty of medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand (grant no. R015933009))
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINATION THERAPY (E.G. ULTRASOUND AND INTERFERENTIAL THERAPY) versus ULTRASOUND	

Protocol outcome 1: Pain at </= 3 months - Actual outcome: Total pain score (VAS) at 2 weeks; Group 1: mean -2.5 (SD 1.8); n=74, Group 2: mean -3 (SD 2); n=74; VAS 0-10 Top=High is poor outcome; Comments: Baseline combination: 5.8 (1.3). Baseline ultrasound: 5.9 (1.3). Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, body weight, BMI, regular use of pain medications, knee exercise, aerobic exercise, duration of knee pain, affected knee: unilateral, pain dimensions; Group 1 Number missing: 10, Reason: Lost to follow up (10) - 3 unable to contact, 7 inconvenient; Group 2 Number missing: 6, Reason: Lost to follow up (6) - 1 severe knee pain, 1 unable to contact, 4 inconvenient Protocol outcome 2: Mild adverse events at </= 3 months - Actual outcome: People with adverse events at 2 weeks; Group 1: 4/64, Group 2: 3/68; Comments: Study group: 4 people had joint swelling, control: 2 people had joint swelling, 1 had a rash Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, body weight, BMI, regular use of pain medications, knee exercise, aerobic exercise, duration of knee pain, affected knee: unilateral, pain dimensions; Group 1 Number missing: 10, Reason: Lost to follow up (10) - 3 unable to contact, 7 inconvenient; Group 2 Number missing: 6, Reason: Lost to follow up (6) - 1 severe knee pain, 1 unable to contact, 4 inconvenient	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Shen 2009[193]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in China; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis of osteoarthritis, radiographic evidence of at least one osteophyte at the tibiofemoral joint, Kellgren-Lawrence grade at least 2, moderate or greater clinically significant knee pain on most days during the previous month
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Male or female, 40 years or older with a diagnosis of osteoarthritis and willingness to sign the consent form for random assignment to either a treatment group or a placebo group
Exclusion criteria	The presence of serious medical conditions that precluded participation int he study; intra-articular corticosteroid or hyaluronate injections (as well as any knee surgeries or concomitant topical use of capsaicin cream) during the past 6 months; previous experience with drug tests; and any plans that would interfere with participation in the entire 4-week study
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 58.3 (7.4). Gender (M:F): 4:36. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade of at least 2 Duration of symptoms (mean [SD]): 5.2 (6.6) years
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. Laser treatment with the tip placed perpendicularly at acupuncture point Dubi (ST 35), which is located in the depression on the lateral side of the patella and the patellar ligament, on the affected knee or both knees if both were affected. Dubi or Xiyan ('eyes' of the knee) is commonly used in clinical trials as a major local point for treating knee-related disorders. The laser device was made to generate 065-0.66 micrometer red light

	transmitted by quartz-glass light fibers with an output power of 36mW, had strong penetrability, and can stimulated acupuncture. The carbon dioxide laser generates a 10.6 micrometer light transmitted by a silver halide light fiber with an output power of 200mW. The carbon dioxide laser was set to a pulse with a frequency of 40Hz and a duty factor of 50% to prevent burns. The laser tip irradiated the skin with a single beam 2mm in diameter to shield adjacent acupuncture points. A 2cm distance between the laser tip and the skin was maintained by a plastic tube 2cm in diameter and 2cm in length, mounted on the tip of the device. In the active group the device was activated for 20 minutes. Both groups were treated once every other day, or three times per week, for 4 weeks with total of 12 treatments.. Duration 4 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=20) Intervention 2: Sham electrotherapy. Sham laser, using the same device but deactivated. Duration 4 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Academic or government funding (The project was partially supported by NSFC (30572306), 973 Program of China (2005CB523306) and by Shanghai Science and Technology Developing Foundation (07DZ19722-2).)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 4 weeks; Group 1: mean 3.8 (SD 3.1); n=18, Group 2: mean 2.5 (SD 2.6); n=9; WOMAC 0-20 Top=High is poor outcome; Comments: Reports individual patient scores. Standard deviation calculated from this. A group (n=18): 1.6, 4.4, 1.6, 1.2, 5, 3.8, 9.2, 1.2, 3.6, 5.2, 7.2, 2, 3.2, 9.6, 1.2, 0, 0, 8. C group (n=9): 1.6, 2.8, 1.2, 6, 0.8, 7.6, 1.8, 0, 0.8
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, disease duration, gender and affected knee; Group 1 Number missing: 2, Reason: 1 lost to follow up ,1 felt treatment was ineffective; Group 2 Number missing: 11, Reason: 4 too busy, 4 felt treatment was ineffective, 3 lost to follow up

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC physical function at 4 weeks; Group 1: mean 13.8 (SD 11.2); n=18, Group 2: mean 10 (SD 6.8); n=9; WOMAC physical function 0-68 Top=High is poor outcome; Comments: Reports individual patient scores. Standard deviation calculated from this. A group (n=18): 10.8, 20.8, 8.8, 3.2, 11.8, 19.8, 37.2, 0, 6.4, 30.8, 15.2, 8.4, 10.8, 26.0, 4.4, 2.4, 2.0, 30.0. C group (n=9): 10.8, 17.2, 3.2, 18.2, 4.8, 15.2, 15.0, 0, 5.2.
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, disease duration, gender and affected knee; Group 1 Number missing: 2, Reason: 1 lost to follow up ,1 felt treatment was ineffective; Group 2 Number missing: 11, Reason: 4 too busy, 4 felt treatment was ineffective, 3 lost to follow up

Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Tascioglu 2010[205]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=90)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with idiopathic knee osteoarthritis according to the American College of Rheumatology criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Ambulant people, between the ages of 54 and 70 years, who had idiopathic knee osteoarthritis who had been symptomatic for at least 3 years and had grade 2-3 bilateral knee osteoarthritis confirmed radiologically according to the Kellgren-Lawrence grading system
Exclusion criteria	Kellgren Lawrence grade 1 and 4 radiological changes; knee joint disease other than osteoarthritis; osteoarthritis of the hip joint; osteoarthritis involvement of the foot joints; serious concomitant systemic diseases; intra-articular fluid effusion; any contraindication for physical therapy; lower limb arthroplasty; previous physical therapy and intra-articular corticosteroid or hyaluronic acid injections during the last 6 months
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 60.5 (3.2). Gender (M:F): 31:59. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 2-3, median grade 2 Duration of symptoms (mean [SD]): 6.5 (1.8) years
Indirectness of population	No indirectness
Interventions	(n=60) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. Continuous or pulsed ultrasonic waves. Continuous ultrasonic waves of 1MHz frequency and 2W/cm² power applied with a 5cm diameter applicator for 5 minutes per session. The people were in a supine position and an acoustic gel that did not contain any pharmacologically active substance was applied. Ultrasound was then applied to the superomedial and lateral parts of the knee in circular movements with the probe at

	right angles to ensure maximum absorption of the energy. The pulsed ultrasound group, the same equipment was set at a frequency of 1MHz and a power of 2W/cm² and a pulsed mode duty cycle of 1:4. The duration of ultrasound applied and the posture of the person treated were as described for the continuous ultrasound group. All treatments were applied once a day, 5 days a week for 2 weeks. Duration 2 weeks. Concurrent medication/care: People were not allowed to use any NSAIDs or analgesics 10 days prior to and throughout the study. Indirectness: No indirectness Comments: The two groups were combined due to class effect as agreed in the protocol (n=30) Intervention 2: Sham electrotherapy. Sham ultrasound group, where the same device was used and seemed to be working, but did not deliver any output. The treatment was applied in the same way otherwise.. Duration 2 weeks. Concurrent medication/care: People were not allowed to use any NSAIDs or analgesics 10 days prior to and throughout the study. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: VAS at 2 weeks; Group 1: mean 5.24 (SD 1.81); n=55, Group 2: mean 6.67 (SD 1.78); n=27; VAS 0-10 Top=High is poor outcome; Comments: Reported continuous: 5.22 (1.70). Reported pulsed: 5.25 (1.90). Baseline continuous: 6.67 (1.41). Baseline pulsed: 6.89 (1.39). Baseline placebo: 7.26 (1.46).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, disease duration, body mass index, gender, Kellgren-Lawrence radiological grade; Group 1 Number missing: 5, Reason: 3 people in the continuous group and 2 people in the pulsed group did not complete the study. 3 of these were due to intolerable pain requiring analgesia, 2 due to not regular attendance to the treatment.; Group 2 Number missing: 3, Reason: 3 people withdrew due to intolerable pain requiring analgesia

Protocol outcome 2: Mild adverse events at </= 3 months
- Actual outcome: Systemic or local side effects at 2 weeks; Group 1: 0/60, Group 2: 0/30
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, disease duration, body mass index, gender, Kellgren-Lawrence radiological grade; Group 1 Number missing: 5, Reason: 3 people in the continuous group and 2 people in the pulsed group did not complete the study. 3 of these were due to intolerable pain requiring analgesia, 2 due to not regular attendance to the treatment.; Group 2 Number missing: 3, Reason: 3 people withdrew due to intolerable pain requiring analgesia

Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at >

	3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Thamsborg 2005[208]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=83)
Countries and setting	Conducted in Denmark; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 6 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Painful knee osteoarthritis of the femorotibial compartment fulfilling the combined clinical and radiological criteria of the American College of Rheumatology
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People older than 45 years with painful knee osteoarthritis of the femorotibial compartment fulfilling the combined clinical and radiological criteria of the American College of Rheumatology
Exclusion criteria	Inflammatory joint disease; acromegaly; Charcot's arthropathy; haemochromatosis; Wilson's disease; ochronosis; terminal illnesses/malignancies; pregnancy or lack of contraception use in women of childbearing age; use of pacemaker or any implanted electrical device; if they were unable to understand/fill out the questionnaires; had received intra-articular glucocorticoid or hyaluronic acid injection 1 month prior to study entry; had hip and/or lumbary spine osteoarthritis with referred pain to the study knee
Recruitment/selection of patients	People recruited from the outpatient clinic at the Department of Rheumatology, Copenhagen University Hospital in Glostrup
Age, gender and ethnicity	Age - Mean (SD): 60.0 (8.7). Gender (M:F): 39:45. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Not stated / Unclear 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Not stated Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=45) Intervention 1: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. Two sets of two adjacent coils placed on the medial and lateral regions of the study knee, resepctively, with the interspace between the coils being at the level of the joint line. The coils were placed on an insulating bandage of 3-5mm thickness that

	could be tightened by use of Velcro material. The coils were constructed to ensure a fast rise time and fast declining phase for current. The use of adjacent coils creates an amplified and focused electromagnetic field. A pulse generator from Biofields Aps, Copenhagen, Denmark was used that yields +/-50V in 50Hz pulses changing voltage in 3ms intervals. This set up results in a maximal electrical gradient sensed by charged particles in tissue of 1-100mV/cm depending on the distance from the coils. . Duration 6 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=45) Intervention 2: Sham electrotherapy. Sham where the same coil is used but a DC current is applied leading to a constant magnetic field rather than a pulsed field. Duration 6 weeks. Concurrent medication/care: No additional information. Indirectness: Serious indirectness; Indirectness comment: The sham intervention sounds like a possible active intervention (still applying a magnetic field)
Funding	Academic or government funding (Economical support from IMK Amene Fond and from Kobenhavns Amts Erhvervskontor)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 12 weeks; Group 1: mean 11.4 (SD 3.69); n=42, Group 2: mean 12.24 (SD 4.03); n=41; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reports final value and standard error. Reported PEMF: 11.40 (0.57). Reported placebo: 12.24 (0.63). Baseline PEMF: 13.15 (0.57). Baseline sham: 14.49 (0.54).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, BMI, gender, disease duration, Kellgren and Lawrence score, analgesic medication and baseline values of outcomes; Group 1 Number missing: 3, Reason: Originally 45 people, 3 were lost to follow up; Group 2 Number missing: 4, Reason: Originally 45 people, 4 were lost to follow up

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC ADL at 12 weeks; Group 1: mean 37.89 (SD 13.87); n=42, Group 2: mean 41.37 (SD 14.54); n=41; WOMAC ADL 0-68 Top=High is poor outcome; Comments: Reports final value and standard error. Reported PEMF: 37.89 (2.14). Reported placebo: 41.37 (2.27). Baseline PEMF: 43.83 (1.93). Baseline sham: 46.49 (2.21).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, BMI, gender, disease duration, Kellgren and Lawrence score, analgesic medication and baseline values of outcomes; Group 1 Number missing: 3, Reason: Originally 45 people, 3 were lost to follow up; Group 2 Number missing: 4, Reason: Originally 45 people, 4 were lost to follow up

Protocol outcome 3: Mild adverse events at </= 3 months

- Actual outcome: Grumbling or throbbing sensation, warming sensation, aggravation of the osteoarthritic pain in the study knee at 12 weeks; Group 1: 12/42, Group 2: 6/41; Comments: PSWT: Grumbling or throbbing sensation = 4, warming sensation = 6, aggravation of the osteoarthritic pain in the study knee = 2. Sham: Grumbling or throbbing sensation = 4, warming sensation = 1, aggravation of the osteoarthritic pain in the study knee = 1 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, BMI, gender, disease duration, Kellgren and Lawrence score, analgesic medication and baseline values of outcomes; Group 1 Number missing: 3, Reason: Originally 45 people, 3 were lost to follow up; Group 2 Number missing: 4, Reason: Originally 45 people, 4 were lost to follow up Protocol outcome 4: Moderate/major adverse events at </= 3 months - Actual outcome: Serious adverse events at 12 weeks; Group 1: 0/42, Group 2: 0/41 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports age, BMI, gender, disease duration, Kellgren and Lawrence score, analgesic medication and baseline values of outcomes; Group 1 Number missing: 3, Reason: Originally 45 people, 3 were lost to follow up; Group 2 Number missing: 4, Reason: Originally 45 people, 4 were lost to follow up	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at > 3 months

Study	Trock 1993[211]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=27)
Countries and setting	Conducted in USA; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 1 month
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis of osteoarthritis according to criteria by Altman, including radiographic evidence for all but one. Types of osteoarthritis included knee, the first carpometacarpal or interphalangeal group of joints in the hand and posttraumatic osteoarthritis of the ankle
Stratum	Overall
Subgroup analysis within study	Not applicable:
Inclusion criteria	People older than 18 years of age with persistent arthritic symptoms of at least one year duration, incompletely relieved by conventional treatment including nonsteroidal antiinflammatory drugs (NSAID), other analgesics and physical therapy modalities.
Exclusion criteria	People receiving a new intervention, including NSAIDs, within one month. People with isolated metacarpal phalangeal joint or single proximal interphalangeal joints, or osteoarthritis of the spine. Use of a cardiac pacemaker. Presence of any serious, unstable medical illness.
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Other: Not stated. Gender (M:F): Not stated. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): Not stated / Unclear 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Systematic review: mixed (Knee, finger and ankle).
Extra comments	Severity: Not stated Duration of symptoms: At least one year duration
Indirectness of population	No indirectness
Interventions	(n=15) Intervention 1: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. Pulsed electromagnetic field therapy with a device that produces an extremely low frequency (less than 30 Hz), varying, pulsed electromagnetic field averaging 10-20 gauss of magnetic energy at a coil current of up to 2 amperes drawn from a power source of 120 volts AC. The pulse phase duration was 67ms, including 15 micropulses with a pause duration of 0.1s. The wave duration varied according to

	the frequency used. The patients rested the joint being treated on a pillow, encircled by the air coil which did not contact the skin. Treatments were given for 30 minutes, 3-5 sessions were given each week for a total of 18 treatments. The entire treatment extended to one month.. Duration 1 month. Concurrent medication/care: People were allowed to continue any treatment on a stable dose at the start of the trial. Indirectness: No indirectness (n=12) Intervention 2: Sham electrotherapy. The same device switched off. Duration 1 month. Concurrent medication/care: People were allowed to continue any treatment on a stable dose at the start of the trial. Indirectness: No indirectness
Funding	Study funded by industry (Funded by Bio-magnetic Therapy Systems, Inc.)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: Overall severity of pain at 2 months (1 month post-treatment); Group 1: mean 3.55 (SD 3.42); n=10, Group 2: mean 7.1 (SD 1.11); n=10; VAS 0-10 Top=High is poor outcome; Comments: Reported mean (standard error). Reported PEMF: 3.55 (1.08). Reported placebo: 7.10 (0.35). Baseline PEMF: 7.65 (0.6405). Baseline sham: 8.07 (0.75). Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported baseline values of outcomes only; Group 1 Number missing: 5, Reason: 1 withdrew before the study (requested unblinded active treatment due to transportation difficulties). 4 did not appear for evaluation (reasons not given).; Group 2 Number missing: 2, Reason: 1 withdrew before the study (requested unblinded active treatment due to hospitalisation due to a hernia). 1 did not appear for evaluation due to hospitalisation for community acquired pneumonia.	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Ulus 2012[213]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=42)
Countries and setting	Conducted in Turkey; Setting: Inpatients
Line of therapy	Unclear
Duration of study	Intervention + follow up: 3 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with bilateral knee osteoarthritis diagnosed in accordance with the American College of Rheumatology criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Inpatients with bilateral knee osteoarthritis diagnosed in accordance with the American College of Rheumatology criteria
Exclusion criteria	Any contraindication for physical therapy; previous history of knee surgery; lower extremity arthroplasty; local dermatological problems; any systemic illness or abnormal laboratory test results; had been on any physiotherapy program or received intra-articular injection of hyaluronic acid or steroids or ultrasound therapy in the last 6 months; had symptoms and signs of acute synovitis
Recruitment/selection of patients	The trial was conducted with inpatients at the Department of Physical Medicine and Rehabilitation, Medical Faculty of Ondokuz Mayis University, Samsun, Turkey
Age, gender and ethnicity	Age - Mean (SD): 60.5 (9.5). Gender (M:F): 6:34. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren and Lawrence grade 2-3, median grade 3 Duration of symptoms (mean [SD]): 106.4 (105.1) months
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. Therapeutic ultrasound using a Sonopuls 434 ultrasound machine. Continuous ultrasonic waves of 1 MHz frequency and intensity of 1W/cm² applied with a 5cm diameter applicator for 10 minutes per session. The person was kept in a supine position with both knees fully extended while ultrasound was applied around the knee joint with full contact for 10 minutes. Aqueous gel was used as a coupling medium in circular movements with the probe at right angles during ultrasound application. Treatment 5 times weekly for 3 weeks.. Duration 3 weeks. Concurrent

	medication/care: All people received 20 minutes of hot packs, 10 minutes of interferential current and 15 minutes of quadriceps isometric exercise of both knees. Non-steroid anti-inflammatory drugs and antidepressant drugs were not permitted throughout the physical therapy sessions; analgesics whenever needed and other medication for comorbid diseases were permitted during the study period.. Indirectness: No indirectness (n=20) Intervention 2: Sham electrotherapy. Sham using a device which when turned on lit the dials but allowed no energy to be delivered to the tissue. The applicator was also disconnected from the back of the machine.. Duration 3 weeks. Concurrent medication/care: All people received 20 minutes of hot packs, 10 minutes of interferential current and 15 minutes of quadriceps isometric exercise of both knees. Non-steroid anti-inflammatory drugs and antidepressant drugs were not permitted throughout the physical therapy sessions; analgesics whenever needed and other medication for comorbid diseases were permitted during the study period.. Indirectness: No indirectness
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 3 weeks; Group 1: mean -6.5 (SD 3.25); n=20, Group 2: mean -4.57 (SD 3.16); n=20; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline ultrasound: 15.70 (3.35). Baseline sham: 14.65 (3.06).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, weight, BMI, duration of symptoms, occupation, education, severity on radiograph and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function at 3 weeks; Group 1: mean -18.85 (SD 9.21); n=20, Group 2: mean -15.05 (SD 15.49); n=20; WOMAC function 0-68 Top=High is poor outcome; Comments: Baseline ultrasound: 47.30 (10.91). Baseline sham: 47.60 (10.97).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, weight, BMI, duration of symptoms, occupation, education, severity on radiograph and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: Psychological distress at </= 3 months
- Actual outcome: HADS anxiety at 3 weeks; Group 1: mean -2.1 (SD 2.77); n=20, Group 2: mean -1.65 (SD 1.92); n=20; HADS anxiety 0-21 Top=High is poor outcome; Comments: Baseline ultrasound: 8.50 (3.84). Baseline sham: 9.05 (5.15).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover -

Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, weight, BMI, duration of symptoms, occupation, education, severity on radiograph and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0 - Actual outcome: HADS depression at 3 weeks; Group 1: mean -1.65 (SD 2.77); n=20, Group 2: mean -1.35 (SD 2.15); n=20; HADS depression 0-21 Top=High is poor outcome; Comments: Baseline ultrasound: 7.20 (4.87). Baseline sham: 7.60 (5.95). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, height, weight, BMI, duration of symptoms, occupation, education, severity on radiograph and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	**Wang 2020[217]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=72)
Countries and setting	Conducted in China; Setting: Outpatient follow up
Line of therapy	5th line
Duration of study	Intervention + follow up: 10 weeks
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis: Chronic knee pain (for more than 3 months) with a duration of morning knee stiffness of less than 30 minutes
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Older than 50 years; had a history of knee pain lasting more than 3 months; had knee pain on most days of the month prior to the study; had an average intensity of knee pain of at least 4 on the numeric rating scale in the month prior to the study; had a duration of morning knee stiffness of less than 30 minutes; had received no alternative therapy, such as ESWT, in the month prior to the study
Exclusion criteria	Were pregnant; had a history of spinal stenosis; had a history of knee surgery; had a history of or were currently suffering from tumours or neurological diseases; had arthritis from secondary causes; had skin disease; had cancer; had a severe mental disorder; had a contraindication to use of magnetic-resonance imaging or radiography

Recruitment/selection of patients	People from two hospitals, the Affiliated Hongqi Hospital of Mudanjiang Medical University and the People's Hospital of Yan'an from January 2016 to April 2017
Age, gender and ethnicity	Age - Mean (SD): 63.9 (10.9). Gender (M:F): 45:27. Ethnicity: not reported
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis without imaging 3. Multimorbidity : Not applicable 4. Site of osteoarthritis: Knee
Extra comments	Severity: Not stated/unclear Duration of symptoms (mean [SD]): 7.9 (3.7) years
Indirectness of population	Serious indirectness: Unclear if people had osteoarthritis
Interventions	(n=36) Intervention 1: Non-invasive electrotherapy interventions - Extracorporeal shockwave therapy. Extracorporeal shockwave therapy using a shockwave of 0.25 mJ/mm² for 4000 pulses in total at a frequency of 15 Hz/s. Therapy three times weekly for a total of 10 weeks.. Duration 10 weeks. Concurrent medication/care: No additional information.. Indirectness: No indirectness (n=36) Intervention 2: Sham electrotherapy. Placebo extracorporeal shockwave therapy using a shockwave of 0 mJ/mm². The probe emitted the same noises as the therapy probe. Therapy three times weekly for a total of 10 weeks. Duration 10 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EXTRACORPOREAL SHOCKWAVE THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 10 weeks; Group 1: mean 2.1 (SD 1); n=36, Group 2: mean 5.6 (SD 2.4); n=36; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline ESWT: 7.8 (1.9). Baseline sham: 7.7 (2.0).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, BMI, duration of symptoms, previous treatments and baseline values of outcomes; Group 1 Number missing: 3, Reason: Consent withdrawn = 2, lost to follow-up = 1; Group 2 Number missing: 5, Reason: Consent withdrawn = 1, lost to follow-up = 2, lack of effect = 2

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function at 10 weeks; Group 1: mean 10.1 (SD 4.9); n=36, Group 2: mean 19.4 (SD 8.8); n=36; WOMAC function 0-68 Top=High is poor outcome; Comments: Baseline ESWT: 25.2 (8.6). Baseline sham: 25.6 (9.3).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, BMI, duration of symptoms, previous treatments and baseline values of outcomes; Group 1 Number missing: 3, Reason: Consent withdrawn = 2, lost to follow-up = 1; Group 2 Number missing: 5, Reason: Consent withdrawn = 1, lost to follow-up = 2, lack of effect = 2

Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Wuschech 2015[220]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=57)
Countries and setting	Conducted in Germany; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 18 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Osteoarthritis in their knee joint according to the American College of Rheumatology criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with osteoarthritis in their knee joint who were willing to take part in the study
Exclusion criteria	In case of pregnancy or possibility thereof; infection in the area treated; presence of general inflammatory processes in area to be treated; not considered to be due to an inflammatory phase of osteoarthritis; people susceptible to thrombosis or spasms
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Mean (SD): 61.1 (12.0). Gender (M:F): 37:20. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Not stated / Unclear 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: American College of Rheumatology severity level (mean [SD]): 2.8 (0.8) Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=44) Intervention 1: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. Pulsed electromagnetic field therapy. Magcell Arthro treatment with a hand-held battery-driven device. The disc area of 28cm² was magnetically active and fully available for treatment. Disc rotation is varied in 2Hz steps to produce frequencies between 4 and 12Hz. By rotating the disc via a direct current motor controlled by a microcontroller, a nearly sinusoidal magnetic field is generated with a magnetic flux density of 420mT (peak-to-peak) on the device surface. At 1cm distance, still 105mT flux density prevails. At 2cm distance, the flux density is 40mT with a corresponding current density of roughly 43mA/m². Treatment took place twice daily for 5 minutes for all. Upon pressing the start button the device ran and stopped automatically after 2.5 minutes (application 2 times consecutively). After the first treatment, the area was changed and the device started for a second time. Treatment areas included anterior

	surface of the joint (cartilage at the top of the lateral femur [Epicondylus lateralis femoris]) and the inferior surface of the joint (directly below the femur cartilage [Epicondylus medialis femoris]).. Duration 18 days. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=13) Intervention 2: Sham electrotherapy. People were given a placebo device. It was identical but the device features a non-magnetic material instead of the four 45 degree segments in a magnetic material.. Duration 18 days. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 18 days; Group 1: mean -5.7 (SD 5.9); n=44, Group 2: mean 1.3 (SD 3.1); n=13; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline active: 14.5 (8.6). Baseline sham: 9.8 (8.2).
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Baseline value for pain is different; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC daily activities at 18 days; Group 1: mean -16.4 (SD 16.1); n=42, Group 2: mean -1.8 (SD 7.8); n=13; WOMAC daily activities 0-68 Top=High is poor outcome; Comments: Baseline active: 47.1 (21.6). Baseline sham: 43.5 (26.8).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Baseline value for pain is different. But the value for function is not.; Group 1 Number missing: 2, Reason: Reason not given; Group 2 Number missing: 0

Protocol outcome 3: Mild adverse events at </= 3 months
- Actual outcome: Undesirable occurrences or side effects at 18 days; Group 1: 0/44, Group 2: 0/13
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Baseline value for pain is different. But the value for function is not.; Group 1 Number missing: 2, Reason: Reason not given; Group 2 Number missing: 0

Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months;

	Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Yegin 2017[224]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=62)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 2 weeks (additional follow up for 1 month)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Primary knee osteoarthritis according to the American Rheumatology Association with a minimum of stage 2 knee osteoarthritis on x-rays taken during the last 12 months according to the Kellgren Lawrence grading scale
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnosed with primary knee osteoarthritis; to be between 40 and 70 years of age; to have evidence of minimum stage 2 knee osteoarthritis in the x-rays taken during the last 12 months according to the Kellgren-Lawrence grading scale
Exclusion criteria	Severe knee trauma in the last 6 months; previous surgical operation on the knee; administration of intra-articular steroid and/or hyaluronate injection in the last 6 months; previous surgical operation on the knee; administration of intra-articular steroid and/or hyaluronate injection int he last 6 months; physical therapy for knee in the last 3 months; existence of acute synovitis; neurologic deficit in lower extremity; inflammatory disease; impaired health condition (cardiac failure, advanced asthma, cancer)
Recruitment/selection of patients	People admitted to the Physical Medicine and Rehabilitation Outpatient Clinic
Age, gender and ethnicity	Age - Range: 40-70 (though not stated explicitly, this was a part of the inclusion criteria). Gender (M:F): 11:51. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: At least Kellgren Lawrence grade 2 Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=32) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. Ultrasound applied to both knees for a total of 10 sessions for 2 weeks using a BTL-4000 Premium Ultrasound device with a 5cm² 1MHz probe. Ultrasound was applied

	continuously in a circular movement (1W/cm², 1MHz) using gel for a total of 8 min to each knee while people were in the supine position and their knees were flexed at 90 degrees. The application was performed on the superomedial and lateral knee regions, covering an area of 25cm². Duration 2 weeks. Concurrent medication/care: The use of analgesics except paracetamol was avoided during the treatment and until the end of the first month following completion of ultrasound treatment. Indirectness: No indirectness (n=33) Intervention 2: Sham electrotherapy. Sham ultrasound with the device switched off but otherwise completing the same procedure. Duration 2 weeks. Concurrent medication/care: The use of analgesics except paracetamol was avoided during the treatment and until the end of the first month following completion of ultrasound treatment. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus SHAM ELECTROTHERAPY

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: SF-36 physical component score at 6 weeks; Group 1: mean 7.9 (SD 9.74); n=30, Group 2: mean 6.1 (SD 9.2); n=32; SF-36 physical component score 0-100 Top=High is good outcome; Comments: Baseline ultrasound: 35.1 (10.56). Baseline sham: 33.9 (6.84).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports baseline values of outcomes only; Group 1 Number missing: 2, Reason: 2 excluded as they failed to come to the post-treatment evaluation; Group 2 Number missing: 1, Reason: 1 excluded as they left the treatment
- Actual outcome: SF-36 mental component score at 6 weeks; Group 1: mean -0.3 (SD 12.78); n=30, Group 2: mean -0.1 (SD 12.14); n=32; SF-36 mental component score 0-100 Top=High is good outcome; Comments: Baseline ultrasound: 45.5 (13.38). Baseline sham: 46.8 (15.21).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports baseline values of outcomes only; Group 1 Number missing: 2, Reason: 2 excluded as they failed to come to the post-treatment evaluation; Group 2 Number missing: 1, Reason: 1 excluded as they left the treatment

Protocol outcome 2: Pain at </= 3 months
- Actual outcome: WOMAC pain at 6 weeks; Group 1: mean -2.9 (SD 3.45); n=30, Group 2: mean -2.6 (SD 4.68); n=32; WOMAC pain 0-20 Top=High is poor outcome; Comments: Baseline ultrasound: 8.5 (3.56). Baseline sham: 9.3 (2.92).
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports baseline values of outcomes only; Group 1 Number missing: 2, Reason: 2 excluded as they failed to come to the post-treatment evaluation; Group 2 Number missing: 1, Reason: 1 excluded as they left the treatment

Protocol outcome 3: Physical function at </= 3 months - Actual outcome: WOMAC physical function at 6 weeks; Group 1: mean -9.3 (SD 10.82); n=30, Group 2: mean -6.5 (SD 14.42); n=32; WOMAC physical function 0-68 Top=High is poor outcome; Comments: Baseline ultrasound: 27.3 (12.36). Baseline sham: 27.7 (10.44). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reports baseline values of outcomes only; Group 1 Number missing: 2, Reason: 2 excluded as they failed to come to the post-treatment evaluation; Group 2 Number missing: 1, Reason: 1 excluded as they left the treatment	
Protocol outcomes not reported by the study	Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Yildiz 2015[225]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=90)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 2 weeks (and an additional 2 months of follow up)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Bilateral stage 2-3 primary knee osteoarthritis according to Kellgren-Lawrence criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with bilateral stage 2 and 3 primary knee osteoarthritis according to the Kellgren-Lawrence criteria
Exclusion criteria	People with secondary knee osteoarthritis; active synovitis; symptomatic hip, foot and ankle disease; neurologic deficits in a lower extremity; recent knee trauma; history of intraarticular steroid and/or hyaluronate injection in the past 6 months; history of hyaluronate injection in the past 6 months; history of knee surgery or arthroscopy to the knee joint in the last year; and application of physical treatment to the knee in the last 3 months
Recruitment/selection of patients	People consulting the outpatient clinic
Age, gender and ethnicity	Age - Mean (SD): 56.2 (6.9). Gender (M:F): 15:75. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 2-3, median grade 3 Duration of symptoms (mean [SD]): 4.0 (3.2) years
Indirectness of population	No indirectness
Interventions	(n=60) Intervention 1: Non-invasive electrotherapy interventions - Ultrasound. Continuous and pulsed ultrasound. Continuous ultrasound (frequency 1 MHz, intensity: 1.5W/cm², duration: 5 min) and pulsed ultrasound (frequency 1 MHz, intensity: 1.5W/cm², mode: 1/5, duration: 5 min) applied to the anterior, medial and lateral areas of the knee bilateral. All treatments were applied for 5 days a week for 2 weeks by the same 5cm² head ultrasound device and physiotherapist.. Duration 2 weeks. Concurrent medication/care: All people were given a home exercise program and were instructed to perform exercises, including quadriceps isometric exercises

	and strengthening exercises, for 10 repetitions of the set, 3 times a day for 8 weeks from the beginning of the treatment. People were informed that they could take 500mg of paracetamol up to 3 times a day in case of pain during treatment.. Indirectness: No indirectness Comments: The two groups were combined due to class effect as agreed in the protocol (n=30) Intervention 2: Sham electrotherapy. Sham ultrasound being the same as the ultrasound group except that the power switch was off. Duration 2 weeks. Concurrent medication/care: All people were given a home exercise program and were instructed to perform exercises, including quadriceps isometric exercises and strengthening exercises, for 10 repetitions of the set, 3 times a day for 8 weeks from the beginning of the treatment. People were informed that they could take 500mg of paracetamol up to 3 times a day in case of pain during treatment.. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRASOUND versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: VAS movement at 10 weeks; Group 1: mean 3.87 (SD 2.58); n=60, Group 2: mean 7.2 (SD 2.66); n=30; VAS movement 0-10 Top=High is poor outcome; Comments: Reported continuous: 3.90 (2.54). Reported pulsed: 3.83 (2.61). Baseline continuous: 8.97 (1.45). Baseline pulsed: 8.60 (1.61). Baseline placebo: 8.93 (1.44). Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, duration, BMI, sex, Kellgren-Lawrence stage and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 2: Mild adverse events at </= 3 months - Actual outcome: Side effects or complications at 10 weeks; Group 1: 0/60, Group 2: 0/30 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, duration, BMI, sex, Kellgren-Lawrence stage and baseline values of outcomes; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Yurtkuran 2007[229]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=55)
Countries and setting	Conducted in Turkey; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 12 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with knee osteoarthritis diagnosed according to the American College of Rheumatology criteria, with Kellgren Lawrence grade 2-3 knee osteoarthritis and an average pain intensity of 40 or more on a 100mm visual analogue scale for the last month before baseline assessment
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with knee osteoarthritis
Exclusion criteria	People who had knee surgery; serious valgus or varus deformity; who had hormonal ,metabolic or systemic rheumatologic problems leading to secondary knee osteoarthritis; physiotherapy in the last 6 months; local oral analgesic or nonsteroidal anti-inflammatory drug use in the previous 4 weeks or people having a systemic disease (cardiac cerebrovascular pulmonary system or malignancy) that contraindicated to physiotherapy and exercise
Recruitment/selection of patients	Recruitment attempts were made by calling people from the Ataturk Rehabilitation and Rheumatology Center outpatient department
Age, gender and ethnicity	Age - Mean (SD): 52.6 (7.0). Gender (M:F): 2:53. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 2-3 Duration of symptoms (mean [SD]): 64.0 (55.0) months.
Indirectness of population	No indirectness
Interventions	(n=28) Intervention 1: Non-invasive electrotherapy interventions - Laser therapy. Low level laser therapy. Performed for 20 minutes per day and 5 days per week (total duration of therapy was 10 days). Using infrared 27 GaAs diode laser instrument, the laser used in the intervention group had an output power of 4mW, 10mW/cm² power density, 0.4cm² spot size, 120s treatment time and 0.48J dose per session. The irradiation was pulsed (duration of 1 pulse was 200nanosecond), and only one point

	was treated with contact application treatment. The treatment was applied to the medial side of the knee to the acupuncture point (Sp9) on the sural nerve, which is associated with knee pain. . Duration 2 weeks. Concurrent medication/care: All people received exercise, consisting of 10 sets of isometric contraction to quadriceps muscle and active range of motion exercises (20 repetitions) for knee. They were instructed not to use any analgesic or non-steroidal anti-inflammatory drugs during the follow-up period.. Indirectness: No indirectness (n=27) Intervention 2: Sham electrotherapy. Sham acupuncture 98same device, voltage applied to the area was 0J/cm². Duration 2 weeks. Concurrent medication/care: All people received exercise, consisting of 10 sets of isometric contraction to quadriceps muscle and active range of motion exercises (20 repetitions) for knee. They were instructed not to use any analgesic or non-steroidal anti-inflammatory drugs during the follow-up period.. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Health-related quality of life at </= 3 months
- Actual outcome: Nottingham Health Profile at 12 weeks; Group 1: mean 7.58 (SD 5.41); n=28, Group 2: mean 6.44 (SD 6.27); n=27; Nottingham Health Profile 0-38 Top=High is good outcome; Comments: Baseline laser: 8.79 (3.77). Baseline sham: 8.06 (4.48).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Baseline values for WOMAC pain and physical function were different at baseline; Group 1 Number missing: 1; Group 2 Number missing: 2

Protocol outcome 2: Pain at </= 3 months
- Actual outcome: WOMAC total pain score at 12 weeks; Group 1: mean 13.47 (SD 5.84); n=28, Group 2: mean 11.5 (SD 5.99); n=27; WOMAC 0-20 Top=High is poor outcome; Comments: Baseline laser: 13.65 (4.77). Baseline sham: 11.63 (4.87).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Baseline values for WOMAC pain and physical function were different at baseline; Group 1 Number missing: 1; Group 2 Number missing: 2

Protocol outcome 3: Physical function at </= 3 months
- Actual outcome: WOMAC total physical function score at 12 weeks; Group 1: mean 44.24 (SD 15.83); n=28, Group 2: mean 35.25 (SD 16.64); n=27; WOMAC 0-68 Top=High is poor outcome; Comments: Baseline laser: 47.53 (12.85). Baseline sham: 35.31 (13.75).
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Baseline values for WOMAC pain and physical function were different at baseline; Group 1 Number missing: 1; Group 2 Number missing: 2

Protocol outcomes not reported by the study	Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	**ChiCTR2,0000030371 trial: Zhang 2021[236]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=89)
Countries and setting	Conducted in China; Setting: Conducted at the outpatient rehabilitation medicine department of the Aerospace Center Hospital, Beijing, China.
Line of therapy	Adjunctive to current care
Duration of study	Follow up (post intervention): 4 sessions of therapy, one week apart, plus 4 week follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosed by 2 expert physicians according to ACR criteria.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Age >45 years,; presence of unilateral knee joint pain unresponsive to conventional treatments for at least 3 months; K-L grade II/ III; and written informed consent to participate in the study.
Exclusion criteria	Bilateral knee joint symptoms; received ESWT in the past; surgery in the involved knee joint or received an intra-articular injection in the preceding 6 months; secondary OA of the knee joint (inflammatory or metabolic); contraindication for ESWT; and severe primary cardiovascular disease, lung disease or other serious diseases that affect survival.
Recruitment/selection of patients	Not reported.
Age, gender and ethnicity	Age - Mean (SD): LD/2000 group: 60.84 (8.36), LD/4000 group: 62.70 (7.50), HD/2000 group: 58.21 (9.47), HD/4000 group: 63.65 (6.94), control group: 61.5 (5.43). Gender (M:F): 36M/53F. Ethnicity: Not reported
Further population details	1. Age (≤/> 75 years): Not stated / Unclear 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity (baseline VAS): LD/2000 group: 5.17(1.17), LD/4000 group: 5.33(1.51), HD/2000 group: 5.6(1.14), HD/4000 group: 5.8(1.79), control group: 5.26(1.66)

	Duration (months): LD/2000 group: 17.15 (5.36), LD/4000 group: 19.92(6.85), HD/2000 group: 18.56(7.48), HD/4000 group: 16.67 (4.72), control group: 15.73 (8.37)
Indirectness of population	No indirectness
Interventions	(n=75) Intervention 1: Non-invasive electrotherapy interventions - Extracorporeal shockwave therapy. Radial extracorporeal shockwave therapy (rESWT) using the Swiss Dolor Clast (EMS Electro Medical Systems, Nyon, Switzerland) device, with the standard radial (blue) handpiece, and a metal applicator with a diameter of 10mm. rEWSt was administered by one physician. Before the treatment, participants were placed in supine and prone positions successively, with the affected knee joint flexed at different angles to expose pain points. Meanwhile, the physician located the pain points by palpating the anatomical marks around the knee joint (i.e. the peripatellar area, the medial and lateral condyles, and the popliteal fossa area, avoiding critical nerves and blood vessels), wiped an aqueous gel on the probe of a radial handpiece, and orientated the probe perpendicularly on the targeted area. There was no application of local anaesthesia or analgesic drugs during the session. Participants received 4 sessions of rEWST, one week apart, with a shock frequency of 8Hs per session. The treatment protocols for the 4 rEWST groups were as follows: LD/2000, with a positive EFD of 0.12mJ/mm2 and 4000 impulses per session; HD/2000, with a positive EFD of 0.24mJ/mm2 and 2000 impulses per session; and HD/4000, with a positive EFD of 0.24mJ/mm2 and 4000 impulses per session.. Duration 4 sessions, one week apart. Concurrent medication/care: All participants were prevented from receiving any additional treatments, such as physical therapy, oral or parenteral steroid medications, anti-inflammatory drugs, stretching, acupuncture, orthotics etc., throughout the treatment sessions.. Indirectness: No indirectness (n=14) Intervention 2: Sham electrotherapy. The placebo group also received 4 sessions of rEWST, one week apart, with a shock frequency of 8Hz per session, but was treated with the minimum positive EFD 0.02mJ/mm2 and 1000 impulses per session.. Duration 4 sessions, one week apart. Concurrent medication/care: All participants were prevented from receiving any additional treatments, such as physical therapy, oral or parenteral steroid medications, anti-inflammatory drugs, stretching, acupuncture, orthotics etc., throughout the treatment sessions.. Indirectness: No indirectness
Funding	Study funded by industry (Supported by a grant from the Medical and Health Research Project of Aerospace Science and Industry Corporation of China (grant no. 2019-LCYL-009).)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EXTRACORPOREAL SHOCKWAVE THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: VAS pain at 4 weeks after intervention; Group 1: mean -3.504 (SD 2.45); n=75, Group 2: mean -0.69 (SD 1.97); n=14; VAS 0-10 Top=High is poor outcome; Comments: SD calculated from 95% CIs reported. Average mean and SD calculated across the 4 intervention groups. Reported reduction in mean change scores (95% CI): HD condition: 4.27 (3.47, 5.08), LD condition: 2.73 (1.99, 3.45), 4000 impulse condition: 3.38 (2.62, 4.14), 2000 impulse condition: 3.62 (2.86, 4.38)
Baseline VAS: LD/2000 group: 5.17 (1.17), LD/4000 group: 5.33(1.51), HD/2000 group: 5.6(1.14), HD/4000 group: 5.8(1.79), control group: 5.26(1.66)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Crossover - Low, Subgroups - Low, Other 1 - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: lost to follow-up; Group 2 Number missing: 0, Reason: N/A	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	Zhao 2013[237]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=70)
Countries and setting	Conducted in China; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 12 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People with a diagnosis of primary symptomatic knee osteoarthritis according to the criteria of the American College of Rheumatology
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with a diagnosis of primary symptomatic knee osteoarthritis according to the criteria of the American College of Rheumatology. This included people aged ≥45 years and had knee pain for the previous 3 months. They had Kellgren and Lawrence grade 2-3 osteoarthritis. For people with both knee symptomatic, the more painful knee or, when symptoms were similar bilaterally, the right knee was chosen as the target knee.
Exclusion criteria	People with a history of spinal stenosis; evidence of neurologic disease by history or physical examination; secondary causes of arthritis (inflammatory or metabolic); those who had a surgical intervention or intra-articular injection in the affected knee in the previous 6 months or any contraindication to magnetic resonance imaging or radiography
Recruitment/selection of patients	People were recruited from two rheumatology clinics
Age, gender and ethnicity	Age - Mean (SD): 60.9 (10.6). Gender (M:F): 25:45. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): </=75 years 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Kellgren Lawrence grade 2-3, median grade 2 Duration of symptoms: At least 3 months
Indirectness of population	No indirectness
Interventions	(n=34) Intervention 1: Non-invasive electrotherapy interventions - Extracorporeal shockwave therapy. Extracorporeal shock wave treatment where people underwent four treatments at weekly intervals. At each treatment session, people were positioned in a supine position with the affected knee unbent or flexed at 90 degrees. The

	shockwave probe was held stationary on a trigger point around the knee or at the patellofemoral and tibiofemoral borders of the target knee, avoiding direct placement on the peroneal nerve or vessel. To reduce loss of shockwave energy at the interface, an aqueous gel was used as a coupling medium between the probe of the device and the skin and applied in circular motions. Shockwaves of 4000 pulses in total were applied at 0.25mJ/mm² and a frequency of 6H/z.. Duration 4 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness (n=36) Intervention 2: Sham electrotherapy. Sham extracorporeal shockwave treatment. Shockwaves at 0mJ/mm² to the same area in the same manner.. Duration 4 weeks. Concurrent medication/care: No additional information. Indirectness: No indirectness
Funding	Academic or government funding (This study was supported by the National natural Science Foundation of China (number 31172169) and China post-doctoral Science Foundation (number 2013M532134))

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EXTRACORPOREAL SHOCKWAVE THERAPY versus SHAM ELECTROTHERAPY

Protocol outcome 1: Pain at </= 3 months
- Actual outcome: WOMAC pain at 12 weeks; Group 1: mean -4.5 (SD 2.7); n=34, Group 2: mean -2.2 (SD 3.1); n=36; WOMAC pain 0-20 Top=High is poor outcome; Comments: Reported change scores and 95% confidence intervals. Reported ESWT: -4.5 (-5.4 to -3.6). Reported placebo: -2.2 (-3.2 to -1.2). Baseline ESWT: 8.1 (2.4). Baseline placebo: 8.0 (2.4).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, weight, height, BMI, Kellgren and Lawrence grade, and baseline values of outcomes; Group 1 Number missing: 4, Reason: 2 lost to follow up, 2 lack of efficacy; Group 2 Number missing: 5, Reason: 2 adverse events, 3 lack of efficacy

Protocol outcome 2: Physical function at </= 3 months
- Actual outcome: WOMAC function at 12 weeks; Group 1: mean -13.9 (SD 9.8); n=34, Group 2: mean -6 (SD 9.8); n=36; WOMAC function 0-68 Top=High is poor outcome; Comments: Reported change scores and 95% confidence intervals. Reported ESWT: -13.9 (-17.2 to -10.6). Reported placebo: -6.0 (-9.2 to -2.8). Baseline ESWT: 25.7 (8.9). Baseline placebo: 22.3 (9.4).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, weight, height, BMI, Kellgren and Lawrence grade, and baseline values of outcomes; Group 1 Number missing: 4, Reason: 2 lost to follow up, 2 lack of efficacy; Group 2 Number missing: 5, Reason: 2 adverse events, 3 lack of efficacy

Protocol outcome 3: Mild adverse events at </= 3 months

- Actual outcome: Increased pain at 12 weeks; Group 1: 0/34, Group 2: 2/36 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Reported age, gender, weight, height, BMI, Kellgren and Lawrence grade, and baseline values of outcomes; Group 1 Number missing: 4, Reason: 2 lost to follow-up, 2 lack of efficacy; Group 2 Number missing: 3, Reason: 3 lack of efficacy	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Study	**Zhong 2019[238]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=63)
Countries and setting	Conducted in China; Setting: Outpatient physical therapy clinics within a hospital network.
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 12 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis by rehabilitation physicians in accordance with ACR criteria and radiographic criteria (K-L grade)
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Men and women with a <6 month history of symptoms of knee osteoarthritis. Mild to moderate knee osteoarthritis was categorised as radiographic alterations in tibiofemoral joints grades II or III based on the K-L scale. Participants had knee pain on most days of >4cm on a 10cm visual analog scale on the worst knee over the past week. The side with more severe symptoms was selected as the target knee in patients with bilateral knee osteoarthritis. When the symptoms of the 2 knees were similar, the right knee was selected as the target knee for evaluation.
Exclusion criteria	Previous joint replacement, a history of intra-articular injection, surgery, ESWT, the commencement of other medications within the past 6 months, loss of independent walking ability, or any major concomitant diseases that could interfere with participation in the trial. Participants with a history of diagnosis of significant neurologic or psychiatric impairments would be excluded in view of their difficulty in objectively answering the questionnaire.

Recruitment/selection of patients	Participants learned about research recruitment from outpatient rehabilitation physicians and recruitment posters.
Age, gender and ethnicity	Age - Mean (SD): 62.8 (7.9). Gender (M:F): Define. Ethnicity: All Mongolian
Further population details	1. Age (≤/> 75 years): Not stated / Unclear (range not given.). 2. Diagnosis : Diagnosis with imaging (diagnosis included radiographic criteria (K-L grade)). 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Duration of knee pain (months): ESWT group: 34.7 (15.4), placebo group: 34.1 (14.2) Severity (WOMAC pain at baseline): ESWT group: 6.6 (1.5), placebo group: 7.0 (1.9) Kellgren-Lawrence grade: II (n): ESWT group: 23, placebo group: 24 Kellgren-Lawrence grade: III (n): ESWT group: 9, placebo group: 7
Indirectness of population	No indirectness
Interventions	(n=32) Intervention 1: Non-invasive electrotherapy interventions - Extracorporeal shockwave therapy. All ESWTs were given by a single, experienced physical therapist. ESWT was conducted using the Swiss DOlorClast instrument once a week for 4 consecutive weeks (4 sessions in total). Participants stayed supine with the target knee flexed at 90 degrees in each session. The physical therapist determined the pain points of the target knee by palpation and marked the pain points and the patellofemoral and tibiofemoral borders. The shockwave probe (15mm) was attached to the marker while avoiding nerves or blood vessels. The ksin contacted by the ESWt probe was coated with ultrasound gel. The parameters of therapy included a total of 2000 pulses of 8Hz frequency at 2.5 bars of pneumatic pressure. The first 1000 pulses were evenly distributed to pain points (the maximum number of pain points is 4). The remaining pulses were slid back and forth on the patellofemoral and tibiofemoral borders. No local anaesthesia or other injections were used.. Duration 4 weeks. Concurrent medication/care: All participants were educated on a simple home exercise programme for the first visit. the programme was comprised of a single knee extensor muscle strengthening. The patient sat in a chair, straightened his/ her knee as far as possible, kept it for 10 seconds, repeated 10 times, and did 3 groups per day. therapist- applied manual forces were not permitted in the exercise programme. The home exercise was supervised by a physiotherapist once every 3 days over the phone. (n=31) Intervention 2: Sham electrotherapy. Participants assigned to the placebo group were managed by the same physical therapist with the same ESWT protocol, but the air pressure was set at 0.2 bar. The stress value was set by the researcher responsible for ranomisation. Participants and therapists could hear a sound similar to that of the regular ESWT, in order to enhance the sham design, but they were not able to see the dashboard.. Duration 4 weeks. Concurrent medication/care: All participants were educated on a simple home exercise programme for the first visit. the programme was comprised of a single knee extensor muscle strengthening. The patient sat in a chair, straightened his/ her knee as far as possible, kept it for 10 seconds, repeated 10 times, and did 3 groups per day. therapist- applied manual forces were not permitted in the exercise programme. The home exercise was supervised by a physiotherapist once every 3 days over the phone.. Indirectness: No indirectness

Funding	Other (Shanghai Qingpu District Science and Technology Development Fund Project (grant no. 2016-03))
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EXTRACORPOREAL SHOCKWAVE THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Pain at </= 3 months - Actual outcome: WOMAC- pain subscale at 12 weeks; Group 1: mean 2.4 (SD 1.4); n=29, Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: lost to follow-up (1), refused to continue (1), unable to contact (1); Group 2 Number missing: 2, Reason: lost to follow-up (1), unable to contact (1) Protocol outcome 2: Physical function at </= 3 months - Actual outcome: WOMAC- physical function subscale at 12 weeks; Group 1: mean 7.9 (SD 4.9); n=29, Group 2: mean 17.3 (SD 7.2); n=29; WOMAC-physical function subscale 0-68 Top=High is poor outcome; Comments: Baseline values: ESWT group: 22.3 (5.1), placebo group: 23.7 (6.4) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: lost to follow-up (1), refused to continue (1), unable to contact (1); Group 2 Number missing: 2, Reason: lost to follow-up (1), unable to contact (1) Protocol outcome 3: Moderate/major adverse events at </= 3 months - Actual outcome: Serious adverse events at 12 weeks; Group 1: 0/32, Group 2: 0/31; Comments: 'No serious adverse events were identified'. Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: lost to follow-up (1), refused to continue (1), unable to contact (1); Group 2 Number missing: 2, Reason: lost to follow-up (1), unable to contact (1)	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at > 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at </= 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at > 3 months

Study	Zizic 1995[240]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=78)
Countries and setting	Conducted in USA; Setting: Outpatient follow up
Line of therapy	Unclear
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Pain in the involved knee that was aggravated by activity and relieved by rest; morning stiffness upon rising or after disuse; at least one physical finding of joint crepitus, tenderness upon motion, swelling, or decreased range of motion; the presence of at least one of the following radiological findings in the involved knee: narrowing of the joint space of either the medial or lateral compartment on standing anteroposterior radiograph, subchondral bony sclerosis, or osteophyte formation.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People over the age of 20 with with knee osteoarthritis that was to be treated and gave informed consent
Exclusion criteria	Other conditions, such as aseptic necrosis of the femoral condyle, juxtaarticular Paget's disease, chondrocalcinosis, hemochromatosis, ochronosis, hemophilic arthropathy, inflammatory arthropathy (such as rheumatoid arthritis, ankylosing spondylitis, or psoriatic arthritis), infectious arthritis, Charcot's knee joint, villonodular tenosynovitis, and synovial chondromatosis
Recruitment/selection of patients	No additional information
Age, gender and ethnicity	Age - Other: Over the age of 20. Gender (M:F): 38:33. Ethnicity: Not stated
Further population details	1. Age (≤/> 75 years): Not stated / Unclear 2. Diagnosis : Diagnosis with imaging 3. Multimorbidity : Not stated / Unclear 4. Site of osteoarthritis: Knee
Extra comments	Severity: Not stated Duration of symptoms: Not stated
Indirectness of population	No indirectness
Interventions	(n=41) Intervention 1: Non-invasive electrotherapy interventions - Pulsed short-wave therapy. Electrical impulse generated by a portable, battery operated device that delivers a low frequency (100Hz), low amplitude, voltage sources monophasic spiked signal to the knee via skin surface electrode. An electrode gel that lowers the

	impedance at the electrode-dermal junction was applied to the skin-electrode interface, allowing the pulsed signal to be effectively delivered at a relatively low voltage. One electrode was placed on the treated knee and the 2nd was placed on the thigh directly above that knee. People were advised to use the instrument for 6 to 10 hours/day during the 4 week treatment period. After positioning the electrodes each person was instructed to activate the device by switch and to adjust the voltage by reducing the @tingling@ sensation produced by the electrical stimulus to a subthreshold level.. Duration 4 weeks. Concurrent medication/care: Background, stable NSAID therapy was permitted as long as people remained symptomatic despite such therapy. Indirectness: No indirectness (n=37) Intervention 2: Sham electrotherapy. Sham device identical to the active device that initially produced an electrical impulse at start up but after the subthreshold level was set was switched off.. Duration 4 weeks. Concurrent medication/care: Background, stable NSAID therapy was permitted as long as people remained symptomatic despite such therapy. Indirectness: No indirectness
Funding	Study funded by industry (This study was supported by Murray Electronics)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PULSED SHORT-WAVE THERAPY versus SHAM ELECTROTHERAPY Protocol outcome 1: Mild adverse events at </= 3 months - Actual outcome: Mild skin reactions (rashes that were transient and disappeared after stopping/changing the conducting gel) at 4 weeks; Group 1: 9/38, Group 2: 7/34; Comments: PSWT: 24%. Sham: 21%. Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Vaguely reported gender, but otherwise completely unreported; Group 1 Number missing: 3, Reason: No reason given; Group 2 Number missing: 4, Reason: No reason given	
Protocol outcomes not reported by the study	Health-related quality of life at </= 3 months; Health-related quality of life at > 3 months; Pain at </= 3 months; Pain at > 3 months; Physical function at </= 3 months; Physical function at > 3 months; Psychological distress at </= 3 months; Psychological distress at > 3 months; Osteoarthritis flares at </= 3 months; Osteoarthritis flares at > 3 months; Mild adverse events at > 3 months; Moderate/major adverse events at </= 3 months ; Moderate/major adverse events at > 3 months

Appendix E – Forest plots

E.1 Pulsed short-wave therapy

E.1.1 Pulsed short-wave therapy compared to sham electrotherapy

Figure 2: Quality of life (EQ-5D, KOOS, AIMS, 0-100, high is good, change score and final values) at ≤3 months

	Pulsed short-wave therapy			Sham electrotherapy				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Callaghan 2005	-53	27	18	-51	17	9	10.8%	-2.00 [-18.70, 14.70]
Fukuda 2011A	38.2	17.5	59	29.7	13.7	23	32.1%	8.50 [1.34, 15.66]
Pipitone 2001	0.59	1.01	34	0.2	1.36	35	57.1%	0.39 [-0.17, 0.95]
Total (95% CI)			**111**			**67**	**100.0%**	**2.73 [-3.37, 8.83]**

Heterogeneity: Tau² = 16.90; Chi² = 4.98, df = 2 (P = 0.08); I² = 60%

Test for overall effect: Z = 0.88 (P = 0.38)

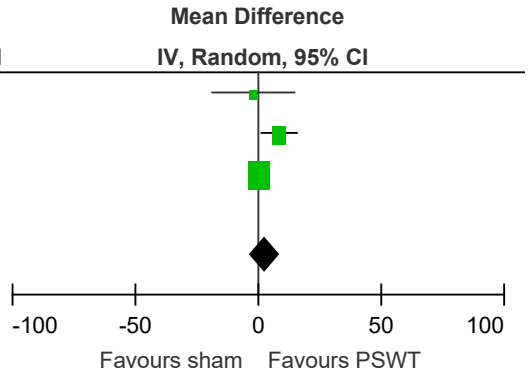


Figure 3: Quality of life (SF-36 physical component, 0-100, high is good, final value) at ≤3 months

	Pulsed short-wave therapy			Sham electrotherapy			Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI
Bagnato 2016	55.8	6.1	30	53.1	6.2	33	2.70 [-0.34, 5.74]

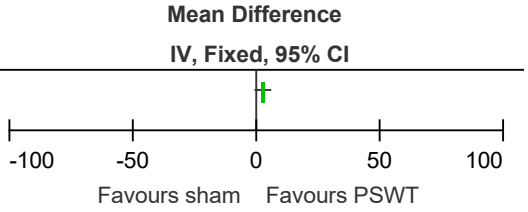


Figure 4: Quality of life (SF-36 mental component, 0-100, high is good, final value) at ≤3 months

	Pulsed short-wave therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Bagnato 2016	43.8	3.6	30	43.6	4.7	30	0.20 [-1.92, 2.32]	

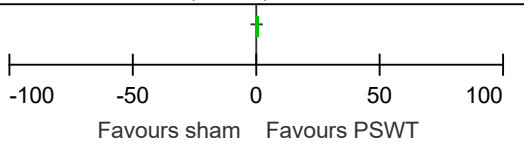


Figure 5: Quality of life (KOOS, 0-100, high is good, final value) at >3 months

	Pulsed short-wave therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Fukuda 2011A	36.4	17	37	33	12.8	14	3.40 [-5.26, 12.06]	

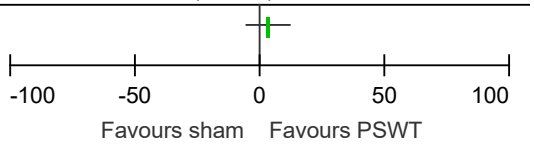


Figure 6: Quality of life (SF-36 physical component, 0-100, high is good, change score) at >3 months

	Pulsed short-wave therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Fary 2011	1	5.6	34	2.6	7.3	36	-1.60 [-4.64, 1.44]	

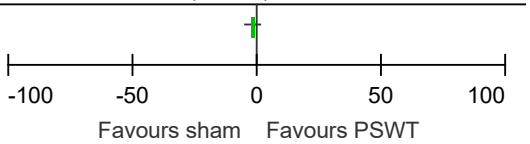


Figure 7: Quality of life (SF-36 mental component, 0-100, high is good, change score) at >3 months

	Pulsed short-wave therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Fary 2011	1.2	9.3	34	2.4	8.1	36	-1.20 [-5.30, 2.90]	

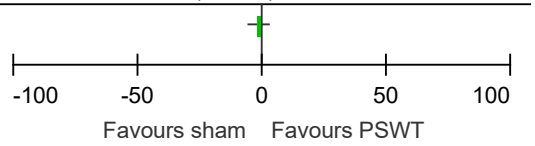


Figure 8: Pain (WOMAC [different scale ranges], high is poor, change scores) at ≤3 months

	Pulsed short-wave therapy			Sham electrotherapy			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Atamaz 2012	-3.6	3.5	32	-4.9	4	31	25.9%	0.34 [-0.16, 0.84]	
Garland 2007	-13.2	22.33	39	-3.1	15.38	19	24.9%	-0.49 [-1.05, 0.07]	
Pipitone 2001	-0.88	2.62	34	-0.49	3.83	35	26.3%	-0.12 [-0.59, 0.36]	
Wuschech 2015	-5.7	5.9	44	1.3	3.1	13	22.9%	-1.28 [-1.94, -0.61]	
Total (95% CI)			**149**			**98**	**100.0%**	**-0.36 [-0.97, 0.26]**	

Heterogeneity: Tau² = 0.32; Chi² = 15.59, df = 3 (P = 0.001); I² = 81%

Test for overall effect: Z = 1.13 (P = 0.26)

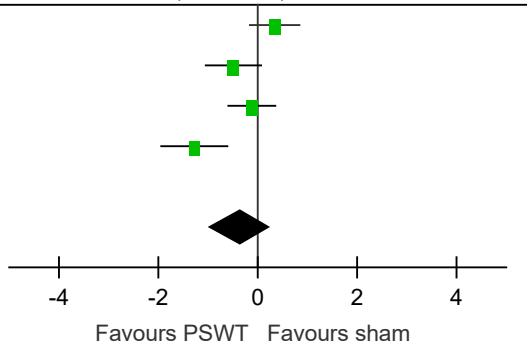


Figure 9: Pain (KOOS, WOMAC, VAS, NRS [different scale ranges], high is poor, final values) at ≤3 months

	Pulsed short-wave therapy			Sham electrotherapy			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Std. Mean Difference	SE	Total	Total	Weight		IV, Random, 95% CI	IV, Random, 95% CI
Bagnato 2016	-0.5749	0.2638	30	30	12.3%		-0.57 [-1.09, -0.06]	
Callaghan 2005	-0.3595	0.4117	18	9	10.0%		-0.36 [-1.17, 0.45]	
de Paula Gomes 2020	0.2646	0.3178	20	20	11.5%		0.26 [-0.36, 0.89]	
Fukuda 2011A	-0.9421	0.2653	59	21	12.3%		-0.94 [-1.46, -0.42]	
Moffett 1996	-0.5685	0.2637	30	30	12.3%		-0.57 [-1.09, -0.05]	
Nelson 2013	-3.023	0.5209	15	19	8.4%		-3.02 [-4.04, -2.00]	
Ozguclu 2010	-0.0369	0.3163	20	20	11.5%		-0.04 [-0.66, 0.58]	
Thamsborg 2005	-0.2155	0.2202	42	41	12.9%		-0.22 [-0.65, 0.22]	
Trock 1993	-1.3373	0.5056	10	10	8.6%		-1.34 [-2.33, -0.35]	
Total (95% CI)			**244**	**200**	**100.0%**		**-0.67 [-1.12, -0.21]**	

Heterogeneity: Tau² = 0.37; Chi² = 38.80, df = 8 (P < 0.00001); I² = 79%

Test for overall effect: Z = 2.86 (P = 0.004)

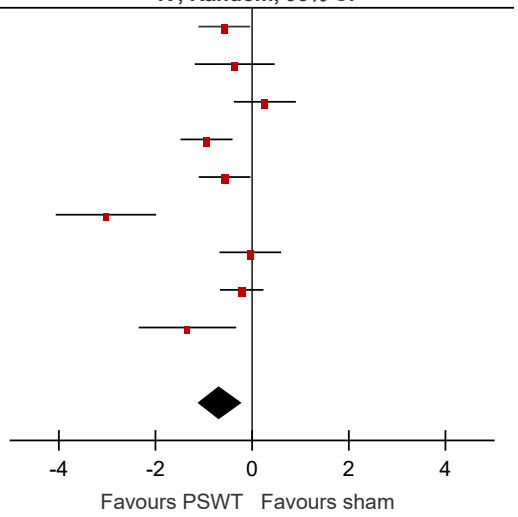


Figure 10: Pain (WOMAC [different scale ranges], high is poor, change scores) at >3 months

	Pulsed short-wave therapy			Sham electrotherapy				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Atamaz 2012	-4.5	4	32	-3.5	3.8	31	48.8%	-0.25 [-0.75, 0.24]	
Fary 2011	-5	20.4	34	-10	18.4	36	51.2%	0.25 [-0.22, 0.73]	
Total (95% CI)			**66**			**67**	**100.0%**	**0.01 [-0.49, 0.50]**	

Heterogeneity: Tau² = 0.07; Chi² = 2.12, df = 1 (P = 0.15); I² = 53%

Test for overall effect: Z = 0.03 (P = 0.98)

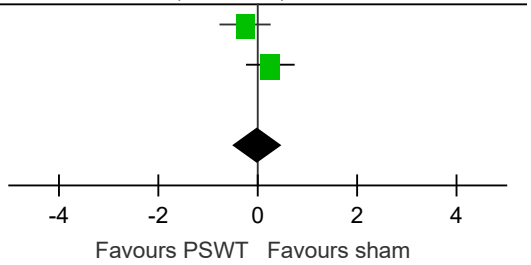


Figure 11: Pain (KOOS, 0-100, high is good, final value) at >3 months

	Pulsed short-wave therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Fukuda 2011A	57.6	18.8	37	33	9.9	14	24.60 [16.63, 32.57]	

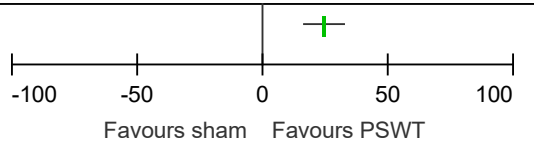


Figure 12: Physical function (WOMAC [different scale ranges], high is poor, change scores) at ≤3 months

	Pulsed short-wave therapy			Sham electrotherapy			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Atamaz 2012	-11.4	12.4	32	-10.3	10.7	31	27.3%	-0.09 [-0.59, 0.40]	
Garland 2007	-12	19.22	39	1.7	13.48	19	23.9%	-0.77 [-1.34, -0.20]	
Pipitone 2001	-3.62	9	34	-0.26	10.7	35	28.3%	-0.34 [-0.81, 0.14]	
Wuschech 2015	-16.4	16.1	42	-1.8	7.8	13	20.5%	-0.98 [-1.63, -0.33]	
Total (95% CI)			**147**			**98**	**100.0%**	**-0.51 [-0.89, -0.12]**	

Heterogeneity: Tau² = 0.08; Chi² = 5.99, df = 3 (P = 0.11); I² = 50%

Test for overall effect: Z = 2.59 (P = 0.010)

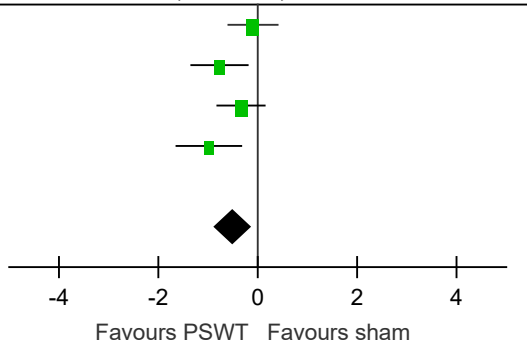


Figure 13: Physical function (KOOS, WOMAC [different scale ranges], high is poor, final values) at ≤3 months

Study or Subgroup	Std. Mean Difference	SE	Pulsed short-wave therapy Total	Sham electrotherapy Total	Weight	Std. Mean Difference IV, Random, 95% CI
Bagnato 2016	-0.2182	0.259	30	30	21.1%	-0.22 [-0.73, 0.29]
de Paula Gomes 2020	-1.6694	0.3723	20	20	16.5%	-1.67 [-2.40, -0.94]
Fukuda 2011A	-0.5837	0.2585	59	21	21.1%	-0.58 [-1.09, -0.08]
Ozguclu 2010	-0.0757	0.3164	20	20	18.7%	-0.08 [-0.70, 0.54]
Thamsborg 2005	-0.2515	0.2205	42	41	22.7%	-0.25 [-0.68, 0.18]
Total (95% CI)			**171**	**132**	**100.0%**	**-0.52 [-0.97, -0.06]**

Heterogeneity: Tau² = 0.19; Chi² = 14.00, df = 4 (P = 0.007); I² = 71%

Test for overall effect: Z = 2.21 (P = 0.03)

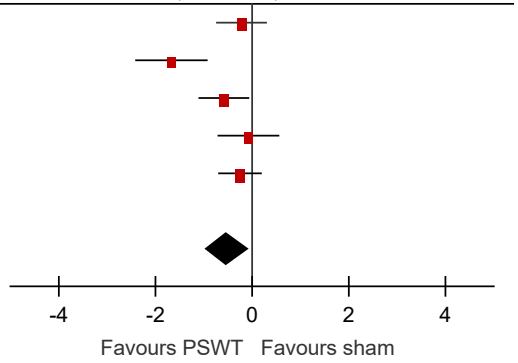


Figure 14: Physical function (WOMAC [different scale ranges], high is poor, change scores) at >3 months

Study or Subgroup	Pulsed short-wave therapy Mean	SD	Total	Sham electrotherapy Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Atamaz 2012	-9.9	13.2	32	-9.9	10.1	31	47.4%	0.00 [-0.49, 0.49]
Fary 2011	-5	16.5	34	-7	16.2	36	52.6%	0.12 [-0.35, 0.59]
Total (95% CI)			**66**			**67**	**100.0%**	**0.06 [-0.28, 0.40]**

Heterogeneity: Chi² = 0.12, df = 1 (P = 0.73); I² = 0%

Test for overall effect: Z = 0.37 (P = 0.71)

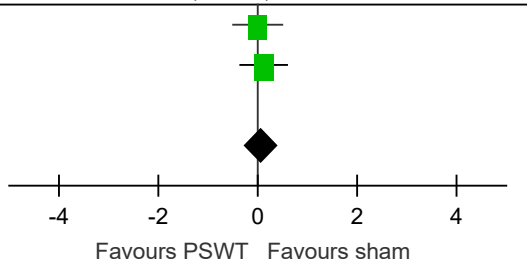


Figure 15: Physical function (KOOS, 0-100, high is good, final value) at >3 months

	Pulsed short-wave therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Fukuda 2011A	60.6	19.8	37	41.6	16.9	14	19.00 [8.09, 29.91]	

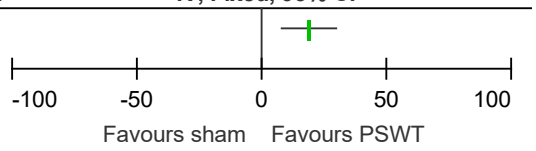


Figure 16: Psychological distress (GHQ, 0-90, high is poor, final value) at ≤3 months

	Pulsed short-wave therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Moffett 1996	30.27	15.8	30	26.79	13.58	30	3.48 [-3.98, 10.94]	

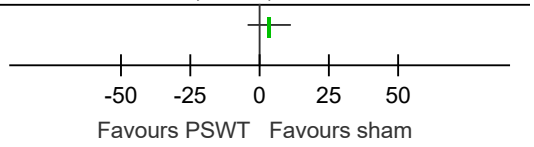


Figure 17: Mild adverse events at ≤3 months

Study or Subgroup	Pulsed short-wave therapy Events	Total	Sham electrotherapy Events	Total	Weight	Risk Difference M-H, Fixed, 95% CI
Garland 2007	7	39	4	19	16.2%	-0.03 [-0.25, 0.19]
Pipitone 2001	2	34	4	35	21.9%	-0.06 [-0.19, 0.08]
Thamsborg 2005	12	42	6	41	26.3%	0.14 [-0.03, 0.31]
Wuschech 2015	0	44	0	13	12.7%	0.00 [-0.10, 0.10]
Zizic 1995	9	38	7	34	22.8%	0.03 [-0.16, 0.22]
Total (95% CI)		**197**		**142**	**100.0%**	**0.03 [-0.05, 0.11]**
Total events	30		21			

Heterogeneity: Chi² = 3.63, df = 4 (P = 0.46); I² = 0%

Test for overall effect: Z = 0.66 (P = 0.51)

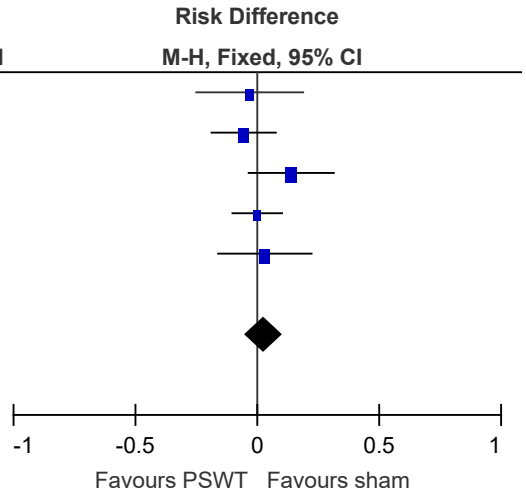
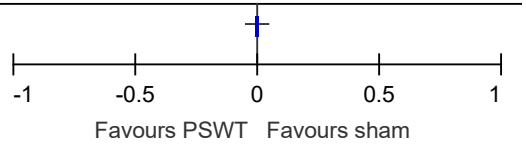


Figure 18: Moderate/major adverse events at ≤3 months

Study or Subgroup	Pulsed short-wave therapy Events	Total	Sham electrotherapy Events	Total	Risk Difference M-H, Fixed, 95% CI
Thamsborg 2005	0	42	0	41	0.00 [-0.05, 0.05]



E.1.2 Pulsed short-wave therapy compared to no treatment

Figure 19: Quality of life (KOOS, 0-100, high is good, final value) at ≤3 months

	Pulsed short-wave therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Fukuda 2011A	38.2	17.5	59	26.4	21.8	32	11.80 [3.03, 20.57]	

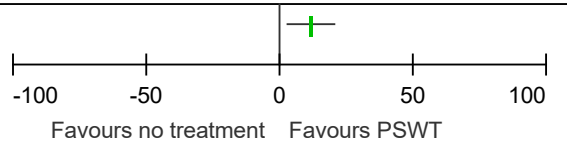


Figure 20: Quality of life (SF-36 physical function, 0-100, high is good, change score) at ≤3 months

	Pulsed short-wave therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Akyol 2010	25.25	18.17	20	19	20.55	20	6.25 [-5.77, 18.27]	

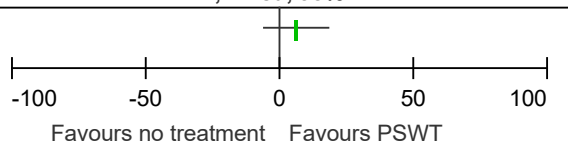


Figure 21: Quality of life (SF-36 bodily pain, 0-100, high is good, change score) at ≤3 months

	Pulsed short-wave therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Akyol 2010	25.85	24.53	20	28.35	19.38	20	-2.50 [-16.20, 11.20]	

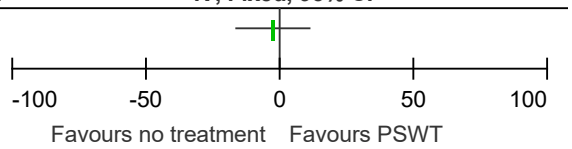


Figure 22: Quality of life (SF-36 vitality, 0-100, high is good, change score) at ≤3 months

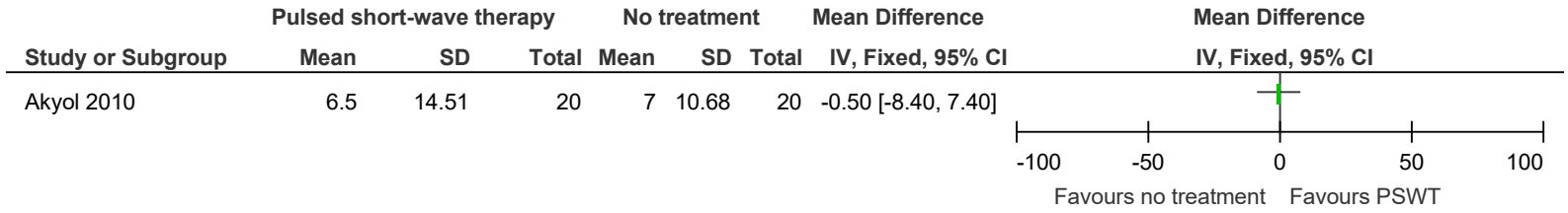


Figure 23: Quality of life (SF-36 general health, 0-100, high is good, change score) at ≤3 months

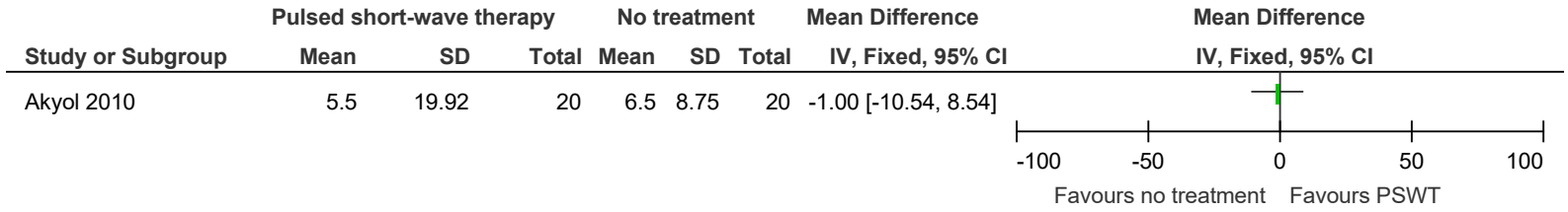


Figure 24: Quality of life (SF-36 social function, 0-100, high is good, final value) at ≤3 months

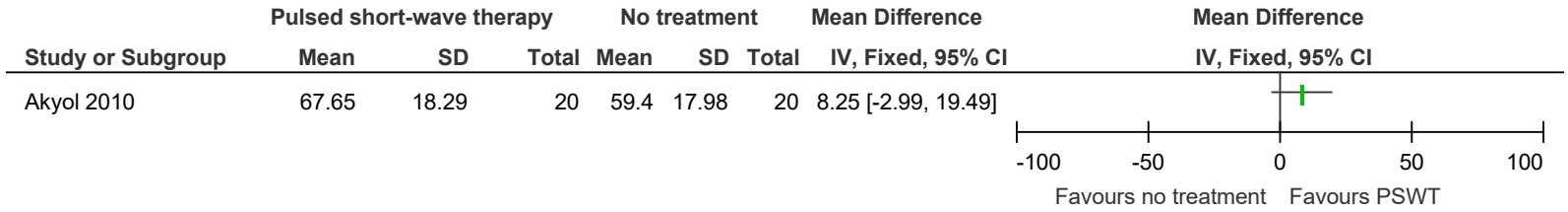


Figure 25: Quality of life (SF-36 physical function, 0-100, high is good, change score) at >3 months

	Pulsed short-wave therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Akyol 2010	24.25	21.16	20	17	18.52	20	7.25 [-5.07, 19.57]	

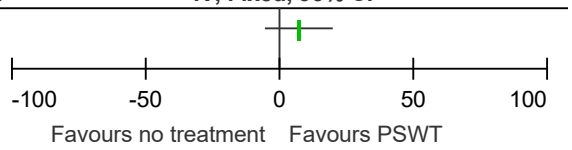


Figure 26: Quality of life (SF-36 bodily pain, 0-100, high is good, change score) at >3 months

	Pulsed short-wave therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Akyol 2010	16.05	29.84	20	28.45	24.2	20	-12.40 [-29.24, 4.44]	

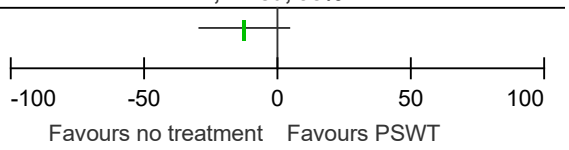


Figure 27: Quality of life (SF-36 vitality, 0-100, high is good, change score) at >3 months

	Pulsed short-wave therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Akyol 2010	-1.25	13.26	20	-0.75	14.71	20	-0.50 [-9.18, 8.18]	

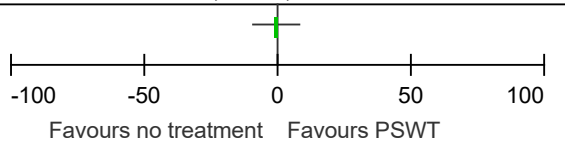


Figure 28: Quality of life (SF-36 general health, 0-100, high is good, change score) at >3 months

	Pulsed short-wave therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Akyol 2010	1	19.77	20	5.75	13.98	20	-4.75 [-15.36, 5.86]	

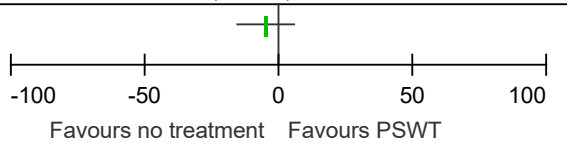


Figure 29: Quality of life (SF-36 social function, 0-100, high is good, final value) at >3 months

	Pulsed short-wave therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Akyol 2010	65.45	20.95	20	59.95	21.84	20	5.50 [-7.76, 18.76]	

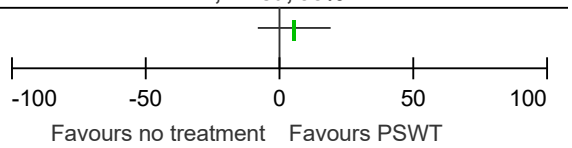


Figure 30: Pain (WOMAC, VAS [different scale ranges], high is poor, change scores) at ≤3 months

	Pulsed short-wave therapy			No treatment			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Akyol 2010	-5.55	4.5	20	-5.3	3.35	20	50.0%	-0.06 [-0.68, 0.56]	
Cetin 2008	-2.33	0.77	20	-2.27	0.88	20	50.0%	-0.07 [-0.69, 0.55]	
Total (95% CI)			**40**			**40**	**100.0%**	**-0.07 [-0.50, 0.37]**	

Heterogeneity: Chi² = 0.00, df = 1 (P = 0.98); I² = 0%

Test for overall effect: Z = 0.30 (P = 0.77)

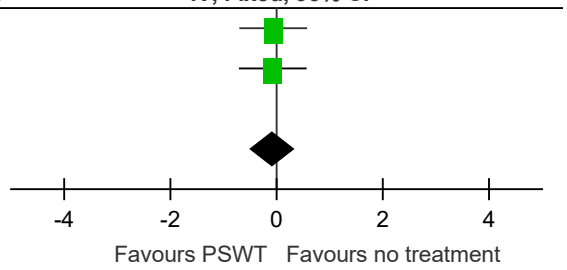


Figure 31: Pain (KOOS, WOMAC [different scale ranges], high is poor, final values) at ≤3 months

Study or Subgroup	Pulsed short-wave therapy Mean	SD	Total	No treatment Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
de Paula Gomes 2020	11.3	1.41	20	9	1.41	20	49.4%	1.60 [0.88, 2.32]
Fukuda 2011A	-59.9	17.2	59	-42.3	17.3	32	50.6%	-1.01 [-1.47, -0.56]
Total (95% CI)			**79**			**52**	**100.0%**	**0.28 [-2.28, 2.84]**

Heterogeneity: Tau² = 3.31; Chi² = 35.98, df = 1 (P < 0.00001); I² = 97%

Test for overall effect: Z = 0.21 (P = 0.83)

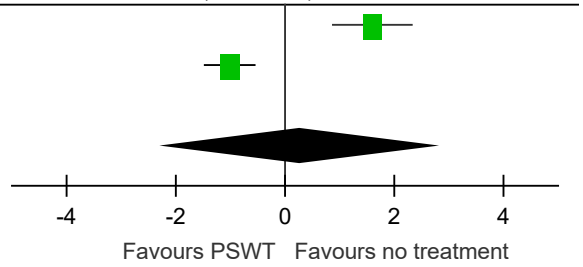


Figure 32: Pain (WOMAC, 0-20, high is poor, change score) at >3 months

Study or Subgroup	Pulsed short-wave therapy Mean	SD	Total	No treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Akyol 2010	-5.5	4.33	20	-5	3.85	20	-0.50 [-3.04, 2.04]

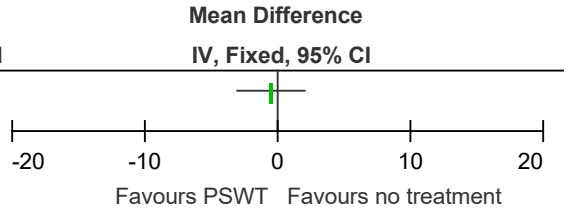


Figure 33: Physical function (WOMAC, 0-68, high is poor, change score and final value) at ≤3 months

	Pulsed short-wave therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Akyol 2010	-19.4	11.03	20	-15.1	12.23	20	6.6%	-4.30 [-11.52, 2.92]	
de Paula Gomes 2020	36.85	2.28	20	38.9	3.72	20	93.4%	-2.05 [-3.96, -0.14]	
Total (95% CI)			**40**			**40**	**100.0%**	**-2.20 [-4.05, -0.35]**	

Heterogeneity: Chi² = 0.35, df = 1 (P = 0.55); I² = 0%

Test for overall effect: Z = 2.33 (P = 0.02)

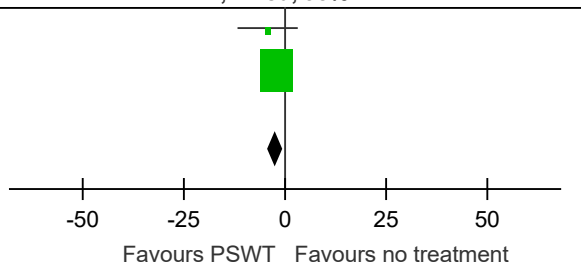


Figure 34: Physical function (KOOS, 0-100, high is good, final value) at ≤3 months

	Pulsed short-wave therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Fukuda 2011A	62.3	18.6	59	48.1	17.7	32	14.20 [6.45, 21.95]	

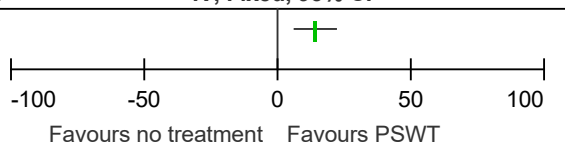


Figure 35: Physical function (WOMAC, 0-68, high is poor, change score) at >3 months

	Pulsed short-wave therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Akyol 2010	-16.9	15.63	20	-15.35	11.27	20	-1.55 [-10.00, 6.90]	

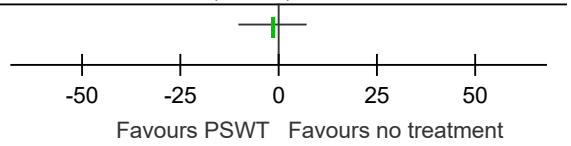


Figure 36: Psychological distress (Beck depression score, 0-63, high is poor, change score) at ≤3 months

	Pulsed short-wave therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Akyol 2010	-2.45	3.74	20	-2.3	3.29	20	-0.15 [-2.33, 2.03]	

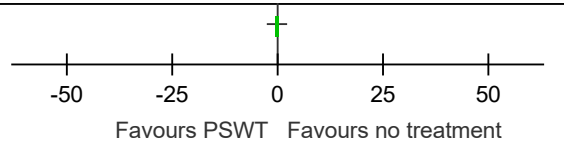


Figure 37: Psychological distress (GHQ, 0-90, high is poor, final value) at ≤3 months

	Pulsed short-wave therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Moffett 1996	30.27	15.8	30	32	14.18	30	-1.73 [-9.33, 5.87]	

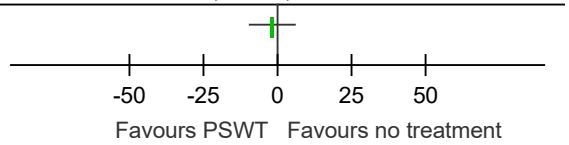
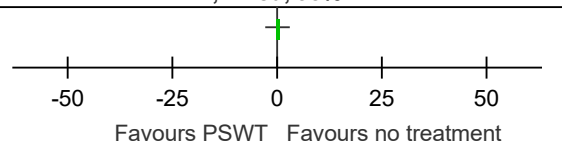


Figure 38: Psychological distress (Beck depression score, 0-63, high is poor, change score) at >3 months

	Pulsed short-wave therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Akyol 2010	-1.15	4.98	20	-1.25	3.68	20	0.10 [-2.61, 2.81]	



E.2 Interferential therapy

E.2.1 Interferential therapy compared to pulsed short-wave therapy

Figure 39: Pain (WOMAC, 0-20, high is poor, final value) at ≤3 months

	Interferential therapy			Pulsed short-wave therapy				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Atamaz 2012	3.3	3.1	31	4.9	4	32	17.1%	-1.60 [-3.36, 0.16]
de Paula Gomes 2020	11	1.16	20	11.3	1.41	20	82.9%	-0.30 [-1.10, 0.50]
Total (95% CI)			**51**			**52**	**100.0%**	**-0.52 [-1.25, 0.21]**

Heterogeneity: Chi² = 1.73, df = 1 (P = 0.19); I² = 42%

Test for overall effect: Z = 1.40 (P = 0.16)

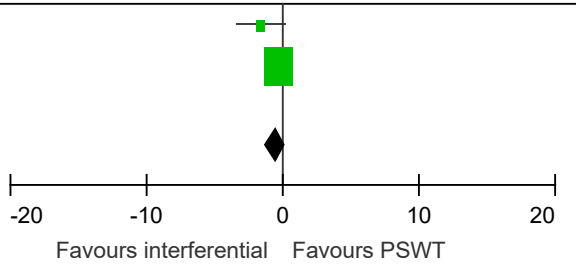


Figure 40: Pain (WOMAC, 0-20, high is poor, final value) at >3 months

	Interferential therapy			Pulsed short-wave therapy			Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI
Atamaz 2012	3.4	3.4	31	4.5	4	32	-1.10 [-2.93, 0.73]

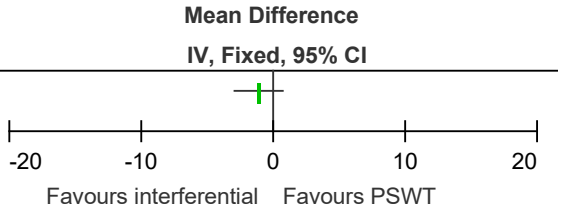


Figure 41: Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months

	Interferential therapy			Pulsed short-wave therapy				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Atamaz 2012	8.1	11.1	31	11.4	12.4	32	8.7%	-3.30 [-9.11, 2.51]
de Paula Gomes 2020	36.2	3.41	20	36.85	2.28	20	91.3%	-0.65 [-2.45, 1.15]
Total (95% CI)			**51**			**52**	**100.0%**	**-0.88 [-2.60, 0.84]**

Heterogeneity: Chi² = 0.73, df = 1 (P = 0.39); I² = 0%

Test for overall effect: Z = 1.01 (P = 0.31)

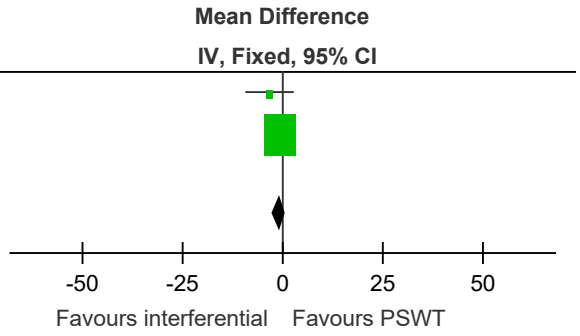
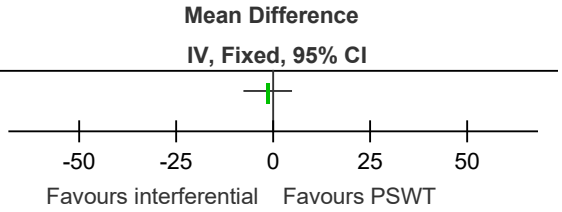


Figure 42: Physical function (WOMAC, 0-68, high is poor, final value) at >3 months

	Interferential therapy			Pulsed short-wave therapy			Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI
Atamaz 2012	8.5	11.1	31	9.9	13.2	32	-1.40 [-7.42, 4.62]



E.2.2 Interferential therapy compared to laser therapy

Figure 43: Pain (WOMAC, NRS [different scale ranges], high is poor, final values) at ≤3 months

	Interferential therapy			Laser therapy			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Fixed, 95% CI**
Alqualo-Costa 2020	3.55	2.9364	42	3.15	2.8004	42	68.4%	0.14 [-0.29, 0.57]
de Paula Gomes 2020	11	1.16	20	10.45	1.05	20	31.6%	0.49 [-0.14, 1.12]
Total (95% CI)			**62**			**62**	**100.0%**	**0.25 [-0.11, 0.60]**

Heterogeneity: Chi² = 0.81, df = 1 (P = 0.37); I² = 0%

Test for overall effect: Z = 1.38 (P = 0.17)

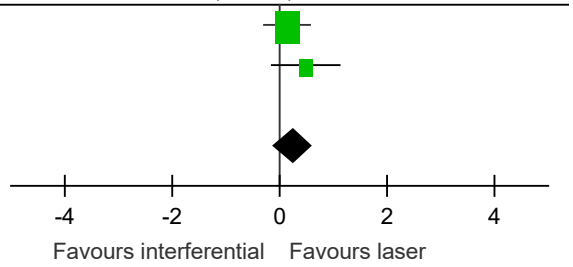


Figure 44: Pain (NRS, 0-10, high is poor, final value) at >3 months

	Interferential therapy			Laser therapy			Mean Difference	Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**IV, Fixed, 95% CI**	**IV, Fixed, 95% CI**
Alqualo-Costa 2020	3.65	2.8614	42	2.95	2.5323	42	0.70 [-0.46, 1.86]	

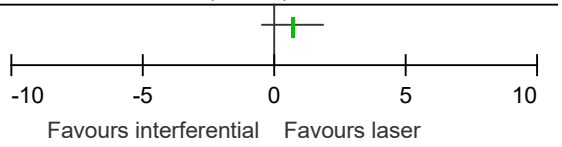
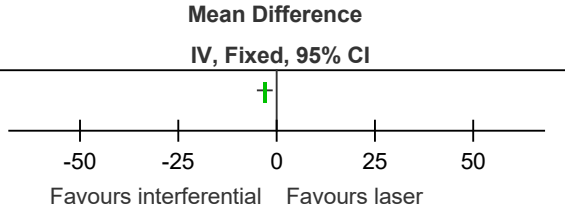


Figure 45: Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months

Study or Subgroup	Interferential therapy Mean	SD	Total	Laser therapy Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
de Paula Gomes 2020	36.2	3.41	20	39.2	2.12	20	-3.00 [-4.76, -1.24]



E.2.3 Interferential therapy compared to sham electrotherapy

Figure 46: Pain (WOMAC, 0-20, high is poor, change score and final value) at ≤3 months

Study or Subgroup	Interferential therapy Mean	SD	Total	Sham electrotherapy Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Atamaz 2012	-3.3	3.1	31	-3.6	3	35	33.1%	0.30 [-1.18, 1.78]
de Paula Gomes 2020	11	1.16	20	10.9	1.55	20	33.5%	0.10 [-0.75, 0.95]
Gundog 2012	7.2	2.3	45	16.1	1.5	15	33.4%	-8.90 [-9.91, -7.89]
Total (95% CI)			**96**			**70**	**100.0%**	**-2.84 [-9.07, 3.39]**

Heterogeneity: Tau² = 29.94; Chi² = 200.58, df = 2 (P < 0.00001); I² = 99%

Test for overall effect: Z = 0.89 (P = 0.37)

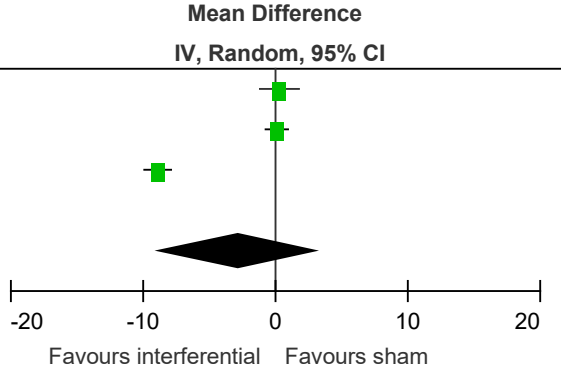


Figure 47: Pain (NRS, 0-10, high is poor, final value) at ≤3 months

	Interferential therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Alqualo-Costa 2020	3.55	2.9364	42	3.85	2.921	42	-0.30 [-1.55, 0.95]	

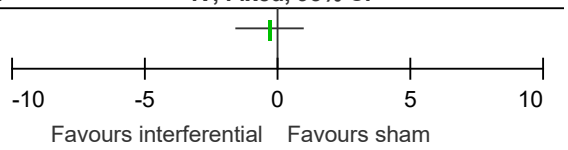


Figure 48: Pain (WOMAC, 0-20, high is poor, change score) at >3 months

	Interferential therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Atamaz 2012	-3.4	3.4	31	-3.2	3.2	35	-0.20 [-1.80, 1.40]	

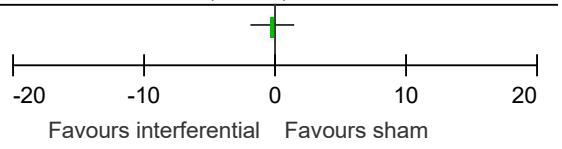


Figure 49: Pain (NRS, 0-10, high is poor, final value) at >3 months

	Interferential therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Alqualo-Costa 2020	3.65	2.8614	42	4.1	3.1064	42	-0.45 [-1.73, 0.83]	

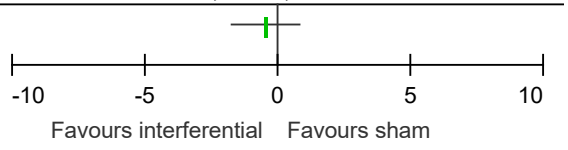


Figure 50: Physical function (WOMAC, 0-68, high is poor, change score and final value) at ≤3 months

	Interferential therapy			Sham electrotherapy				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Atamaz 2012	-8.1	11.1	31	-11	8.9	35	33.0%	2.90 [-2.00, 7.80]
de Paula Gomes 2020	36.2	3.41	20	41.35	2.96	20	33.7%	-5.15 [-7.13, -3.17]
Gundog 2012	27.5	7.2	45	57.8	6.1	15	33.3%	-30.30 [-34.04, -26.56]
Total (95% CI)			**96**			**70**	**100.0%**	**-10.88 [-28.56, 6.80]**

Heterogeneity: Tau² = 240.55; Chi² = 162.11, df = 2 (P < 0.00001); I² = 99%

Test for overall effect: Z = 1.21 (P = 0.23)

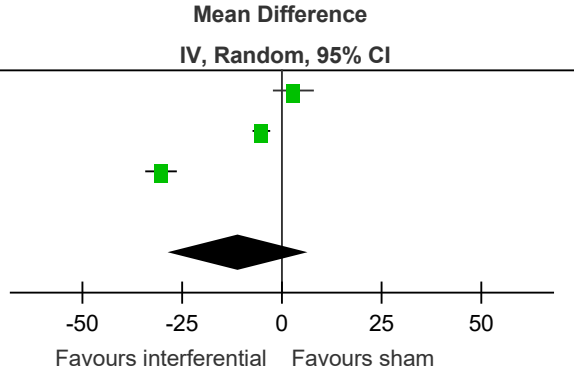
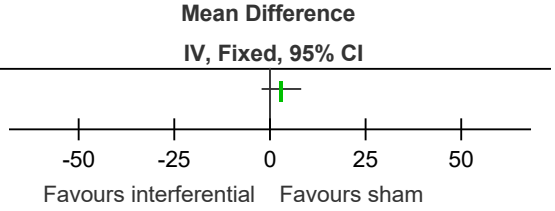


Figure 51: Physical function (WOMAC, 0-68, high is poor, change score) at >3 months

	Interferential therapy			Sham electrotherapy			Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI
Atamaz 2012	-8.5	11.1	31	-11.5	9.1	35	3.00 [-1.94, 7.94]



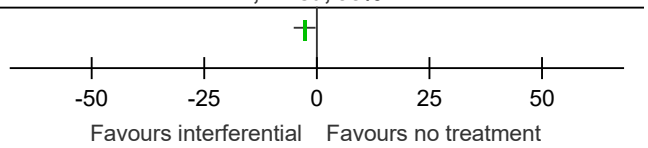
E.2.4 Interferential therapy compared to no treatment

Figure 52: Pain (WOMAC, 0-20, high is poor, final value) at ≤3 months

Study or Subgroup	Interferential therapy Mean	SD	Total	No treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
de Paula Gomes 2020	11	1.16	20	9	1.41	20	2.00 [1.20, 2.80]

Figure 53: Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months

Study or Subgroup	Interferential therapy Mean	SD	Total	No treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
de Paula Gomes 2020	36.2	3.41	20	38.9	3.72	20	-2.70 [-4.91, -0.49]



E.3 Neuromuscular electrical stimulation

E.3.1 Neuromuscular electrical stimulation compared to no treatment

Figure 54: Quality of life (SF-36 physical component, 0-100, high is good, final value) at ≤3 months

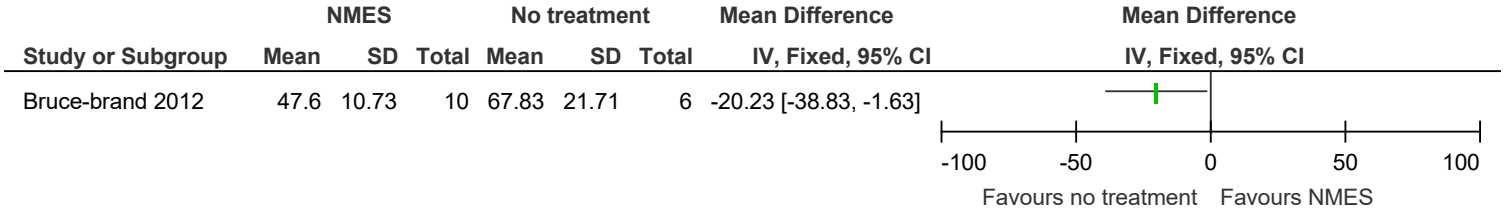


Figure 55: Quality of life (SF-36 mental component, 0-100, high is good, final value) at ≤3 months

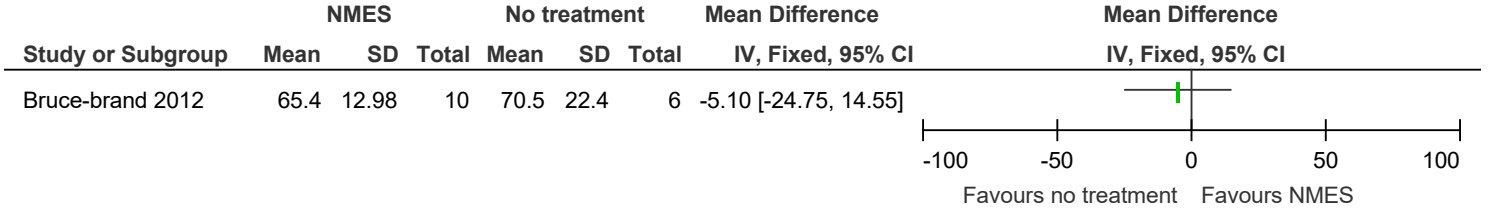


Figure 56: Quality of life (NHP pain, scale range unclear, high is poor, final value) at ≤3 months

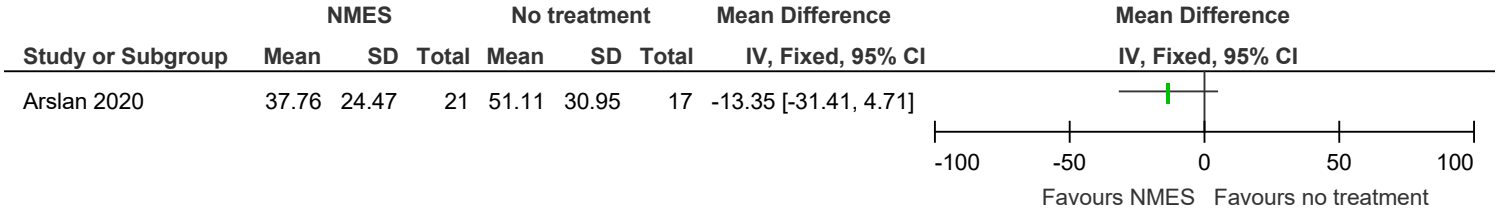


Figure 57: Quality of life (NHP physical mobility, scale range unclear, high is poor, final value) at ≤3 months

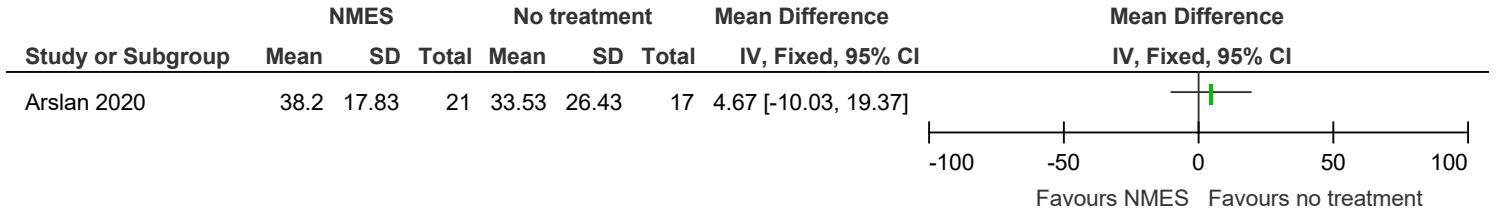


Figure 58: Quality of life (NHP energy level, scale range unclear, high is poor, final value) at ≤3 months

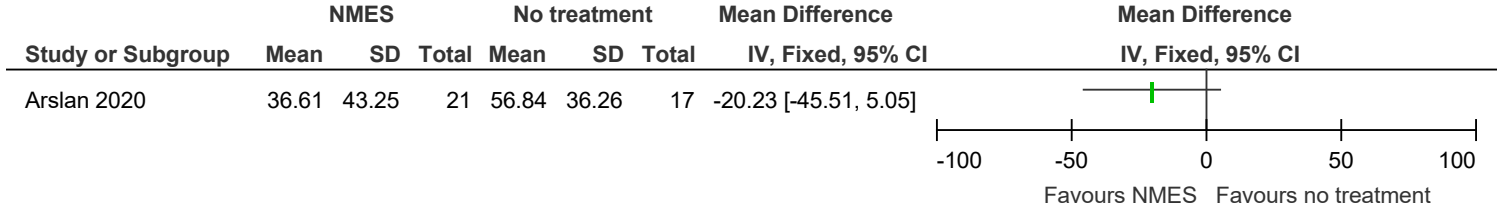


Figure 59: Quality of life (NHP sleep, scale range unclear, high is poor, final value) at ≤3 months

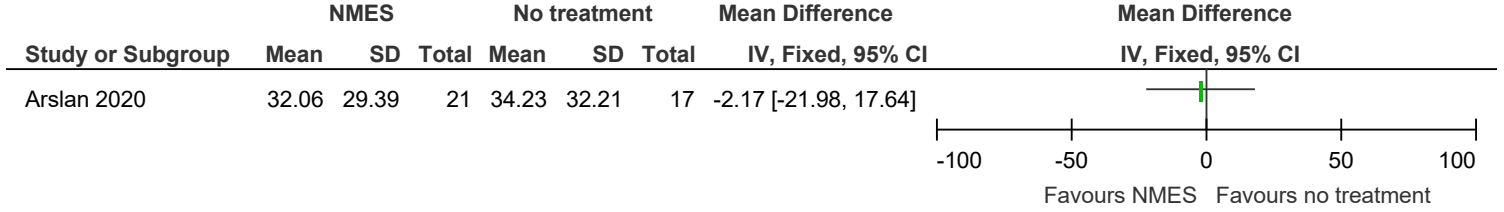


Figure 60: Quality of life (NHP social isolation, scale range unclear, high is poor, final value) at ≤3 months

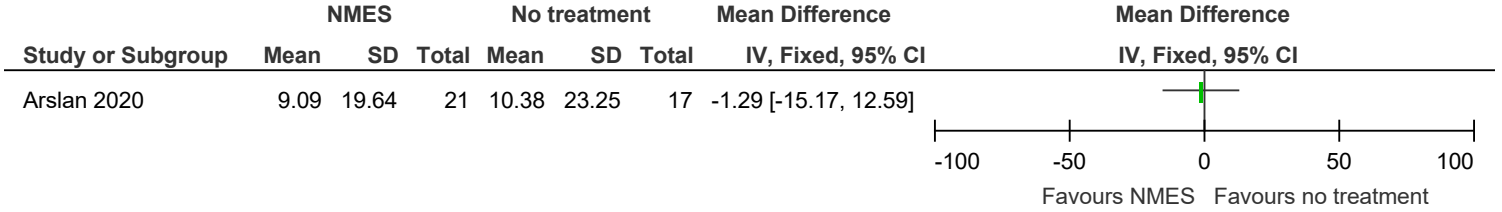


Figure 61: Quality of life (NHP total score, scale range unclear, high is poor, final value) at ≤3 months

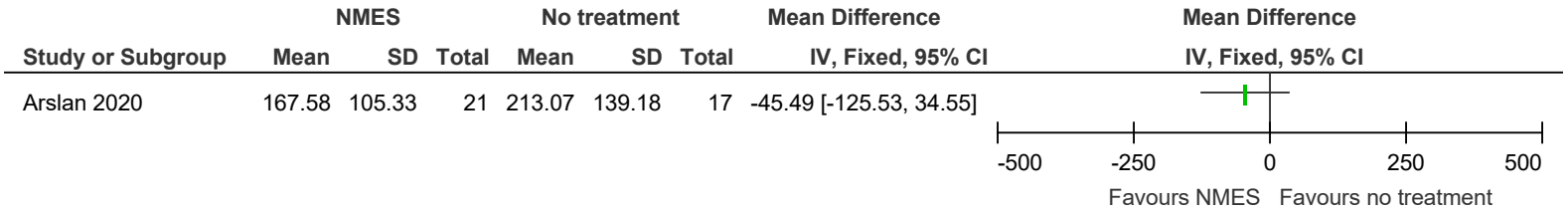


Figure 62: Pain (WOMAC, [different scale ranges], high is poor, change scores) at ≤3 months

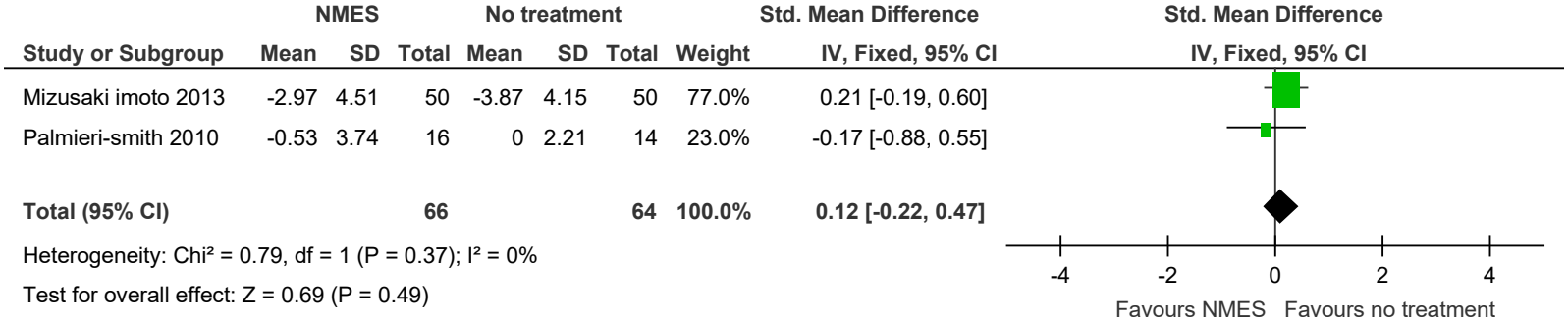


Figure 63: Pain (WOMAC, VAS [different scale ranges], high is poor, final values) at ≤3 months

	NMES			No treatment				Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Fixed, 95% CI**
Arslan 2020	6.23	3.3	21	7.78	9.65	17	25.9%	-0.22 [-0.86, 0.42]
Bruce-brand 2012	8.5	2.72	10	8.33	4.08	6	10.4%	0.05 [-0.96, 1.06]
Elboim-gabyzon 2013	3.3	2.4	25	5	2.2	25	32.3%	-0.73 [-1.30, -0.15]
Laufer 2014	3.3	1.3	25	5	2.4	25	31.4%	-0.87 [-1.45, -0.29]
Total (95% CI)			**81**			**73**	**100.0%**	**-0.56 [-0.89, -0.23]**

Heterogeneity: Chi² = 3.86, df = 3 (P = 0.28); I² = 22%

Test for overall effect: Z = 3.36 (P = 0.0008)

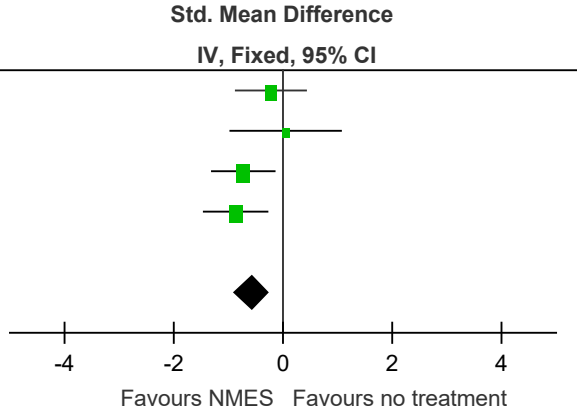


Figure 64: Pain (WOMAC, 5-25, high is poor, change score) at >3 months

	NMES			No treatment			Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**IV, Fixed, 95% CI**
Palmieri-smith 2010	-0.54	2.63	16	1.4	3.17	14	-1.94 [-4.04, 0.16]

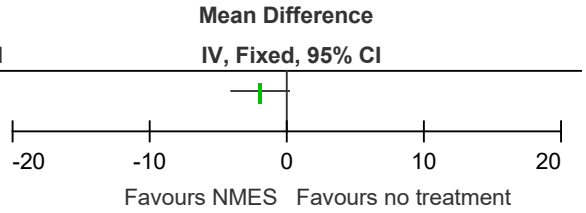


Figure 65: Pain (VAS, 0-10, high is poor, final value) at >3 months

Study or Subgroup	NMES Mean	NMES SD	NMES Total	No treatment Mean	No treatment SD	No treatment Total	Mean Difference IV, Fixed, 95% CI
Laufer 2014	3.4	2.4	23	5.3	2.3	21	-1.90 [-3.29, -0.51]

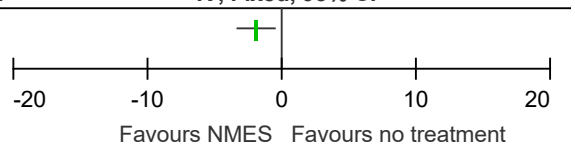


Figure 66: Physical function (WOMAC [different scale ranges], high is poor, change scores) at ≤3 months

Study or Subgroup	NMES Mean	NMES SD	NMES Total	No treatment Mean	No treatment SD	No treatment Total	Weight	Std. Mean Difference IV, Random, 95% CI
Mizusaki imoto 2013	-8.02	12	50	-10.95	14.1	50	62.2%	0.22 [-0.17, 0.62]
Palmieri-smith 2010	-4.86	13.1	16	0	9.5	14	37.8%	-0.41 [-1.13, 0.32]
Total (95% CI)			**66**			**64**	**100.0%**	**-0.02 [-0.62, 0.58]**

Heterogeneity: Tau² = 0.11; Chi² = 2.24, df = 1 (P = 0.13); I² = 55%

Test for overall effect: Z = 0.05 (P = 0.96)

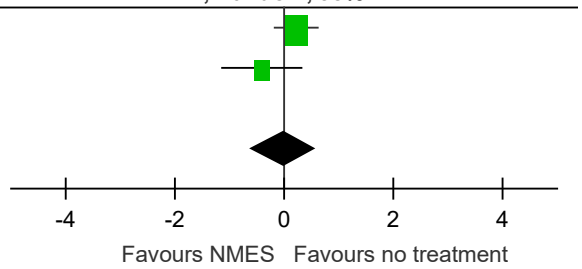


Figure 67: Physical function (WOMAC, 0-68, high is poor, final values) at ≤3 months

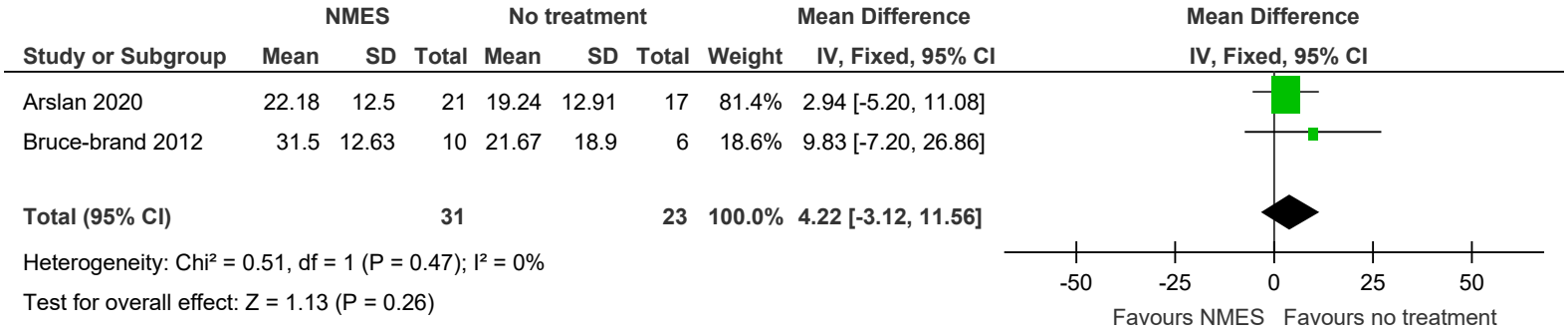


Figure 68: Physical function (WOMAC, 17-85, high is poor, change score) at >3 months

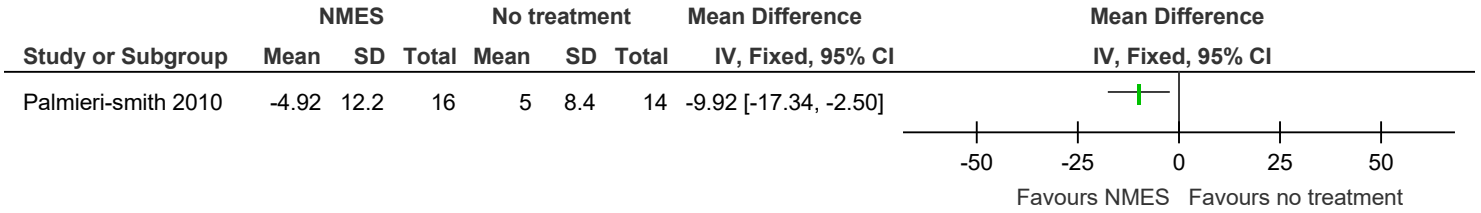
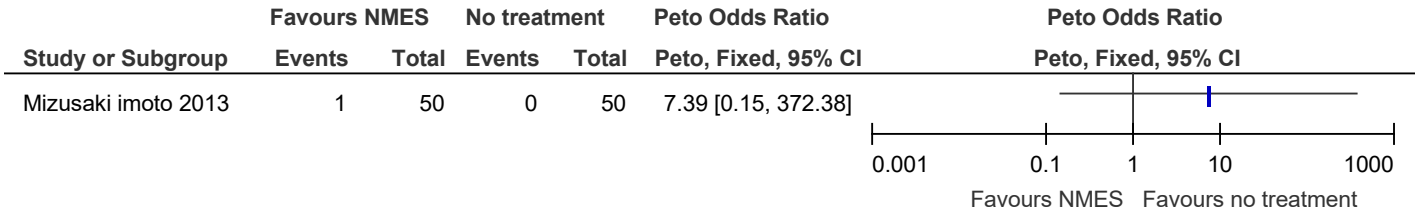


Figure 69: Mild adverse events at ≤3 months



E.4 Extracorporeal shockwave therapy

E.4.1 Extracorporeal shockwave therapy compared to sham electrotherapy

Figure 70: Pain (WOMAC, 0-20, high is poor, change score and final values) at ≤3 months

	ESWT			Sham electrotherapy				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Wang 2020	2.1	1	36	5.6	2.4	36	45.6%	-3.50 [-4.35, -2.65]
Zhao 2013	-4.5	2.7	34	-2.2	3.1	36	17.8%	-2.30 [-3.66, -0.94]
Zhong 2019	2.4	1.4	29	5.1	2.2	29	36.6%	-2.70 [-3.65, -1.75]
Total (95% CI)			**99**			**101**	**100.0%**	**-2.99 [-3.57, -2.42]**

Heterogeneity: Chi² = 2.73, df = 2 (P = 0.26); I² = 27%

Test for overall effect: Z = 10.23 (P < 0.00001)

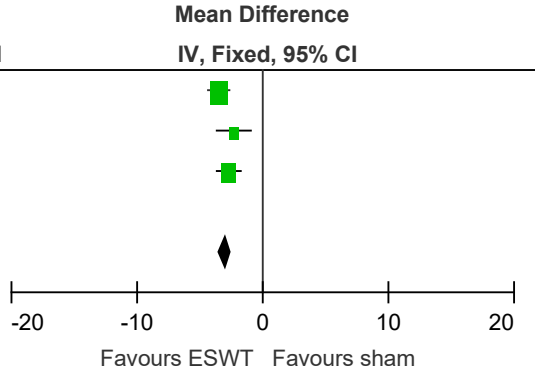


Figure 71: Pain (VAS, 0-10, high is poor, change score and final value) at ≤3 months

	ESWT			Sham electrotherapy				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Cho 2016	2.7	1.4	9	4.1	1.7	9	45.5%	-1.40 [-2.84, 0.04]
Zhang 2021	-3.504	2.45	75	-0.69	1.97	14	54.5%	-2.81 [-3.99, -1.64]
Total (95% CI)			**84**			**23**	**100.0%**	**-2.17 [-3.55, -0.79]**

Heterogeneity: Tau² = 0.55; Chi² = 2.23, df = 1 (P = 0.14); I² = 55%

Test for overall effect: Z = 3.08 (P = 0.002)

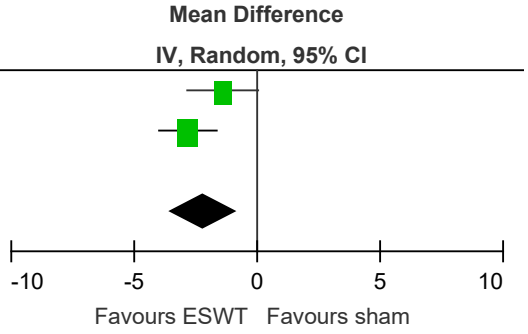


Figure 72: Physical function (WOMAC, 0-68, high is poor, change score and final values) at ≤3 months

Study or Subgroup	ESWT Mean	SD	Total	Sham electrotherapy Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Wang 2020	10.1	4.9	36	19.4	8.8	36	38.6%	-9.30 [-12.59, -6.01]
Zhao 2013	-13.9	9.8	34	-6	9.8	36	19.8%	-7.90 [-12.49, -3.31]
Zhong 2019	7.9	4.9	29	17.3	7.2	29	41.6%	-9.40 [-12.57, -6.23]
Total (95% CI)			**99**			**101**	**100.0%**	**-9.06 [-11.11, -7.02]**

Heterogeneity: Chi² = 0.31, df = 2 (P = 0.86); I² = 0%

Test for overall effect: Z = 8.69 (P < 0.00001)

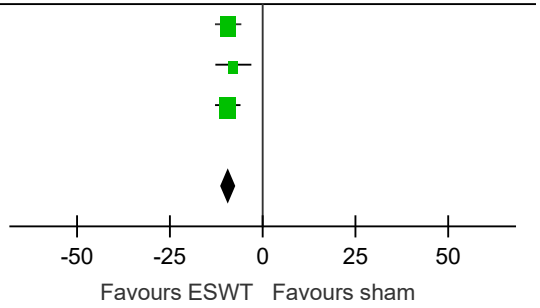


Figure 73: Mild adverse events at ≤3 months

Study or Subgroup	ESWT Events	Total	Sham electrotherapy Events	Total	Risk Difference M-H, Fixed, 95% CI
Zhao 2013	0	34	2	36	-0.06 [-0.15, 0.03]

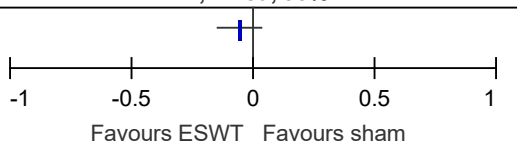
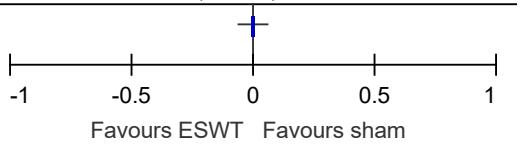


Figure 74: Moderate/major adverse events at ≤3 months

Study or Subgroup	ESWT Events	ESWT Total	Sham electrotherapy Events	Sham electrotherapy Total	Risk Difference M-H, Fixed, 95% CI
Zhong 2019	0	32	0	31	0.00 [-0.06, 0.06]



E.4.2 Extracorporeal shockwave therapy compared to no treatment

Figure 75: Pain (WOMAC, VAS [different scale ranges], high is poor, final values) at ≤3 months

Study or Subgroup	ESWT Mean	ESWT SD	ESWT Total	No treatment Mean	No treatment SD	No treatment Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Eftekharsadat 2019	12.3	4.84	23	10.61	4.91	22	66.9%	0.34 [-0.25, 0.93]
Gunaydin 2020	4.13	2.36	8	2.74	2.16	20	33.1%	0.61 [-0.23, 1.45]
Total (95% CI)			**31**			**42**	**100.0%**	**0.43 [-0.05, 0.91]**

Heterogeneity: Chi² = 0.26, df = 1 (P = 0.61); I² = 0%

Test for overall effect: Z = 1.75 (P = 0.08)

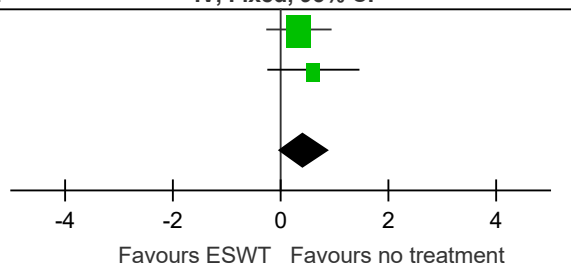
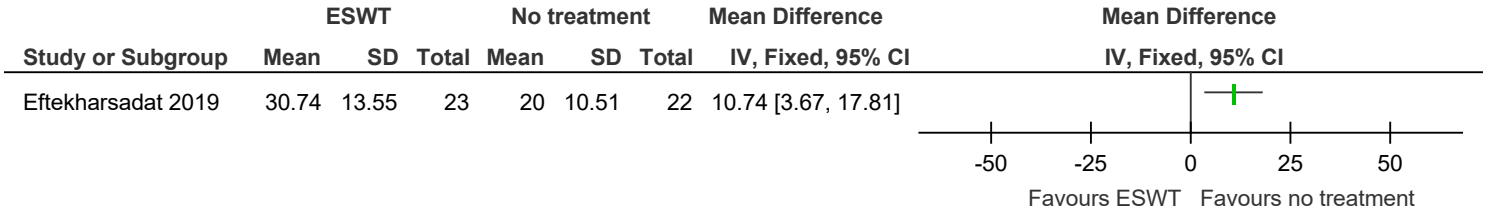


Figure 76: Physical function (WOMAC, 0-68, high is poor, final score) at ≤3 months



E.5 Laser therapy

E.5.1 Laser therapy compared to pulsed short-wave therapy

Figure 77: Pain (WOMAC, 0-20, high is poor, final value) at ≤3 months

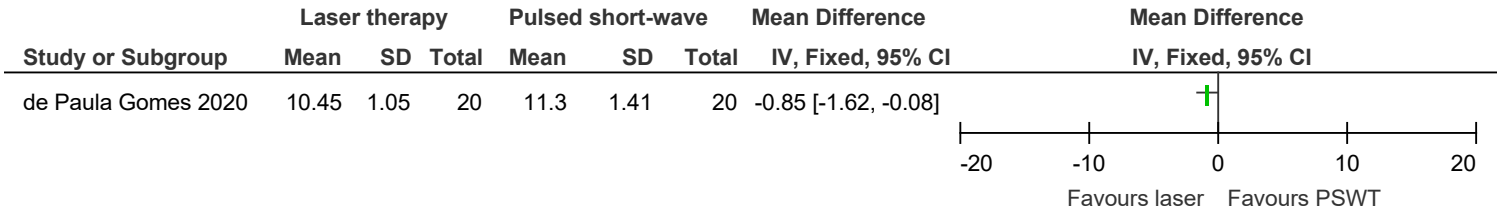
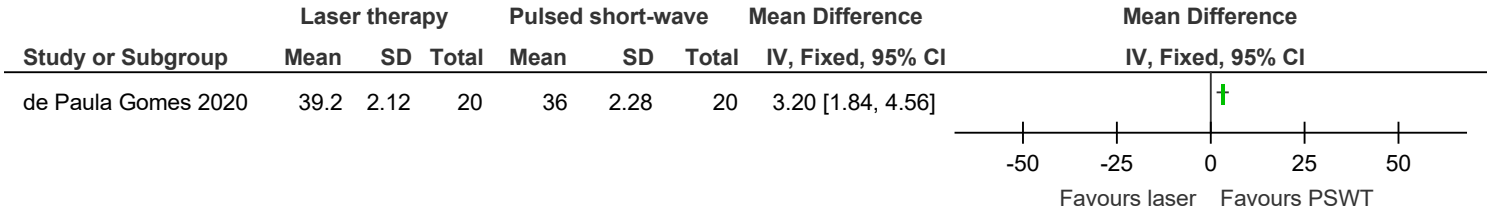
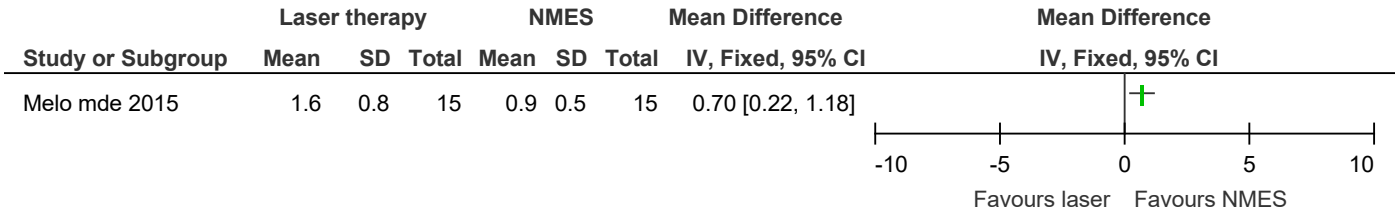


Figure 78: Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months



E.5.2 Laser therapy compared to neuromuscular electrical stimulation

Figure 79: Pain (VAS, 0-10, high is poor, final value) at ≤3 months



E.5.3 Laser therapy compared to sham electrotherapy

Figure 80: Quality of life (KOOS, NHP [different scale ranges], high is good, final values) at ≤3 months

	Laser therapy			Sham electrotherapy			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Fixed, 95% CI**
Hsieh 2012	61.3	13.3	37	61.4	14.7	35	56.8%	-0.01 [-0.47, 0.46]
Yurtkuran 2007	7.58	5.41	28	6.44	6.27	27	43.2%	0.19 [-0.34, 0.72]
Total (95% CI)			**65**			**62**	**100.0%**	**0.08 [-0.27, 0.43]**

Heterogeneity: Chi² = 0.31, df = 1 (P = 0.58); I² = 0%

Test for overall effect: Z = 0.44 (P = 0.66)

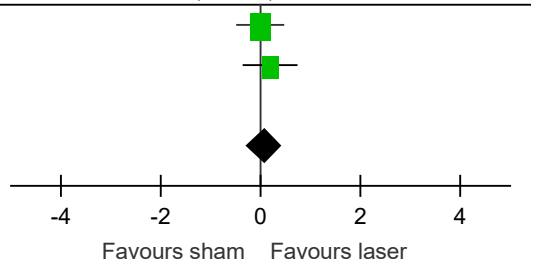


Figure 81: Quality of life (SF-36 physical component, 0-50, high is good, change score) at ≤3 months

	Laser therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**IV, Fixed, 95% CI**	**IV, Fixed, 95% CI**
Mahler 2019	0.1	7	27	2.4	6.9	28	-2.30 [-5.97, 1.37]	

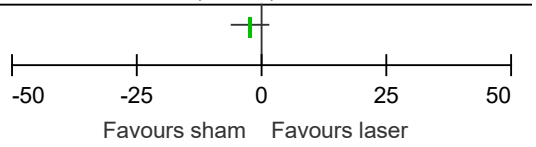


Figure 82: Quality of life (SF-36 mental component, 0-50, high is good, change score) at ≤3 months

	Laser therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Mahler 2019	0.9	9.4	27	-4.2	10	28	5.10 [-0.03, 10.23]	

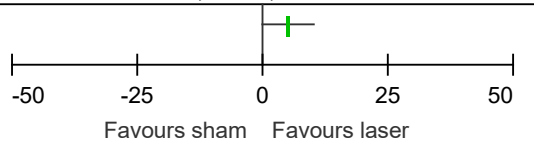


Figure 83: Quality of life (SF-12 physical component, 0-100, high is good, final value) at ≤3 months

	Laser therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Hinman 2014	39.4	9.5	65	40.2	10.1	58	-0.80 [-4.28, 2.68]	

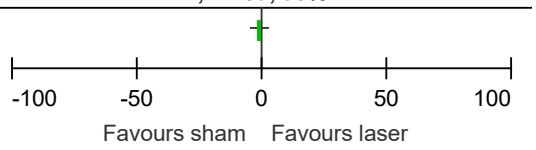


Figure 84: Quality of life (SF-12 mental component, 0-100, high is good, final value) at ≤3 months

	Laser therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Hinman 2014	53	9.9	65	53.2	10.4	58	-0.20 [-3.80, 3.40]	

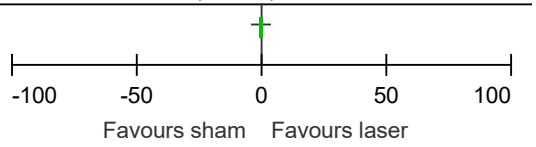


Figure 85: Quality of life (SF-12 physical component, 0-100, high is good, final value) at >3 months

	Laser therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Hinman 2014	38.8	10.2	58	38.2	9.9	51	0.60 [-3.18, 4.38]	

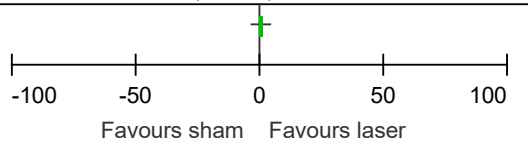


Figure 86: Quality of life (SF-12 mental component, 0-100, high is good, final value) at >3 months

	Laser therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Hinman 2014	52.1	9.8	58	52.8	9.1	51	-0.70 [-4.25, 2.85]	

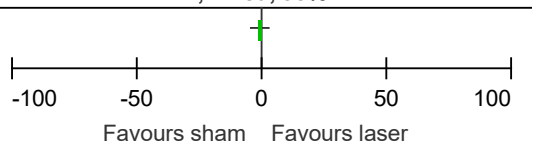


Figure 87: Pain (WOMAC, AUSCAN, VAS [different scale ranges], high is poor, change scores) at ≤3 months

	Laser therapy			Sham electrotherapy				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Brosseau 2005	-0.48	0.71	41	-0.29	0.71	45	25.6%	-0.27 [-0.69, 0.16]
Gworys 2012	-2.3	1.6	94	-1.5	1	31	25.7%	-0.54 [-0.95, -0.13]
Helianthi 2016	-40.5	14.8	31	-1.3	6	31	23.5%	-3.43 [-4.23, -2.63]
Mahler 2019	-8	13	27	-11	14	28	25.1%	0.22 [-0.31, 0.75]
Total (95% CI)			**193**			**135**	**100.0%**	**-0.96 [-2.09, 0.18]**

Heterogeneity: Tau² = 1.26; Chi² = 59.77, df = 3 (P < 0.00001); I² = 95%

Test for overall effect: Z = 1.65 (P = 0.10)

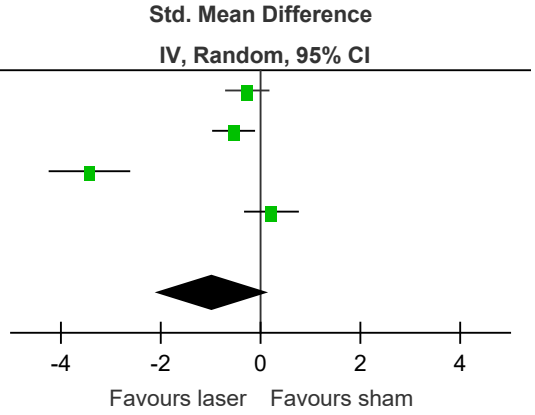


Figure 88: Pain (KOOS, WOMAC, VNPS, VAS [different scale ranges], high is poor, final values) at ≤3 months

	Laser therapy			Sham electrotherapy				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Alfredo 2012	4.8	4.36	20	6.35	3.48	20	6.7%	-0.39 [-1.01, 0.24]
Alghadir 2014	3.25	2.61	20	5.5	2.5	20	6.4%	-0.86 [-1.51, -0.21]
Alqualo-Costa 2020	3.15	2.8004	42	3.85	2.921	42	8.6%	-0.24 [-0.67, 0.19]
Cantero-Tellez 2019	5.6	1	18	5.8	1.1	17	6.3%	-0.19 [-0.85, 0.48]
de Paula Gomes 2020	10.45	1.05	20	10.9	1.55	20	6.7%	-0.33 [-0.96, 0.29]
Fukuda 2011B	4.4	2.9	25	5.3	2.8	22	7.1%	-0.31 [-0.89, 0.27]
Gur 2003	3.69	1	60	4.3	1.38	30	8.5%	-0.53 [-0.98, -0.09]
Hinman 2014	6.6	3.9	65	6.6	3.9	58	9.4%	0.00 [-0.35, 0.35]
Hsieh 2012	79.2	12	37	77.5	14	35	8.3%	0.13 [-0.33, 0.59]
Kheshie 2014	3.92	1.39	36	6.26	1.22	12	5.7%	-1.70 [-2.45, -0.96]
Madani 2014	1.5	2.3	10	1.6	2.2	10	4.7%	-0.04 [-0.92, 0.83]
Marquina 2012	2.8	2.4	53	4.6	2.6	48	8.9%	-0.72 [-1.12, -0.31]
Shen 2009	3.8	3.1	18	2.5	2.6	9	5.2%	0.43 [-0.38, 1.24]
Yurtkuran 2007	13.47	5.84	28	11.5	5.99	27	7.6%	0.33 [-0.20, 0.86]
Total (95% CI)			**452**			**370**	**100.0%**	**-0.31 [-0.55, -0.06]**

Heterogeneity: Tau² = 0.14; Chi² = 36.73, df = 13 (P = 0.0005); I² = 65%

Test for overall effect: Z = 2.45 (P = 0.01)

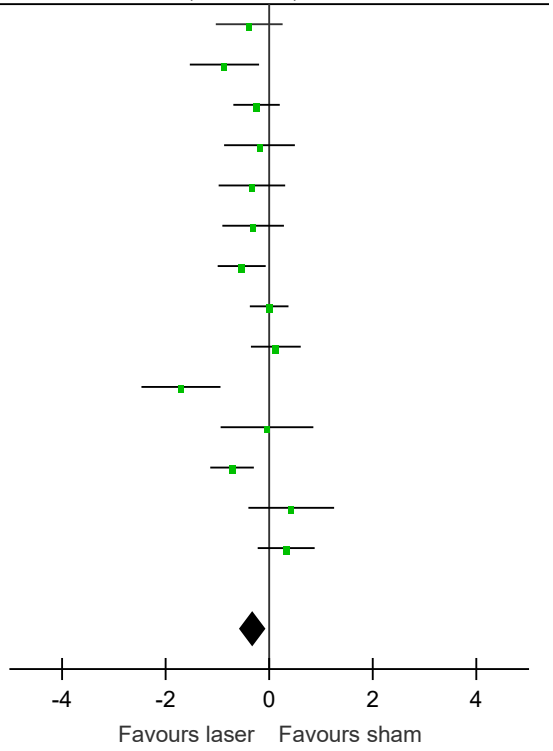


Figure 89: Pain (AUSCAN, 0-4, high is poor, change score) at >3 months

	Laser therapy			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Brosseau 2005	-0.41	0.83	41	-0.35	0.71	45	-0.06 [-0.39, 0.27]	

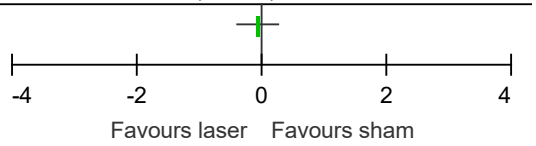


Figure 90: Pain (WOMAC, NRS [different scale ranges], high is poor, final values) >3 months

	Laser therapy			Sham electrotherapy			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Alfredo 2012	5.3	4.68	20	5.35	4.38	20	17.3%	-0.01 [-0.63, 0.61]	
Alqualo-Costa 2020	2.95	2.5323	42	4.1	3.1064	42	35.6%	-0.40 [-0.83, 0.03]	
Hinman 2014	7.1	4.1	58	6.9	4	51	47.0%	0.05 [-0.33, 0.43]	
Total (95% CI)			**120**			**113**	**100.0%**	**-0.12 [-0.38, 0.14]**	

Heterogeneity: Chi² = 2.53, df = 2 (P = 0.28); I² = 21%

Test for overall effect: Z = 0.93 (P = 0.35)

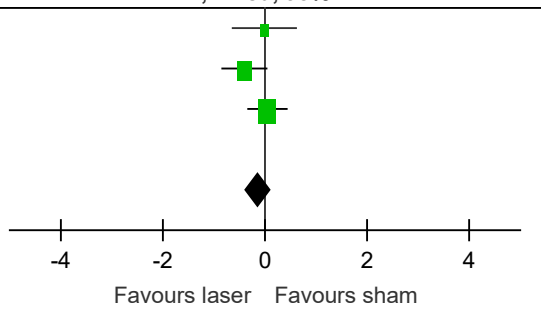


Figure 91: Physical function (WOMAC, AUSCAN [different scale ranges], high is poor, change score) at ≤3 months

	Laser therapy			Sham electrotherapy				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Brosseau 2005	-0.35	0.71	41	-0.31	0.82	45	61.2%	-0.05 [-0.47, 0.37]
Mahler 2019	-9.7	8	27	-6.3	14	28	38.8%	-0.29 [-0.82, 0.24]
Total (95% CI)			**68**			**73**	**100.0%**	**-0.15 [-0.48, 0.19]**

Heterogeneity: Chi² = 0.48, df = 1 (P = 0.49); I² = 0%

Test for overall effect: Z = 0.86 (P = 0.39)

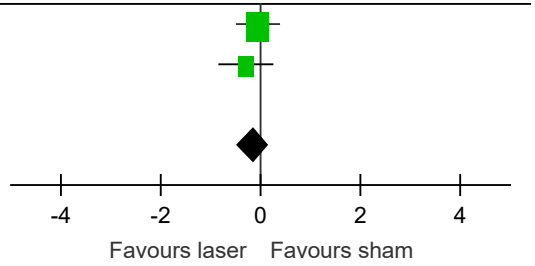


Figure 92: Physical function (KOOS, WOMAC [different scale ranges], high is poor, final values) at ≤3 months

	Laser therapy			Sham electrotherapy				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Alfredo 2012	19.5	14.04	20	23.35	12.18	20	12.4%	-0.29 [-0.91, 0.34]
Alghadir 2014	10	7.39	20	18.2	9	20	12.2%	-0.98 [-1.64, -0.32]
de Paula Gomes 2020	39.2	2.12	20	41.35	2.96	20	12.2%	-0.82 [-1.47, -0.17]
Hinman 2014	21.9	12.3	65	21.7	12	58	14.1%	0.02 [-0.34, 0.37]
Hsieh 2012	78.9	15.5	37	76.5	16.1	35	13.4%	0.15 [-0.31, 0.61]
Kheshie 2014	15.3	2.48	38	20.6	2.44	15	11.7%	-2.11 [-2.84, -1.39]
Shen 2009	13.8	11.2	18	10	6.8	9	11.1%	0.37 [-0.44, 1.18]
Yurtkuran 2007	44.24	15.83	28	35.25	16.64	27	13.0%	0.55 [0.01, 1.09]
Total (95% CI)			**246**			**204**	**100.0%**	**-0.37 [-0.89, 0.16]**

Heterogeneity: Tau² = 0.48; Chi² = 48.24, df = 7 (P < 0.00001); I² = 85%

Test for overall effect: Z = 1.36 (P = 0.17)

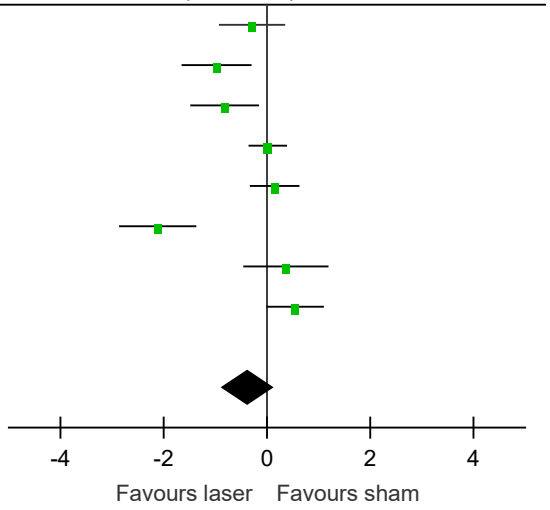


Figure 93: Physical function (AUSCAN, 0-4, high is poor, change score) at >3 months

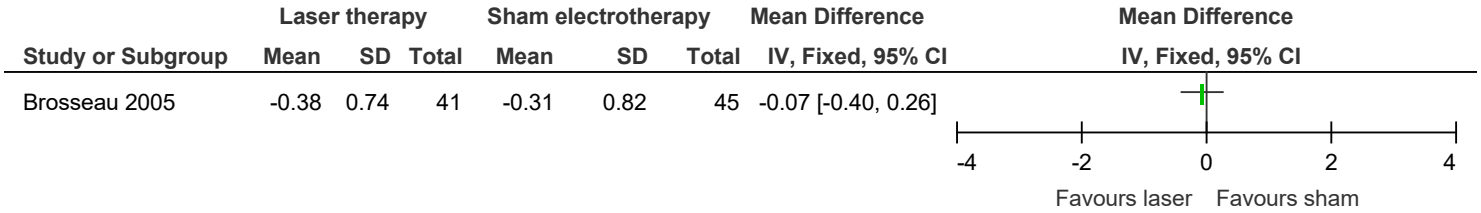


Figure 94: Physical function (WOMAC, 0-68, high is poor, final values) at >3 months

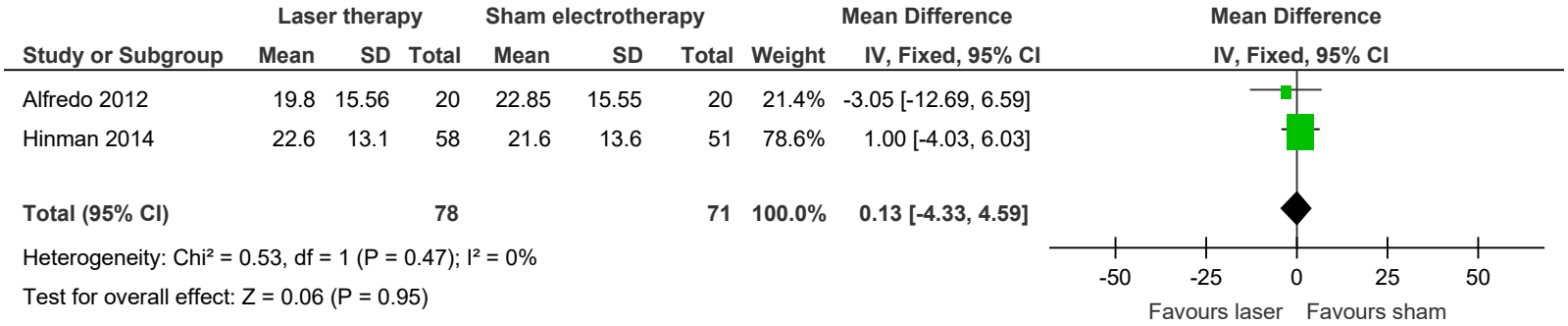


Figure 95: Mild adverse events at ≤3 months

Study or Subgroup	Laser therapy Events	Total	Sham electrotherapy Events	Total	Weight	Risk Difference M-H, Fixed, 95% CI
Basford 1987	1	47	1	34	35.1%	-0.01 [-0.08, 0.06]
Brosseau 2005	2	31	0	33	28.4%	0.06 [-0.04, 0.17]
Bulow 1994	0	13	0	14	12.0%	0.00 [-0.13, 0.13]
Mahler 2019	7	27	5	28	24.5%	0.08 [-0.14, 0.30]
Total (95% CI)		**118**		**109**	**100.0%**	**0.04 [-0.03, 0.10]**
Total events	10		6			

Heterogeneity: Chi² = 2.22, df = 3 (P = 0.53); I² = 0%

Test for overall effect: Z = 1.02 (P = 0.31)

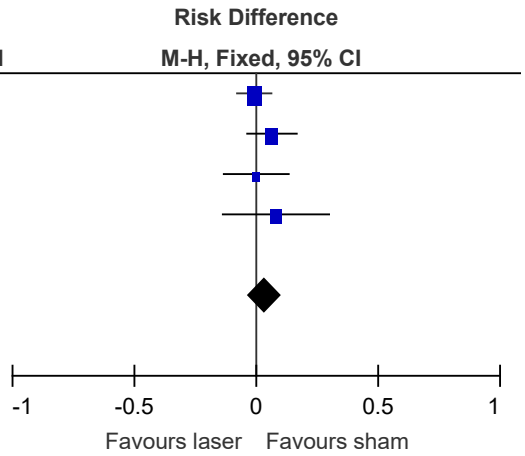


Figure 96: Mild adverse event at >3 months

Study or Subgroup	Laser therapy Events	Total	Sham electrotherapy Events	Total	Risk Difference M-H, Fixed, 95% CI
Brosseau 2005	0	32	0	34	0.00 [-0.06, 0.06]

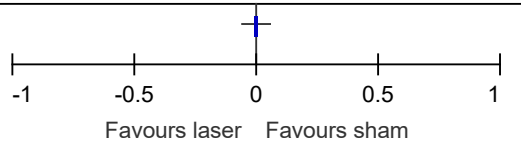
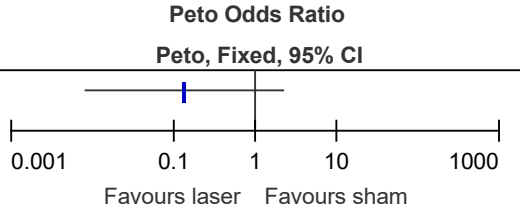


Figure 97: Moderate/major adverse events at ≤3 months

Study or Subgroup	Laser therapy Events	Laser therapy Total	Sham electrotherapy Events	Sham electrotherapy Total	Peto Odds Ratio Peto, Fixed, 95% CI
Mahler 2019	0	27	2	28	0.14 [0.01, 2.22]



E.5.4 Laser therapy compared to no treatment

Figure 98: Quality of life (SF-12 physical component, 0-100, high is good, final value) at ≤3 months

Study or Subgroup	Laser therapy Mean	SD	Total	No treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Hinman 2014	39.4	9.5	65	39.5	10.7	69	-0.10 [-3.52, 3.32]

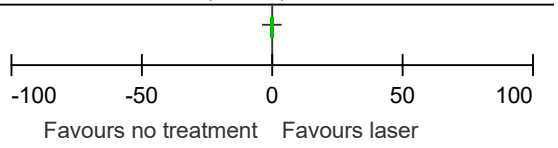


Figure 99: Quality of life (SF-12 mental component, 0-100, high is good, final value) at ≤3 months

Study or Subgroup	Laser therapy Mean	SD	Total	No treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Hinman 2014	53	9.9	65	55.8	9.1	69	-2.80 [-6.03, 0.43]

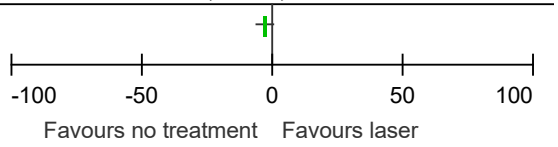


Figure 100: Quality of life (SF-12 physical component, 0-100, high is good, final value) at >3 months

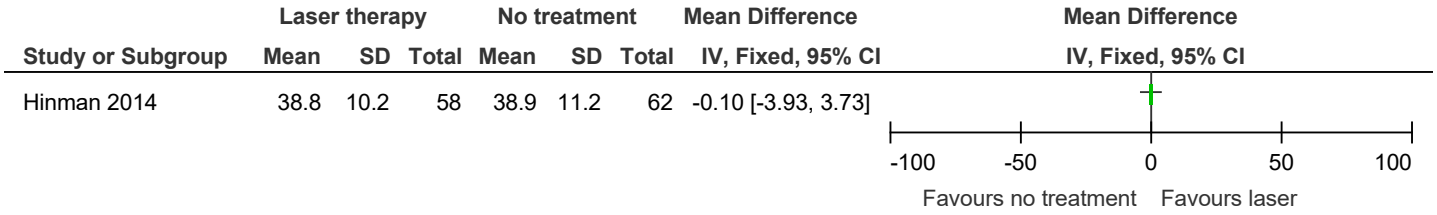


Figure 101: Quality of life (SF-12 mental component, 0-100, high is good, final value) at >3 months

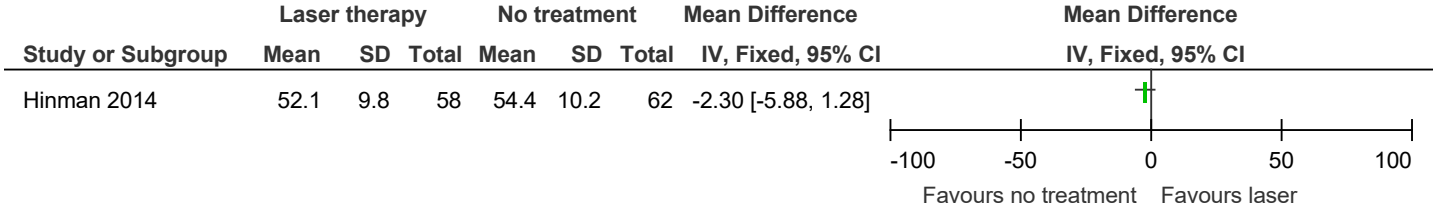


Figure 102: Pain (WOMAC [different scale ranges], high is poor, final values) at ≤3 months

Study or Subgroup	Laser therapy Mean	SD	Total	No treatment Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Alayat 2017	4.77	0.92	23	4.14	0.71	22	23.6%	0.75 [0.14, 1.36]
De matos brunelli braghin 2018	15.67	18.87	30	15.17	19.75	30	25.6%	0.03 [-0.48, 0.53]
de Paula Gomes 2020	10.45	1.05	20	9	1.41	20	22.3%	1.14 [0.47, 1.82]
Hinman 2014	6.6	3.9	65	7.3	3.9	69	28.5%	-0.18 [-0.52, 0.16]
Total (95% CI)			**138**			**141**	**100.0%**	**0.39 [-0.20, 0.98]**

Heterogeneity: Tau² = 0.29; Chi² = 15.90, df = 3 (P = 0.001); I² = 81%

Test for overall effect: Z = 1.29 (P = 0.20)

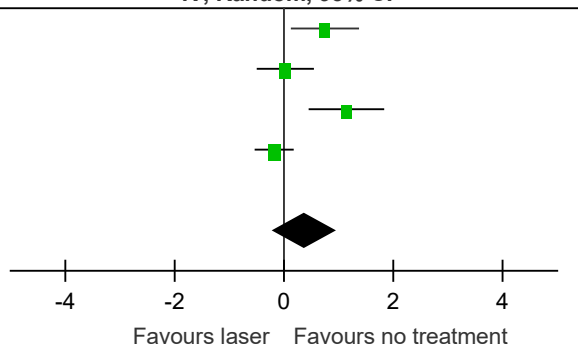


Figure 103: Pain (WOMAC, 0-20, high is poor, final value) at >3 months

Study or Subgroup	Laser therapy Mean	SD	Total	No treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Hinman 2014	7.1	4.1	58	7.4	4.1	62	-0.30 [-1.77, 1.17]

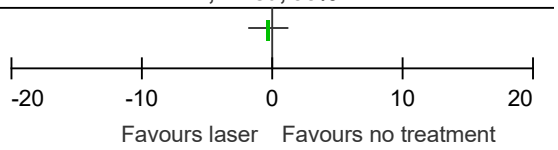


Figure 104: Physical function (WOMAC [different scale ranges], high is poor, final values) at ≤3 months

Study or Subgroup	Laser therapy Mean	SD	Total	No treatment Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Alayat 2017	14.78	1.2	23	21.82	1.8	22	22.0%	-4.54 [-5.68, -3.40]
De matos brunelli braghin 2018	9.12	13.58	30	10.89	17.01	30	26.0%	-0.11 [-0.62, 0.39]
de Paula Gomes 2020	39.2	2.12	20	38.9	3.72	20	25.4%	0.10 [-0.52, 0.72]
Hinman 2014	21.9	12.3	65	21.7	12	69	26.6%	0.02 [-0.32, 0.36]
Total (95% CI)			**138**			**141**	**100.0%**	**-1.00 [-2.23, 0.23]**

Heterogeneity: Tau² = 1.46; Chi² = 57.96, df = 3 (P < 0.00001); I² = 95%

Test for overall effect: Z = 1.59 (P = 0.11)

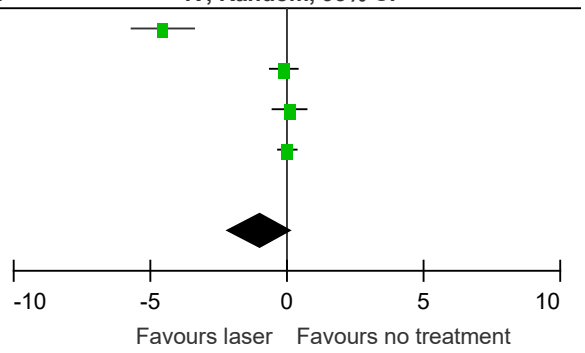
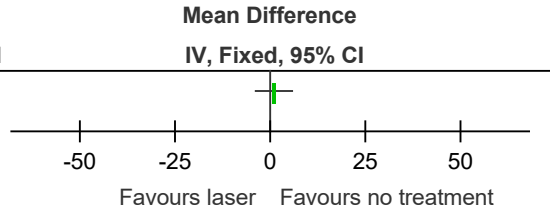


Figure 105: Physical function (WOMAC, 0-68, high is poor, final value) at >3 months

Study or Subgroup	Laser therapy Mean	SD	Total	No treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Hinman 2014	22.6	13.1	58	21.6	13.6	62	1.00 [-3.78, 5.78]



E.6 Transcutaneous electrical nerve stimulation

E.6.1 Transcutaneous electrical nerve stimulation compared to pulsed short-wave therapy

Figure 106: Pain (WOMAC, VAS [different scale ranges], high is poor, change score) at ≤3 months

	TENS			Pulsed-short wave therapy				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Atamaz 2012	-3.6	3	37	-4.9	4	32	62.8%	0.37 [-0.11, 0.84]
Cetin 2008	-2.32	0.6	20	-2.33	0.77	20	37.2%	0.01 [-0.61, 0.63]
Total (95% CI)			**57**			**52**	**100.0%**	**0.24 [-0.14, 0.61]**

Heterogeneity: Chi² = 0.78, df = 1 (P = 0.38); I² = 0%

Test for overall effect: Z = 1.22 (P = 0.22)

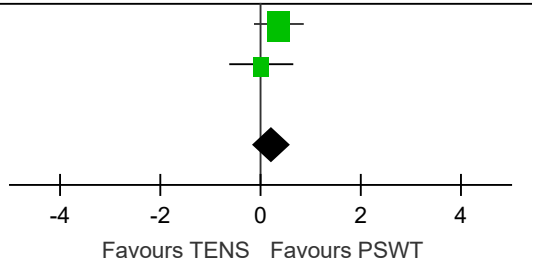


Figure 107: Pain (WOMAC, 0-20, high is poor, change score) at >3 months

	TENS			Pulsed-short wave therapy			Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI
Atamaz 2012	-3	3.1	37	-4.5	4	32	1.50 [-0.21, 3.21]

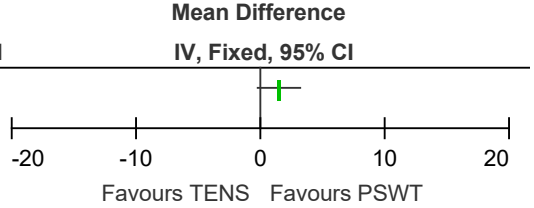


Figure 108: Physical function (WOMAC, 0-68, high is poor, change score) at ≤3 months

	TENS			Pulsed-short wave therapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Atamaz 2012	-8.7	11.6	37	-11.4	12.4	32	2.70 [-2.99, 8.39]	

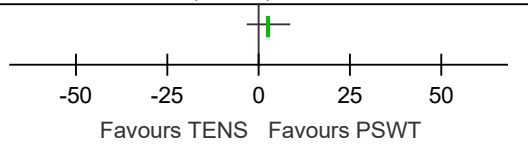
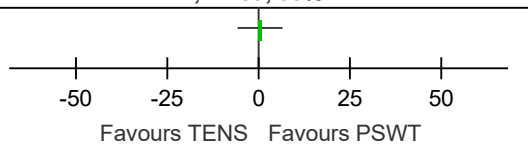


Figure 109: Physical function (WOMAC, 0-68, high is poor, change score) at >3 months

	TENS			Pulsed-short wave therapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Atamaz 2012	-9.5	11.5	37	-9.9	13.2	32	0.40 [-5.49, 6.29]	



E.6.2 Transcutaneous electrical nerve stimulation compared to interferential therapy

Figure 110: Pain (WOMAC, 0-20, high is poor, change scores) at ≤3 months

Study or Subgroup	Mean Difference	SE	TENS Total	Interferential therapy Total	Weight	Mean Difference IV, Random, 95% CI
Atamaz 2012	0.3	0.7438	37	31	47.6%	0.30 [-1.16, 1.76]
Burch 2008	2.02	0.64	53	52	52.4%	2.02 [0.77, 3.27]
Total (95% CI)			**90**	**83**	**100.0%**	**1.20 [-0.48, 2.89]**

Heterogeneity: Tau² = 1.00; Chi² = 3.07, df = 1 (P = 0.08); I² = 67%

Test for overall effect: Z = 1.40 (P = 0.16)

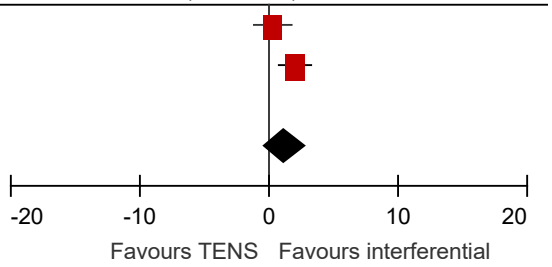


Figure 111: Pain (WOMAC, 0-20, high is poor, change score) at >3 months

Study or Subgroup	TENS Mean	SD	Total	Interferential therapy Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Atamaz 2012	3.7	3.7	37	3.4	3.4	31	0.30 [-1.39, 1.99]

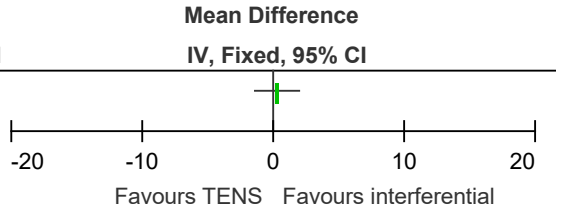


Figure 112: Physical function (WOMAC, 0-68, high is poor, change scores) at ≤3 months

	TENS			Interferential therapy			Mean Difference	Mean Difference
Study or Subgroup	Mean Difference	SE	Total	Total	Weight		IV, Random, 95% CI	IV, Random, 95% CI
Atamaz 2012	0.6	2.7589	37	31	44.1%		0.60 [-4.81, 6.01]	
Burch 2008	6.12	2.01	53	52	55.9%		6.12 [2.18, 10.06]	
Total (95% CI)			**90**	**83**	**100.0%**		**3.68 [-1.69, 9.06]**	

Heterogeneity: Tau² = 9.41; Chi² = 2.62, df = 1 (P = 0.11); I² = 62%

Test for overall effect: Z = 1.34 (P = 0.18)

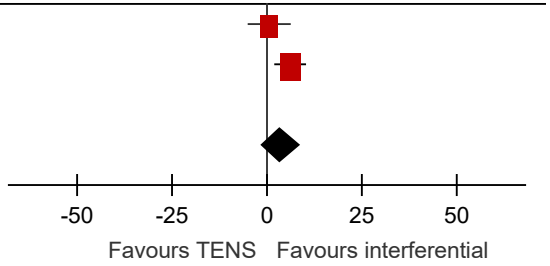


Figure 113: Physical function (WOMAC, 0-68, high is poor, change score) at >3 months

	TENS			Interferential therapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Atamaz 2012	9.5	11.5	37	8.5	11.1	31	1.00 [-4.39, 6.39]	

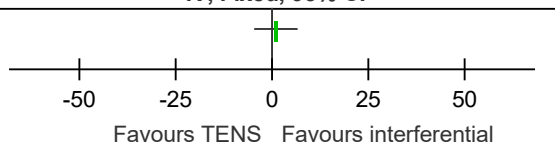
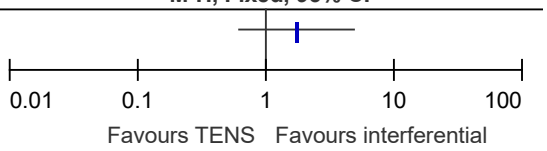


Figure 114: Mild adverse events at ≤3 months

	TENS		Interferential therapy		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Burch 2008	9	59	5	57	1.74 [0.62, 4.88]	



E.6.3 Transcutaneous electrical nerve stimulation compared to sham electrotherapy

Figure 115: Quality of life (SF-36 physical function, 0-1, high is good, final value) at ≤3 months

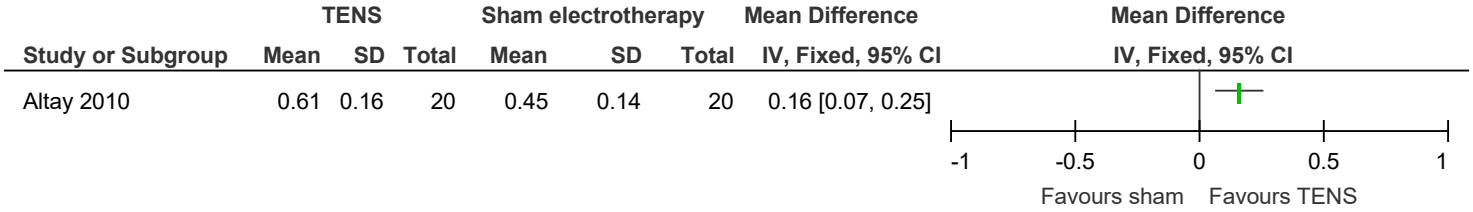


Figure 116: Quality of life (SF-36 vitality, 0-1, high is good, final value) at ≤3 months

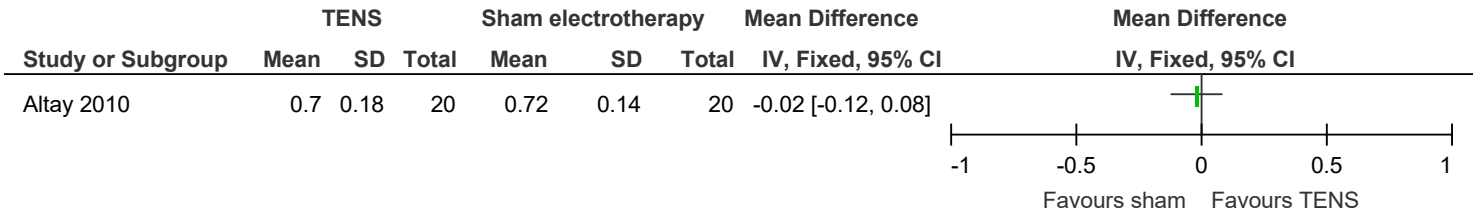


Figure 117: Quality of life (SF-36 general health, 0-1, high is good, final value) at ≤3 months

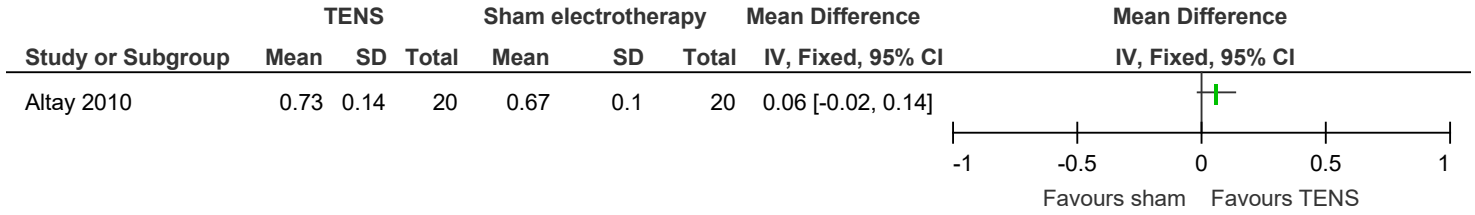


Figure 118: Quality of life (SF-36 mental health, 0-1, high is good, final value) at ≤3 months

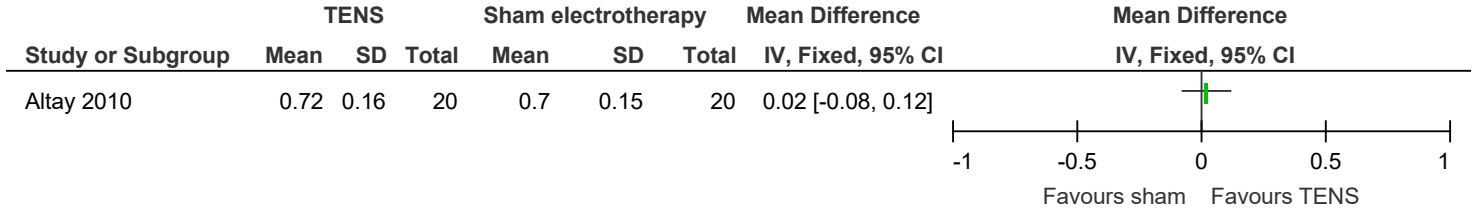


Figure 119: Quality of life (SF-36 social function, 0-1, high is good, final value) at ≤3 months

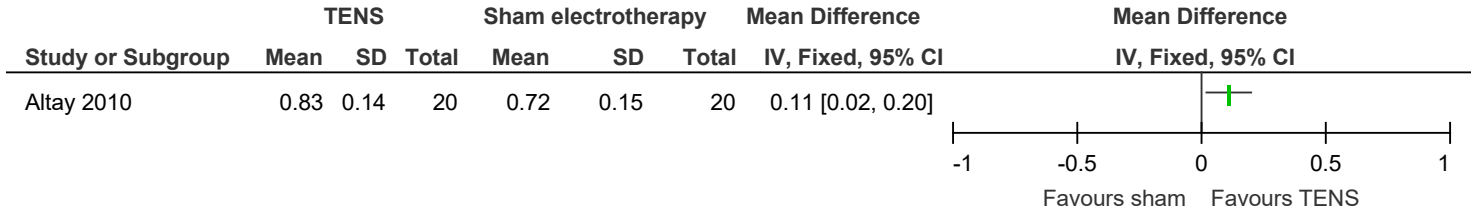


Figure 120: Pain (WOMAC, 0-20, high is poor, change score) at ≤3 months

	TENS			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Atamaz 2012	2.8	3.4	37	3.6	3	37	-0.80 [-2.26, 0.66]	

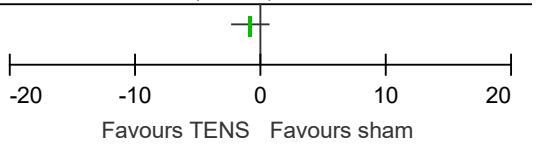


Figure 121: Pain (WOMAC, VAS [different scale ranges], high is poor, final values) at ≤3 months

	TENS			Sham electrotherapy			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Inal 2016	6.5	4.8	60	7.1	4.7	30	23.1%	-0.12 [-0.56, 0.31]	
Law 2004	1.4	1.8	38	4.4	3	10	16.0%	-1.41 [-2.17, -0.66]	
Palmer 2014	7	7.8	73	7	7	74	25.7%	0.00 [-0.32, 0.32]	
Pietrosimone 2011	10	3	12	12.3	3.9	12	14.7%	-0.64 [-1.46, 0.19]	
Pietrosimone 2020	29.3	21.6	30	26.5	15.2	22	20.4%	0.14 [-0.41, 0.69]	
Total (95% CI)			**213**			**148**	**100.0%**	**-0.32 [-0.76, 0.13]**	

Heterogeneity: Tau² = 0.17; Chi² = 13.95, df = 4 (P = 0.007); I² = 71%

Test for overall effect: Z = 1.41 (P = 0.16)

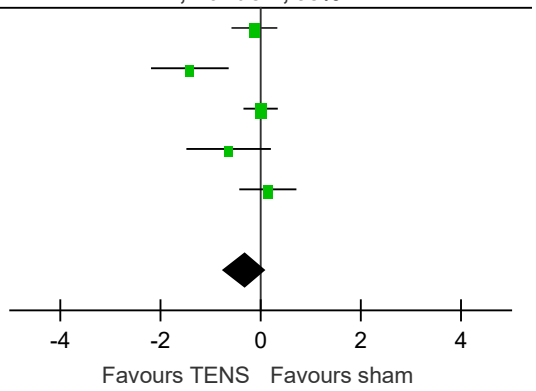


Figure 122: Pain (WOMAC, 0-20, high is poor, change score and final value) at >3 months

	TENS			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Atamaz 2012	3.7	3.7	37	3	3.1	37	70.4%	0.70 [-0.86, 2.26]	
Palmer 2014	7	7.8	73	7	7	74	29.6%	0.00 [-2.40, 2.40]	
Total (95% CI)			**110**			**111**	**100.0%**	**0.49 [-0.81, 1.80]**	

Heterogeneity: Chi² = 0.23, df = 1 (P = 0.63); I² = 0%

Test for overall effect: Z = 0.74 (P = 0.46)

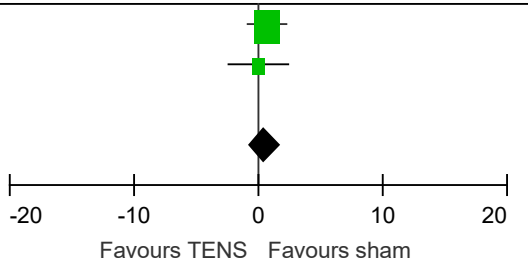


Figure 123: Physical function (WOMAC, 0-68, high is poor, change score) at ≤3 months

	TENS			Sham electrotherapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Atamaz 2012	8.7	11.6	37	9.4	10.7	37	-0.70 [-5.78, 4.38]	

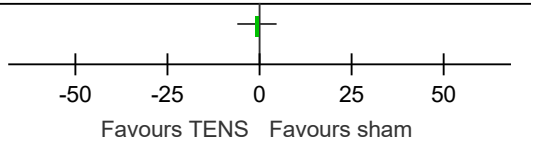


Figure 124: Physical function (WOMAC [different scale ranges], high is poor, final values) at ≤3 months

	TENS			Sham electrotherapy				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Inal 2016	24.8	15.6	60	25.7	14.1	30	28.7%	-0.06 [-0.50, 0.38]
Palmer 2014	25.3	14.1	73	25.7	14.1	74	36.1%	-0.03 [-0.35, 0.30]
Pietrosimone 2011	22.5	5.1	12	31.1	8.7	12	12.3%	-1.16 [-2.04, -0.29]
Pietrosimone 2020	30.3	17.5	30	30.2	17	22	22.9%	0.01 [-0.54, 0.56]
Total (95% CI)			**175**			**138**	**100.0%**	**-0.17 [-0.52, 0.18]**

Heterogeneity: Tau² = 0.06; Chi² = 6.01, df = 3 (P = 0.11); I² = 50%

Test for overall effect: Z = 0.94 (P = 0.35)

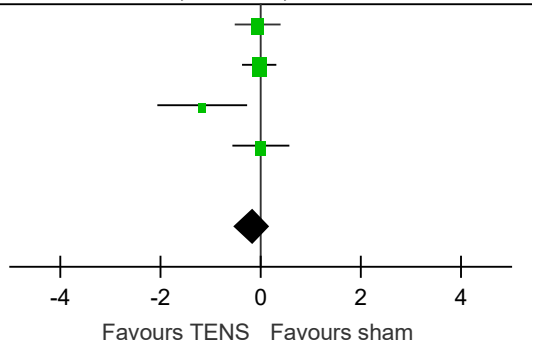


Figure 125: Physical function (WOMAC, 0-68, high is poor, change score and final value) at >3 months

	TENS			Sham electrotherapy				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Atamaz 2012	9.5	11.5	37	9.1	10.7	37	45.9%	0.40 [-4.66, 5.46]
Palmer 2014	25.8	13.8	73	25.3	15	74	54.1%	0.50 [-4.16, 5.16]
Total (95% CI)			**110**			**111**	**100.0%**	**0.45 [-2.97, 3.88]**

Heterogeneity: Chi² = 0.00, df = 1 (P = 0.98); I² = 0%

Test for overall effect: Z = 0.26 (P = 0.80)

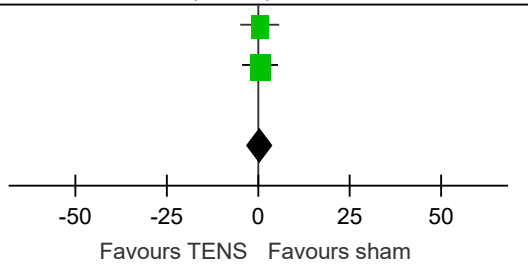
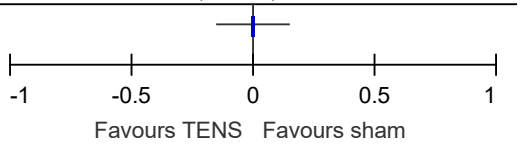


Figure 126: Mild adverse events at ≤3 months

Study or Subgroup	TENS Events	TENS Total	Sham electrotherapy Events	Sham electrotherapy Total	Risk Difference M-H, Fixed, 95% CI
Pietrosimone 2011	0	12	0	12	0.00 [-0.15, 0.15]



E.6.4 Transcutaneous electrical nerve stimulation compared to no treatment

Figure 127: Pain (VAS, 0-10, high is poor, change score) at ≤3 months

Study or Subgroup	TENS Mean	TENS SD	TENS Total	No treatment Mean	No treatment SD	No treatment Total	Mean Difference IV, Fixed, 95% CI
Cetin 2008	-2.32	0.6	20	-2.27	0.88	20	-0.05 [-0.52, 0.42]

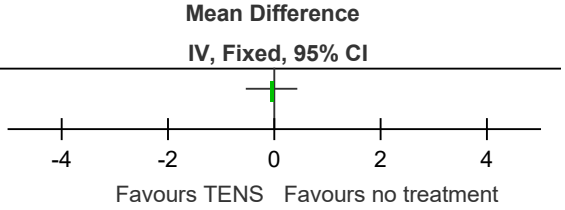


Figure 128: Pain (WOMAC [different scale ranges], high is poor, final values) at ≤3 months

	TENS			No treatment				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Mascarin 2012	3.3	2.9	12	2	2.3	16	27.5%	0.49 [-0.27, 1.25]
Pietrosimone 2011	10	3	12	11.8	4.8	12	24.9%	-0.43 [-1.25, 0.38]
Pietrosimone 2020	29.3	21.6	30	30.3	17.9	29	47.7%	-0.05 [-0.56, 0.46]
Total (95% CI)			**54**			**57**	**100.0%**	**0.00 [-0.45, 0.46]**

Heterogeneity: Tau² = 0.04; Chi² = 2.73, df = 2 (P = 0.25); I² = 27%

Test for overall effect: Z = 0.01 (P = 0.99)

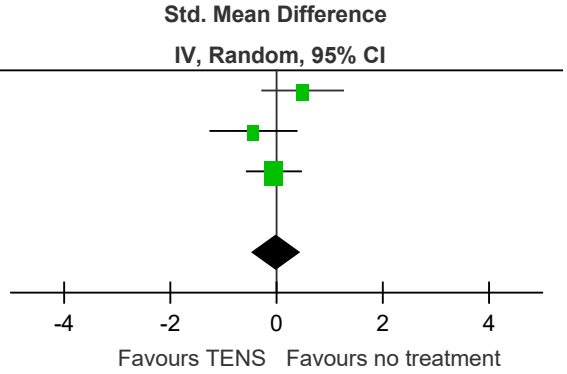


Figure 129: Physical function (WOMAC [different scale ranges], high is poor, final values) at ≤3 months

	TENS			No treatment				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Mascarin 2012	10.1	8.3	12	4.6	5.9	16	29.8%	0.76 [-0.02, 1.54]
Pietrosimone 2011	22.5	5.1	12	24.9	7.1	12	28.7%	-0.37 [-1.18, 0.43]
Pietrosimone 2020	30.3	17.5	30	31.9	14.4	29	41.5%	-0.10 [-0.61, 0.41]
Total (95% CI)			**54**			**57**	**100.0%**	**0.08 [-0.53, 0.68]**

Heterogeneity: Tau² = 0.16; Chi² = 4.59, df = 2 (P = 0.10); I² = 56%

Test for overall effect: Z = 0.25 (P = 0.80)

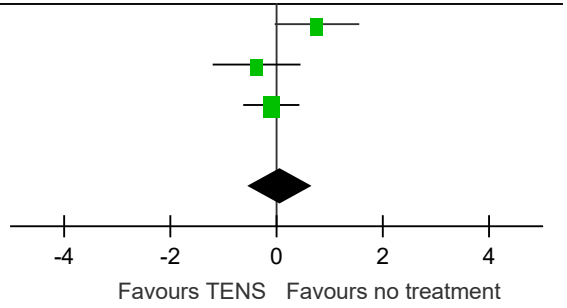
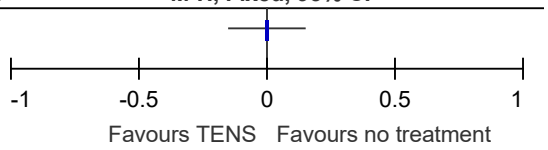


Figure 130: Mild adverse events at ≤3 months

Study or Subgroup	TENS Events	TENS Total	No treatment Events	No treatment Total	Risk Difference M-H, Fixed, 95% CI
Pietrosimone 2011	0	12	0	12	0.00 [-0.15, 0.15]

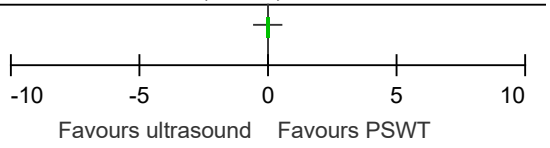


E.7 Ultrasound

E.7.1 Ultrasound compared to pulsed short-wave therapy

Figure 131: Pain (VAS, 0-10, high is poor, change score) at ≤3 months

Study or Subgroup	Ultrasound Mean	Ultrasound SD	Ultrasound Total	Pulsed short-wave therapy Mean	Pulsed short-wave therapy SD	Pulsed short-wave therapy Total	Mean Difference IV, Fixed, 95% CI
Cetin 2008	-2.34	0.94	20	-2.33	0.77	20	-0.01 [-0.54, 0.52]



E.7.2 Ultrasound compared to neuromuscular electrical stimulation

Figure 132: Pain (WOMAC, 0-20, high is poor, final value) at ≤3 months

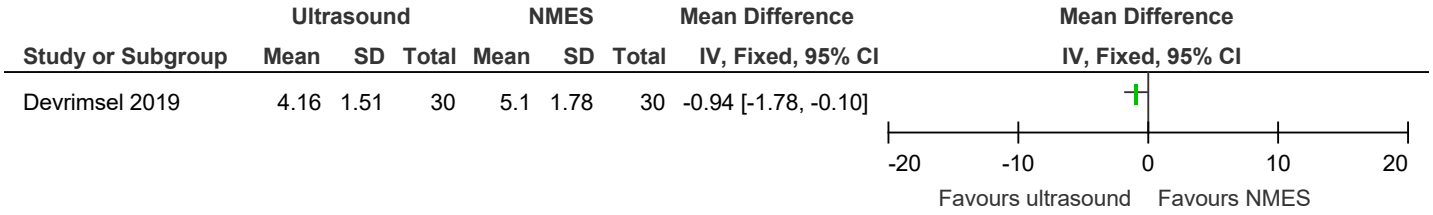
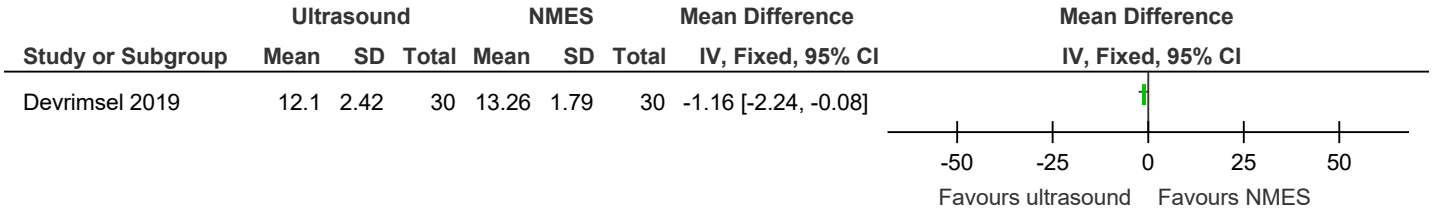


Figure 133: Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months



E.7.3 Ultrasound compared to transcutaneous electrical nerve stimulation

Figure 134: Pain (VAS, 0-10, high is poor, change score) at ≤3 months

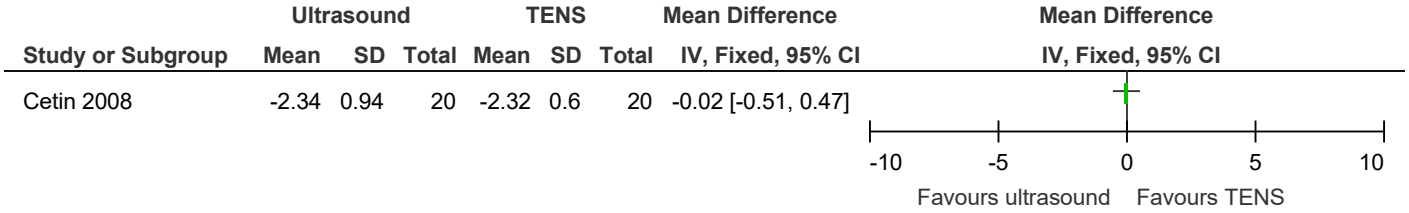


Figure 135: Pain (WOMAC, 0-20, high is poor, final value) at ≤3 months

	Ultrasound			TENS			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Mascarin 2012	6.2	4.2	12	3.2	2.9	12	3.00 [0.11, 5.89]	

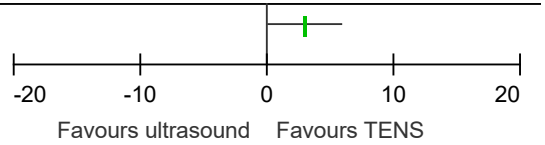
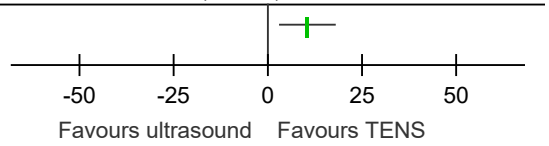


Figure 136: Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months

	Ultrasound			TENS			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Mascarin 2012	20.6	9.8	12	10.1	8.3	12	10.50 [3.23, 17.77]	



E.7.4 Ultrasound compared to sham electrotherapy

Figure 137: Quality of life (SF-36 physical function, 0-100, high is good, change score) at ≤3 months

	Ultrasound			Sham			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Jia 2016	26.9	13.32	49	15.4	12.32	48	11.50 [6.40, 16.60]	

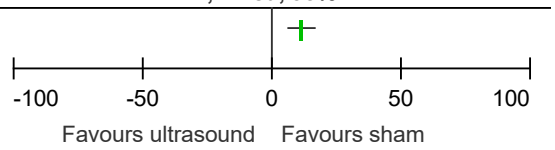


Figure 138: Quality of life (SF-36 bodily pain, 0-100, high is good, change score and final value) at ≤3 months

	Ultrasound			Sham				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Jia 2016	37.01	14.44	49	20.76	9.49	48	55.8%	16.25 [11.40, 21.10]	
Kiraly 2021	46.251	26.202	38	47.15	20.02	18	44.2%	-0.90 [-13.35, 11.55]	
Total (95% CI)			**87**			**66**	**100.0%**	**8.67 [-8.02, 25.36]**	

Heterogeneity: Tau² = 123.81; Chi² = 6.33, df = 1 (P = 0.01); I² = 84%

Test for overall effect: Z = 1.02 (P = 0.31)

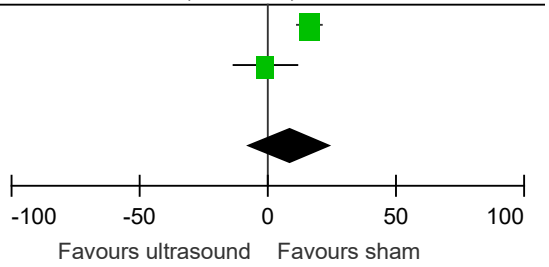


Figure 139: Quality of life (SF-36 role physical, 0-100, high is good, change score) at ≤3 months

	Ultrasound			Sham			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Jia 2016	13	16.24	49	12.33	17.69	48	0.67 [-6.09, 7.43]	

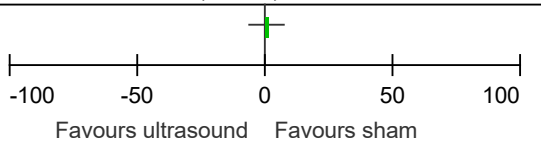


Figure 140: Quality of life (SF-36 vitality, 0-100, high is good, change score) at ≤3 months

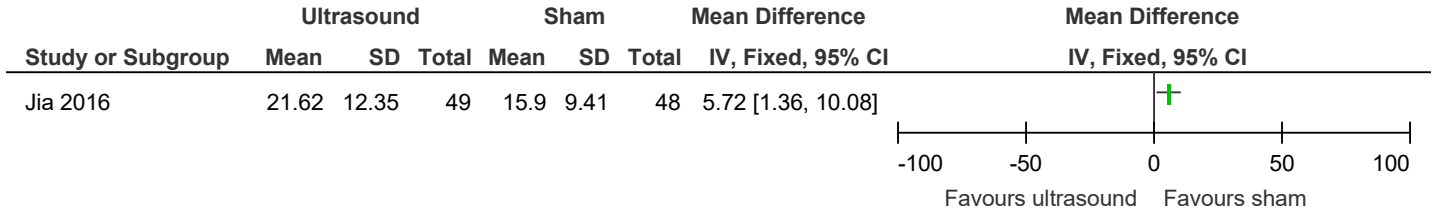


Figure 141: Quality of life (SF-36 general health, 0-100, high is good, change score and final value) at ≤3 months

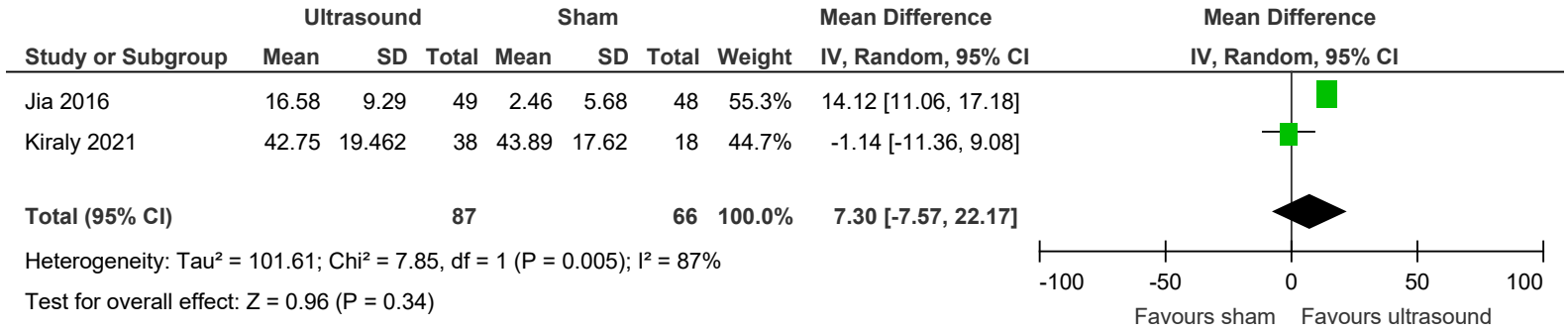


Figure 142: Quality of life (SF-36 mental health, 0-100, high is good, change score) at ≤3 months

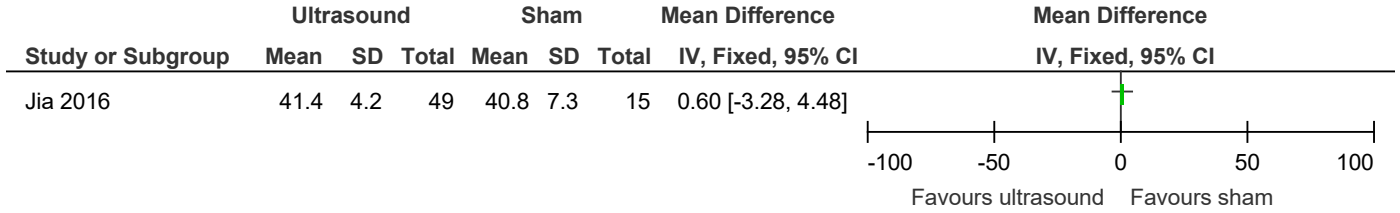


Figure 143: Quality of life (SF-36 role emotional, 0-100, high is good, change score) at ≤3 months

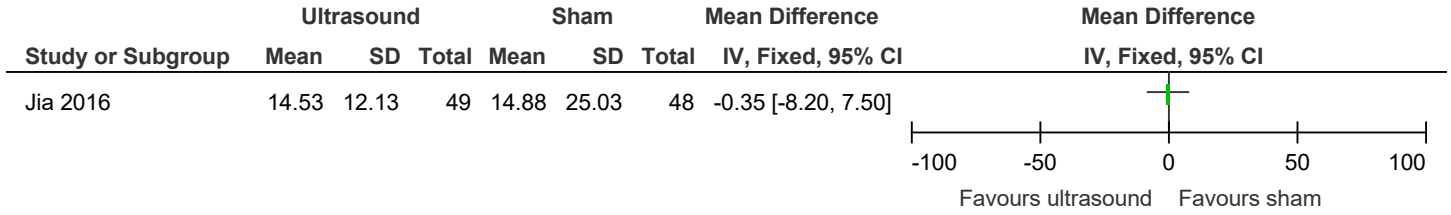


Figure 144: Quality of life (SF-36 social function, 0-100, high is good, change score) at ≤3 months

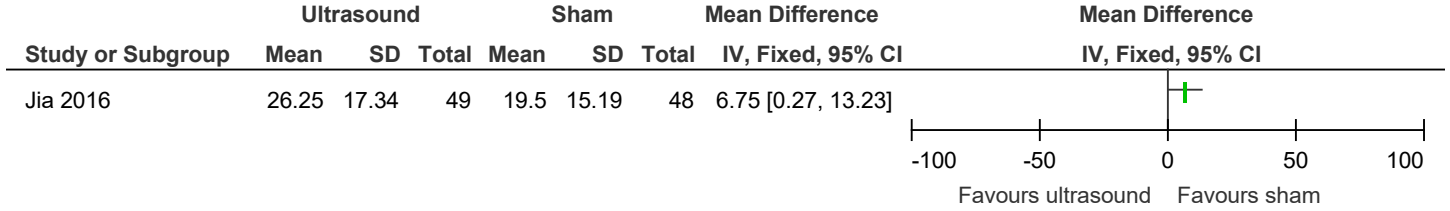


Figure 145: Quality of life (SF-36 physical component, 0-100, high is good, change score and final value) at ≤3 months

	Ultrasound			Sham				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Koybasi 2010	40.9	6.6	15	39.2	6.4	15	50.8%	1.70 [-2.95, 6.35]
Yegin 2017	7.9	9.74	30	6.1	9.2	32	49.2%	1.80 [-2.92, 6.52]
Total (95% CI)			**45**			**47**	**100.0%**	**1.75 [-1.57, 5.06]**

Heterogeneity: Chi² = 0.00, df = 1 (P = 0.98); I² = 0%

Test for overall effect: Z = 1.03 (P = 0.30)

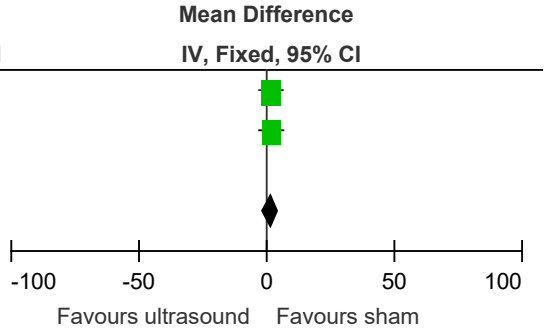


Figure 146: Quality of life (SF-36 mental component, 0-100, high is good, change score and final value) at ≤3 months

	Ultrasound			Sham				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Koybasi 2010	41.4	4.2	15	40.8	7.3	15	68.0%	0.60 [-3.66, 4.86]
Yegin 2017	-0.3	12.78	30	-0.1	12.14	32	32.0%	-0.20 [-6.41, 6.01]
Total (95% CI)			**45**			**47**	**100.0%**	**0.34 [-3.17, 3.86]**

Heterogeneity: Chi² = 0.04, df = 1 (P = 0.84); I² = 0%

Test for overall effect: Z = 0.19 (P = 0.85)

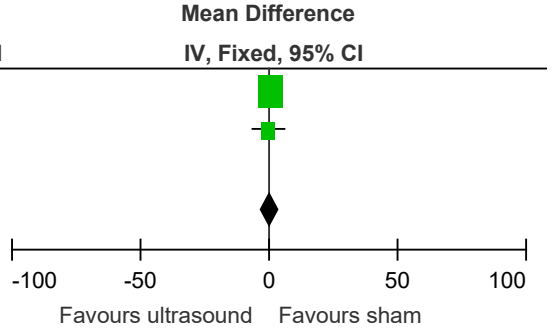


Figure 147: Pain (WOMAC, VAS [different scale ranges], high is poor, change scores) at ≤3 months

	Ultrasound			Sham				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Cakir 2014	-6.2	6	40	-4.3	7.2	20	19.2%	-0.29 [-0.83, 0.25]
Draper 2018	-107.3	97.5	51	-60.8	80.95	31	21.6%	-0.50 [-0.96, -0.05]
Jia 2016	-5.44	0.84	49	-4.48	0.84	48	22.2%	-1.13 [-1.56, -0.70]
Ulus 2012	-6.5	3.25	20	-4.57	3.16	20	16.7%	-0.59 [-1.22, 0.04]
Yegin 2017	-2.9	3.45	30	-2.6	4.68	32	20.3%	-0.07 [-0.57, 0.43]
Total (95% CI)			**190**			**151**	**100.0%**	**-0.53 [-0.91, -0.15]**

Heterogeneity: Tau² = 0.12; Chi² = 11.54, df = 4 (P = 0.02); I² = 65%

Test for overall effect: Z = 2.71 (P = 0.007)

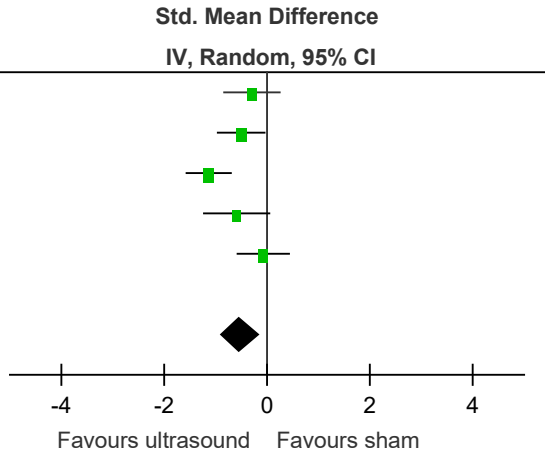


Figure 148: Pain (WOMAC, VAS [different scale ranges], high is poor, final values) at ≤3 months

	Ultrasound			Sham				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Karakas 2020	5.26	3.94	39	5.92	3.26	36	14.1%	-0.18 [-0.63, 0.27]
Kiraly 2021	38.445	28.485	38	40.22	20.88	18	12.9%	-0.07 [-0.63, 0.49]
Koybasi 2010	47.8	18	15	73.6	14.6	15	9.9%	-1.53 [-2.36, -0.70]
Loyola-sanchez 2012	6.92	3.96	12	5.62	4.33	13	10.3%	0.30 [-0.49, 1.09]
Ozgonenel 2009	6.9	3.6	34	8.4	4.2	33	13.7%	-0.38 [-0.86, 0.10]
Ozgonenel 2018	5.93	0.8	15	5.89	0.68	18	11.4%	0.05 [-0.63, 0.74]
Tascioglu 2010	5.24	1.81	55	6.67	1.78	27	13.8%	-0.79 [-1.26, -0.31]
Yildiz 2015	3.87	2.58	60	7.2	2.66	30	13.8%	-1.27 [-1.74, -0.79]
Total (95% CI)			**268**			**190**	**100.0%**	**-0.48 [-0.89, -0.08]**

Heterogeneity: Tau² = 0.24; Chi² = 28.17, df = 7 (P = 0.0002); I² = 75%

Test for overall effect: Z = 2.36 (P = 0.02)

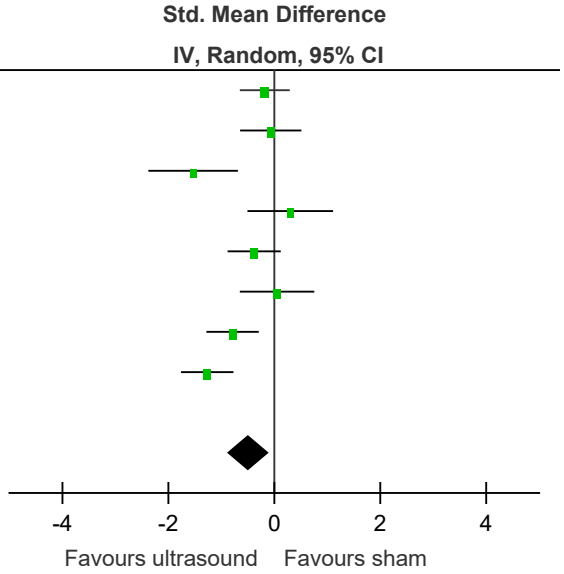


Figure 149: Pain (VAS, 0-100, high is poor, change score) at >3 months

	Ultrasound			Sham			Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI
Cakir 2014	-35.5	15.1	40	-34.1	12.3	20	-1.40 [-8.54, 5.74]

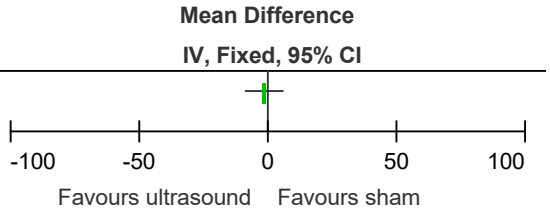


Figure 150: Physical function (WOMAC [different scale ranges], high is poor, change scores) at ≤3 months

	Ultrasound			Sham				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Cakir 2014	-17.7	6	40	-13.6	5.9	20	22.3%	-0.68 [-1.23, -0.13]
Draper 2018	-352.3	309.6	51	-220.1	233.6	31	33.1%	-0.46 [-0.91, -0.01]
Ulus 2012	-18.85	9.21	20	-15.05	15.49	20	17.4%	-0.29 [-0.92, 0.33]
Yegin 2017	-9.3	10.82	30	-6.5	14.42	32	27.1%	-0.22 [-0.72, 0.28]
Total (95% CI)			**141**			**103**	**100.0%**	**-0.41 [-0.67, -0.15]**

Heterogeneity: Chi² = 1.68, df = 3 (P = 0.64); I² = 0%

Test for overall effect: Z = 3.12 (P = 0.002)

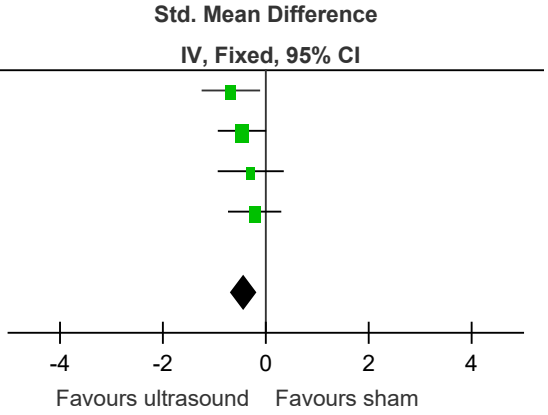


Figure 151: Physical function (WOMAC, 0-68, high is poor, final values) at ≤3 months

	Ultrasound			Sham				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Karakas 2020	18.92	13.79	39	21.39	10.1	36	47.5%	-2.47 [-7.91, 2.97]
Loyola-sanchez 2012	23.92	11.3	12	20.38	13	13	15.5%	3.54 [-5.99, 13.07]
Ozgonenel 2009	23.6	11.6	34	27.1	14	33	37.0%	-3.50 [-9.67, 2.67]
Total (95% CI)			**85**			**82**	**100.0%**	**-1.92 [-5.67, 1.83]**

Heterogeneity: Chi² = 1.55, df = 2 (P = 0.46); I² = 0%

Test for overall effect: Z = 1.00 (P = 0.32)

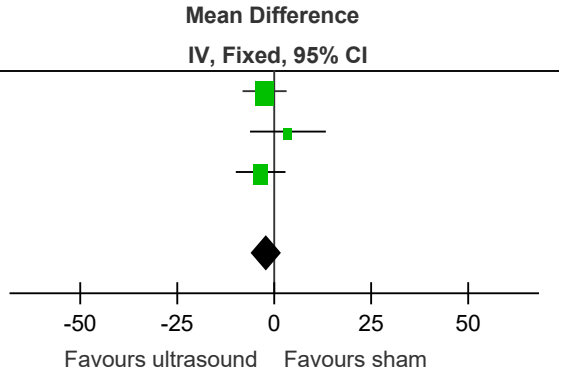


Figure 152: Physical function (WOMAC, 0-68, high is poor, change score) at >3 months

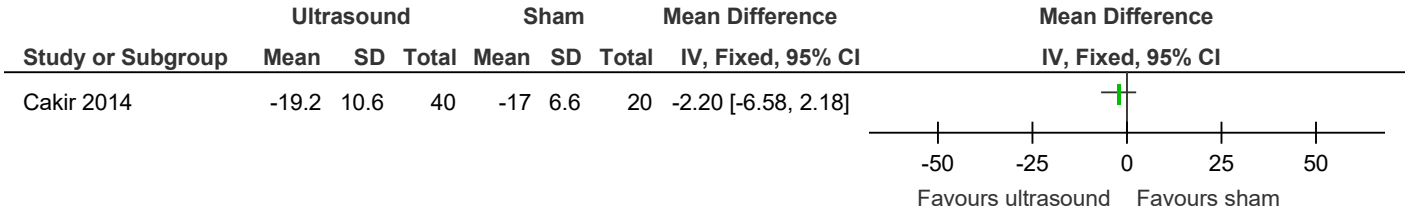


Figure 153: Psychological distress (HADS anxiety, 0-21, high is poor, change score) at ≤3 months

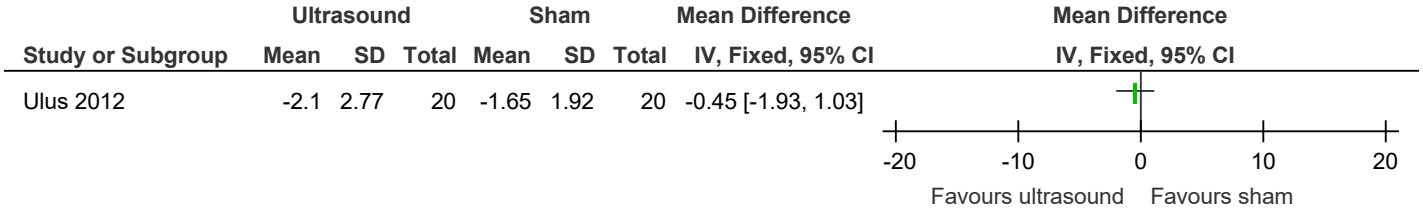


Figure 154: Psychological distress (HADS depression, 0-21, high is poor, change score) at ≤3 months

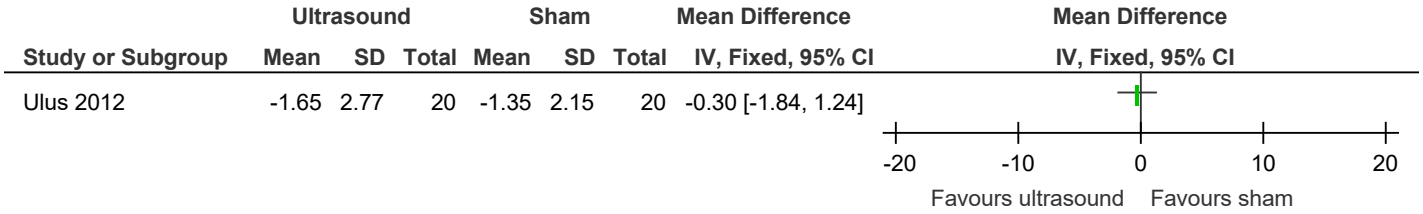


Figure 155: Mild adverse events at ≤3 months

Study or Subgroup	Ultrasound Events	Ultrasound Total	Sham Events	Sham Total	Weight	Risk Difference M-H, Fixed, 95% CI
Kiraly 2021	0	38	0	18	16.1%	0.00 [-0.08, 0.08]
Loyola-sanchez 2012	2	14	2	13	8.9%	-0.01 [-0.28, 0.26]
Ozgonenel 2009	0	34	2	33	22.1%	-0.06 [-0.16, 0.04]
Tascioglu 2010	0	60	0	30	26.4%	0.00 [-0.05, 0.05]
Yildiz 2015	0	60	0	30	26.4%	0.00 [-0.05, 0.05]
Total (95% CI)		**206**		**124**	**100.0%**	**-0.01 [-0.05, 0.03]**
Total events	2		4			

Heterogeneity: Chi² = 1.65, df = 4 (P = 0.80); I² = 0%

Test for overall effect: Z = 0.70 (P = 0.48)

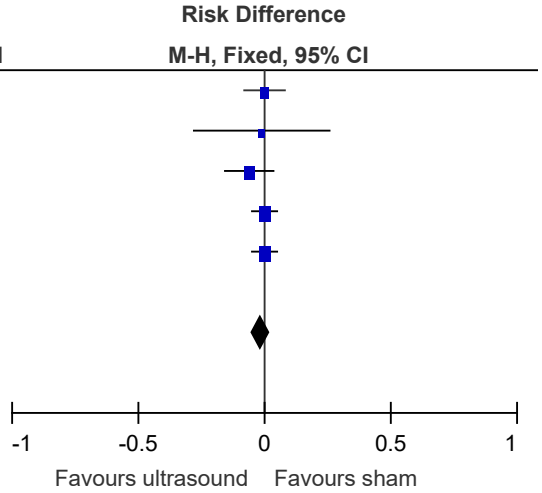
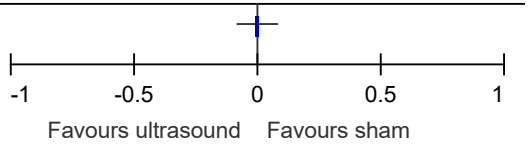


Figure 156: Moderate/major adverse events at ≤3 months

Study or Subgroup	Ultrasound Events	Ultrasound Total	Sham Events	Sham Total	Risk Difference M-H, Fixed, 95% CI
Kiraly 2021	0	38	0	18	0.00 [-0.08, 0.08]



E.7.5 Ultrasound compared to no treatment

Figure 157: Quality of life (SF-36 physical component, 0-100, high is poor, final value) at ≤3 months

	Ultrasound			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Koybasi 2010	40.9	6.6	15	40.9	5.1	15	0.00 [-4.22, 4.22]	

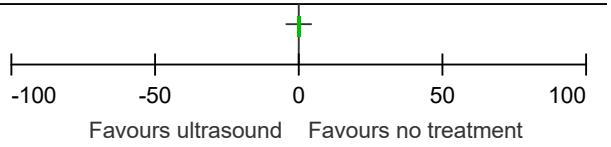


Figure 158: Quality of life (SF-36 mental component, 0-100, high is poor, final value) at ≤3 months

	Ultrasound			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Koybasi 2010	41.4	4.2	15	39.3	4.8	15	2.10 [-1.13, 5.33]	

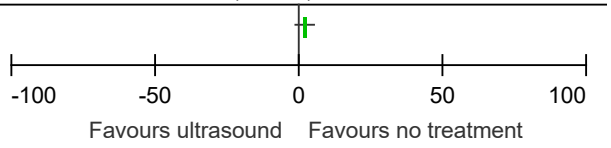


Figure 159: Pain (VAS, 0-10, high is poor, change scores) at ≤3 months

	Ultrasound			No treatment				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Alfredo 2020	-6.5	4.8946	80	-0.8	3.1	20	25.0%	-1.23 [-1.75, -0.71]
Cetin 2008	-2.34	0.94	20	-2.27	0.88	20	23.9%	-0.08 [-0.70, 0.54]
Huang 2005A	-1.6	1.5	60	-2.4	1.8	30	25.8%	0.49 [0.05, 0.94]
Huang 2005B	-2.5	1.9	35	-1.2	1.6	35	25.4%	-0.73 [-1.22, -0.25]
Total (95% CI)			**195**			**105**	**100.0%**	**-0.38 [-1.16, 0.40]**

Heterogeneity: Tau² = 0.57; Chi² = 27.98, df = 3 (P < 0.00001); I² = 89%

Test for overall effect: Z = 0.96 (P = 0.34)

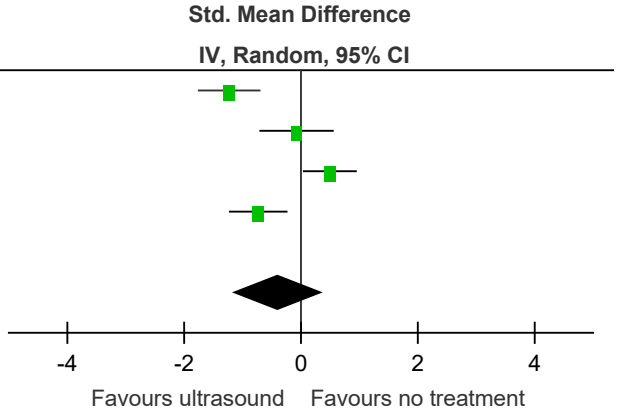


Figure 160: Pain (WOMAC, VAS [different scale ranges], high is poor, final values) at ≤3 months

	Ultrasound			No treatment				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Koybasi 2010	47.8	18	15	74.3	13.6	15	50.0%	-1.62 [-2.46, -0.78]
Mascarin 2012	6.2	4.2	12	2	2.3	16	50.0%	1.26 [0.43, 2.09]
Total (95% CI)			**27**			**31**	**100.0%**	**-0.18 [-2.99, 2.64]**

Heterogeneity: Tau² = 3.95; Chi² = 22.80, df = 1 (P < 0.00001); I² = 96%

Test for overall effect: Z = 0.12 (P = 0.90)

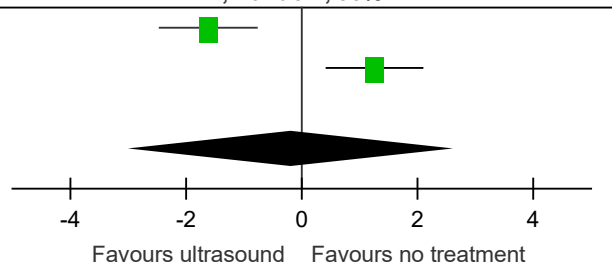


Figure 161: Pain (VAS, 0-10, high is poor, final values) at >3 months

	Ultrasound			No treatment				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Huang 2005A	3.1	1.6	60	2.2	1.8	30	49.7%	0.90 [0.14, 1.66]
Huang 2005B	2.6	1.5	35	3.9	1.4	35	50.3%	-1.30 [-1.98, -0.62]
Total (95% CI)			**95**			**65**	**100.0%**	**-0.21 [-2.36, 1.95]**

Heterogeneity: Tau² = 2.28; Chi² = 17.86, df = 1 (P < 0.0001); I² = 94%

Test for overall effect: Z = 0.19 (P = 0.85)

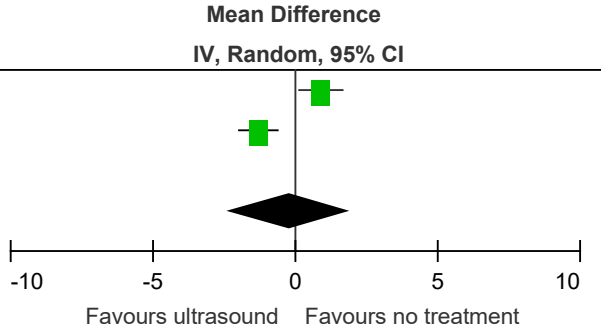
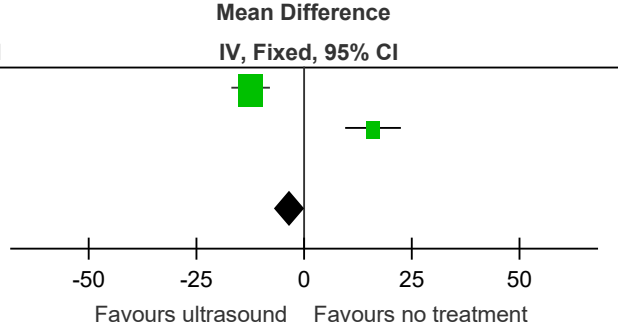


Figure 162: Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months

	Ultrasound			No treatment				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Alfredo 2020	-14.8	12.465	80	-2.4	7.44	20	68.4%	-12.40 [-16.65, -8.15]
Mascarin 2012	20.6	9.8	12	4.6	5.9	16	31.6%	16.00 [9.75, 22.25]
Total (95% CI)			**92**			**36**	**100.0%**	**-3.42 [-6.93, 0.10]**

Heterogeneity: Chi² = 54.17, df = 1 (P < 0.00001); I² = 98%

Test for overall effect: Z = 1.90 (P = 0.06)



E.8 Combination therapy

E.8.1 Combination therapy compared to interferential therapy

Figure 163: Pain (VAS, 0-10, high is poor, final value) at ≤3 months

	Combination therapy			Interferential therapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Alqualo-Costa 2021	2.45	2.8004	42	3.55	2.9364	42	-1.10 [-2.33, 0.13]	

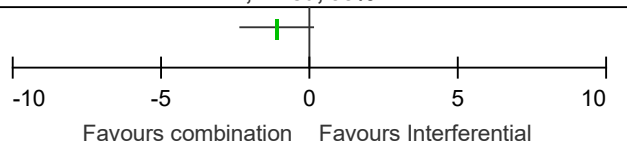
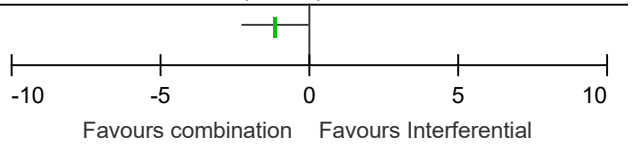


Figure 164: Pain (VAS, 0-10, high is poor, final value) at >3 months

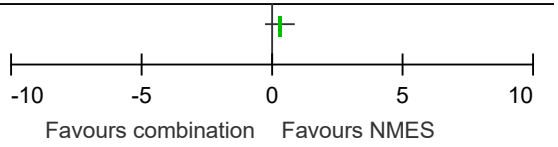
	Combination therapy			Interferential therapy			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Alqualo-Costa 2021	2.5	2.2383	42	3.65	2.8614	42	-1.15 [-2.25, -0.05]	



E.8.2 Combination therapy compared to neuromuscular electrical stimulation

Figure 165: Pain (VAS, 0-10, high is poor, final value) at ≤3 months

	Combination therapy			NMES			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Melo mde 2015	1.2	0.9	14	0.9	0.5	15	0.30 [-0.24, 0.84]	



E.8.3 Combination therapy compared to laser therapy

Figure 166: Pain (VAS, NRS, 0-10, high is poor, final values) at ≤3 months

	Combination therapy			Laser				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Alqualo-Costa 2020	2.45	2.8004	42	3.15	2.8004	42	21.2%	-0.70 [-1.90, 0.50]	
Melo mde 2015	1.2	0.9	14	1.6	0.8	15	78.8%	-0.40 [-1.02, 0.22]	
Total (95% CI)			**56**			**57**	**100.0%**	**-0.46 [-1.02, 0.09]**	

Heterogeneity: Chi² = 0.19, df = 1 (P = 0.66); I² = 0%

Test for overall effect: Z = 1.65 (P = 0.10)

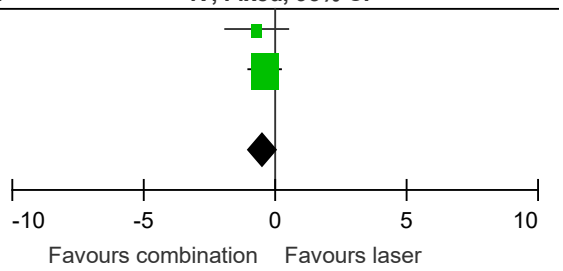
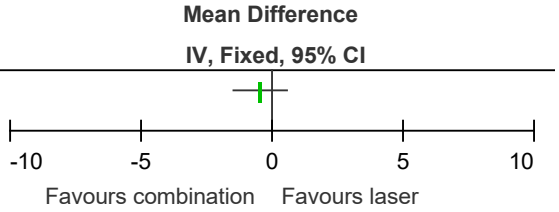


Figure 167: Pain (NRS, 0-10, high is poor, final value) at >3 months

Study or Subgroup	Combination therapy Mean	SD	Total	Laser Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Alqualo-Costa 2020	2.5	2.2383	42	2.95	2.5323	42	-0.45 [-1.47, 0.57]



E.8.4 Combination therapy compared to transcutaneous electrical nerve stimulation

Figure 168: Quality of life (SF-36, 0-100, high is good, final value) at ≤3 months

Study or Subgroup	Combination therapy Mean	SD	Total	TENS Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Kim 2019	67.8	11.03	19	67.34	18.22	19	0.46 [-9.12, 10.04]

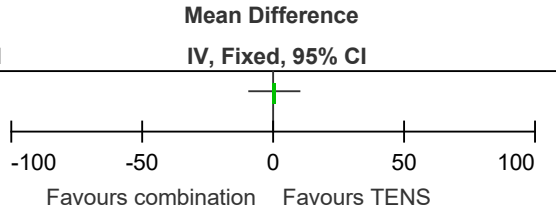


Figure 169: Pain (WOMAC, 0-20, high is poor, final value) at ≤3 months

	Combination therapy			TENS			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Kim 2019	5.32	3.09	19	4.26	3.75	19	1.06 [-1.12, 3.24]	

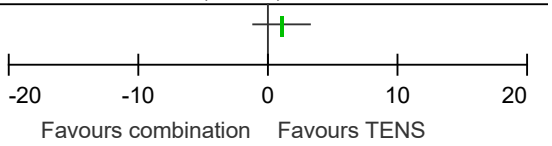


Figure 170: Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months

	Combination therapy			TENS			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Kim 2019	15.84	10.07	19	10.79	9.63	19	5.05 [-1.22, 11.32]	

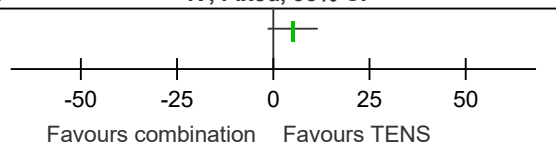


Figure 171: Mild adverse events at ≤3 months

	Combination therapy		TENS		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Kim 2019	0	20	0	20	0.00 [-0.09, 0.09]	

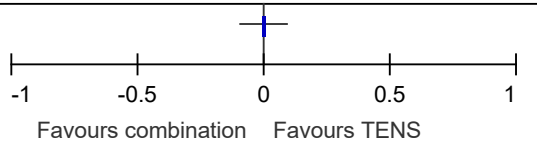
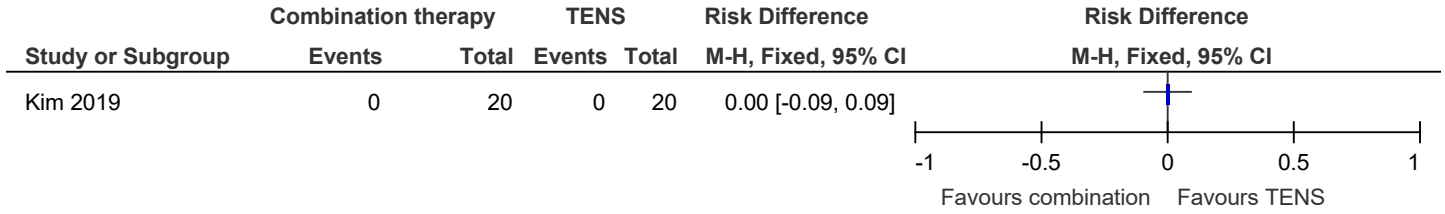


Figure 172: Moderate/major adverse events at ≤3 months



E.8.5 Combination therapy compared to ultrasound

Figure 173: Quality of life (SF-36 pain, 0-100, high is good, final value) at ≤3 months

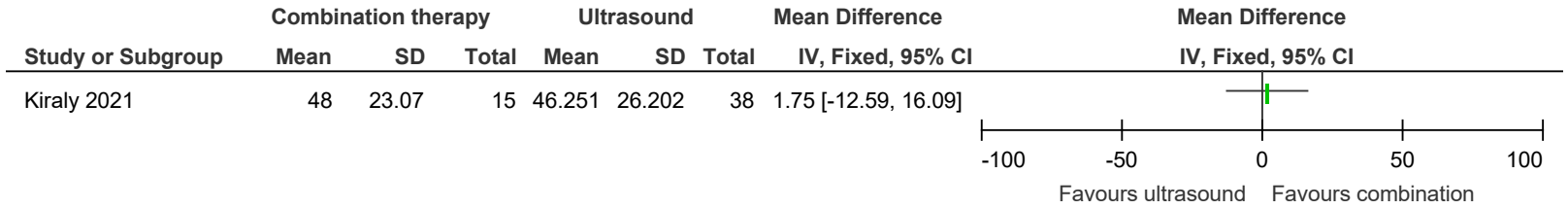


Figure 174: Quality of life (SF-36 general health, 0-100, high is good, final value) at ≤3 months

	Combination therapy			Ultrasound			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Kiraly 2021	51.63	18.2	15	42.75	19.462	38	8.88 [-2.22, 19.98]	

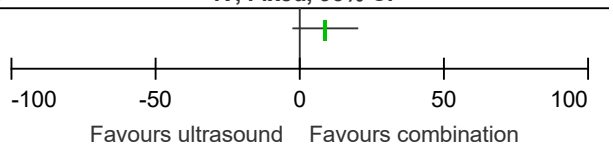


Figure 175: Pain (VAS, 0-100, high is poor, change score and final value) at ≤3 months

	Combination therapy			Ultrasound				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Kiraly 2021	31.13	22.26	15	38.445	28.485	38	35.3%	-7.32 [-21.77, 7.14]	
Sangtong 2019	-25	18	74	-30	20	74	64.7%	5.00 [-1.13, 11.13]	
Total (95% CI)			**89**			**112**	**100.0%**	**0.65 [-10.88, 12.19]**	

Heterogeneity: Tau² = 43.74; Chi² = 2.36, df = 1 (P = 0.12); I² = 58%

Test for overall effect: Z = 0.11 (P = 0.91)

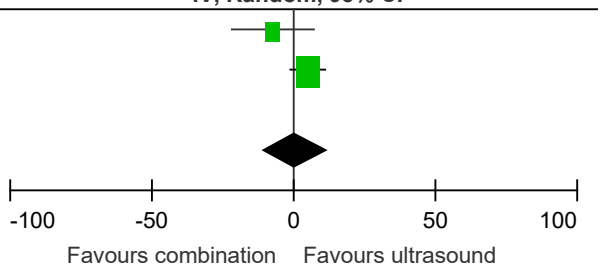


Figure 176: Mild adverse events at ≤3 months

Study or Subgroup	Combination therapy Events	Total	Ultrasound Events	Total	Weight	Risk Difference M-H, Fixed, 95% CI
Kiraly 2021	0	15	0	38	24.6%	0.00 [-0.09, 0.09]
Sangtong 2019	4	64	3	68	75.4%	0.02 [-0.06, 0.10]
Total (95% CI)		**79**		**106**	**100.0%**	**0.01 [-0.05, 0.08]**
Total events	4		3			

Heterogeneity: Chi² = 0.10, df = 1 (P = 0.75); I² = 0%

Test for overall effect: Z = 0.43 (P = 0.66)

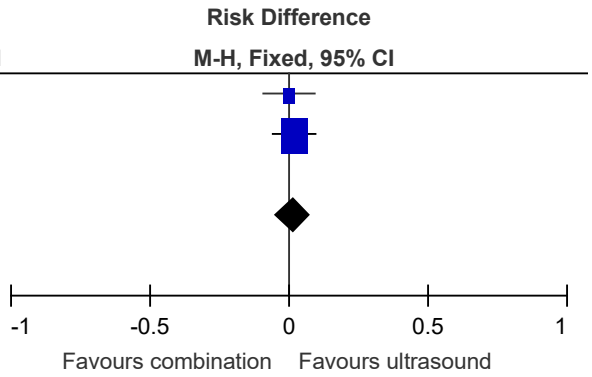
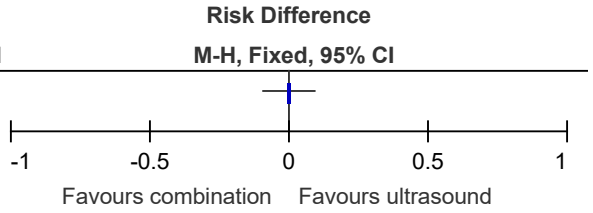


Figure 177: Moderate/major adverse events at ≤3 months

Study or Subgroup	Combination therapy Events	Total	Ultrasound Events	Total	Risk Difference M-H, Fixed, 95% CI
Kiraly 2021	0	15	0	38	0.00 [-0.09, 0.09]



E.8.6 Combination therapy compared to sham electrotherapy

Figure 178: Quality of life (SF-36 pain, 0-100, high is good, final values) at ≤3 months

	Combination therapy			Sham			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Kiraly 2021	48	23.07	15	47.15	20.02	18	0.85 [-14.04, 15.74]	

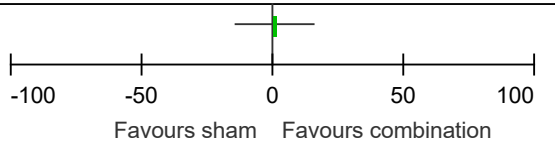


Figure 179: Quality of life (SF-36 general health, 0-100, high is good, final values) at ≤3 months

	Combination therapy			Sham			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Kiraly 2021	51.63	18.2	15	43.89	17.62	18	7.74 [-4.55, 20.03]	

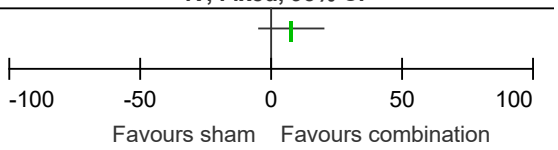


Figure 180: Pain (VAS, 0-100, high is poor, final value) at ≤3 months

	Combination therapy			Sham electrotherapy				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Fixed, 95% CI**
Alqualo-Costa 2020	32	29	42	52	23	42	63.7%	-20.00 [-31.19, -8.81]
Kiraly 2021	31.13	22.26	15	40.22	20.88	18	36.3%	-9.09 [-23.92, 5.74]
Total (95% CI)			**57**			**60**	**100.0%**	**-16.04 [-24.97, -7.11]**

Heterogeneity: Chi² = 1.32, df = 1 (P = 0.25); I² = 24%

Test for overall effect: Z = 3.52 (P = 0.0004)

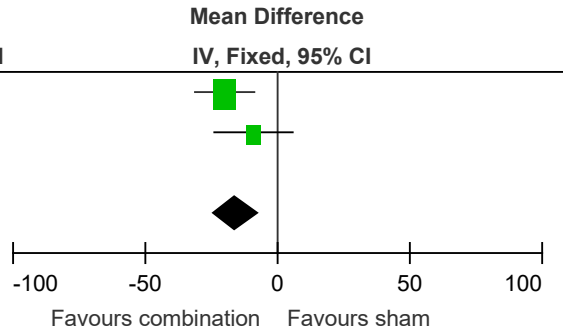


Figure 181: Pain (VAS, 0-10, high is poor, final value) at >3 months

	Combination therapy			Sham combination therapy			Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**IV, Fixed, 95% CI**
Alqualo-Costa 2020	1.9	2.2	42	4.9	2.6	42	-3.00 [-4.03, -1.97]

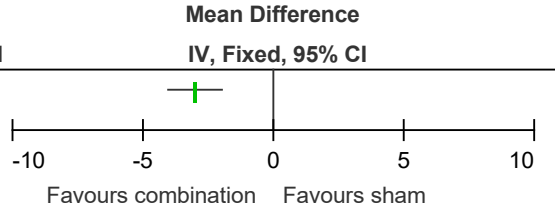


Figure 182: Mild adverse events at ≤3 months

Study or Subgroup	Combination therapy Events	Total	Sham electrotherapy Events	Total	Risk Difference M-H, Fixed, 95% CI
Kiraly 2021	0	15	0	18	0.00 [-0.11, 0.11]

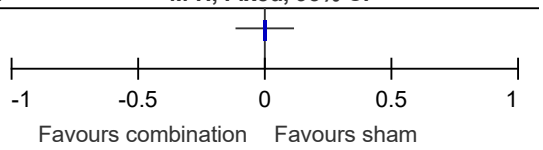
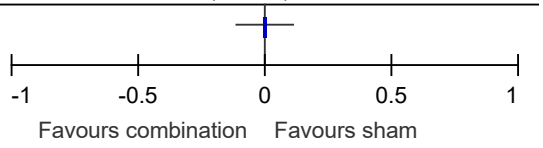


Figure 183: Moderate/major adverse events at ≤3 months

Study or Subgroup	Combination therapy Events	Total	Sham electrotherapy Events	Total	Risk Difference M-H, Fixed, 95% CI
Kiraly 2021	0	15	0	18	0.00 [-0.11, 0.11]



E.8.7 Combination therapy compared to no treatment

Figure 184: Quality of life (SF-36 physical function, 0-100, high is good, final value) at ≤3 months

	Combination therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Atlas 2020	83	13.8	20	59	13.6	20	24.00 [15.51, 32.49]	

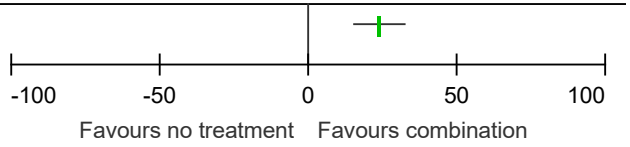


Figure 185: Quality of life (SF-36 pain, 0-100, high is good, final value) at ≤3 months

	Combination therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Atlas 2020	55.6	12.6	20	45.4	15.1	20	10.20 [1.58, 18.82]	

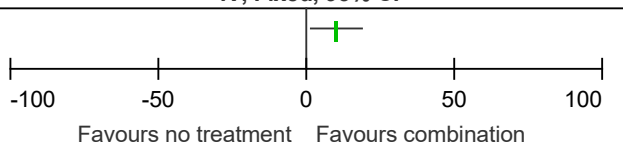


Figure 186: Quality of life (SF-36 role physical, 0-100, high is good, final value) at ≤3 months

Study or Subgroup	Combination therapy Mean	SD	Total	No treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Atlas 2020	66.3	29.6	20	28.75	3	20	37.55 [24.51, 50.59]

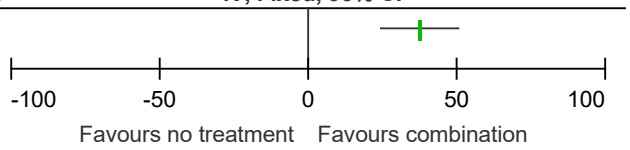


Figure 187: Quality of life (SF-36 vitality, 0-100, high is good, final value) at ≤3 months

Study or Subgroup	Combination therapy Mean	SD	Total	No treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Atlas 2020	62	15.3	20	40	13.7	20	22.00 [13.00, 31.00]

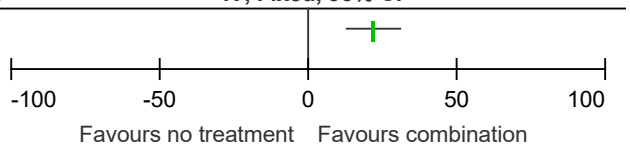


Figure 188: Quality of life (SF-36 general health, 0-100, high is good, final value) at ≤3 months

Study or Subgroup	Combination therapy Mean	SD	Total	No treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Atlas 2020	43.8	9.2	20	40.9	16.7	20	2.90 [-5.46, 11.26]

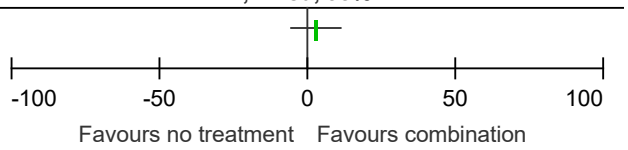


Figure 189: Quality of life (SF-36 role emotion, 0-100, high is good, final value) at ≤3 months

Study or Subgroup	Combination therapy Mean	SD	Total	No treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Atlas 2020	79.7	22.9	20	47.9	22.8	20	31.80 [17.64, 45.96]

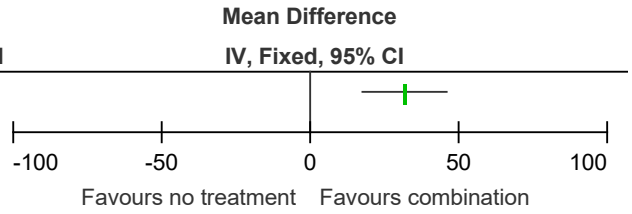


Figure 190: Quality of life (SF-36 mental health, 0-100, high is good, final value) at ≤3 months

Study or Subgroup	Combination therapy Mean	SD	Total	No treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Atlas 2020	69	9.4	20	56	16.8	20	13.00 [4.56, 21.44]

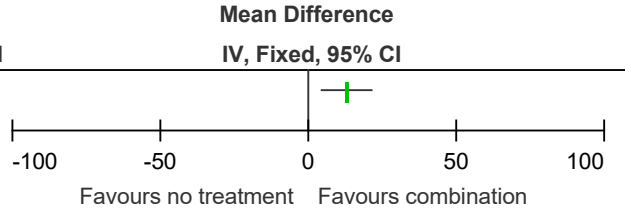


Figure 191: Quality of life (SF-36 social function, 0-100, high is good, final value) at ≤3 months

	Combination therapy			No treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Atlas 2020	76.2	17.1	20	50	21.5	20	26.20 [14.16, 38.24]	

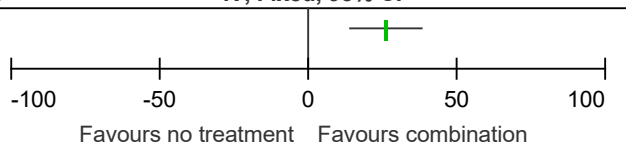


Figure 192: Pain (WOMAC, NRS [different scale ranges], high is poor, final values) at ≤3 months

	Combination therapy			No treatment			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Atlas 2020	4.1	1.3	20	6.4	1.4	20	49.5%	-1.67 [-2.40, -0.94]	
Eftekharsadat 2019	13.18	5.66	22	10.61	4.91	22	50.5%	0.48 [-0.12, 1.08]	
Total (95% CI)			**42**			**42**	**100.0%**	**-0.59 [-2.69, 1.52]**	

Heterogeneity: Tau² = 2.18; Chi² = 19.80, df = 1 (P < 0.00001); I² = 95%

Test for overall effect: Z = 0.55 (P = 0.58)

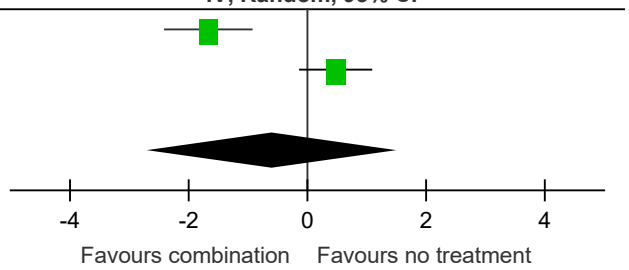


Figure 193: Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months

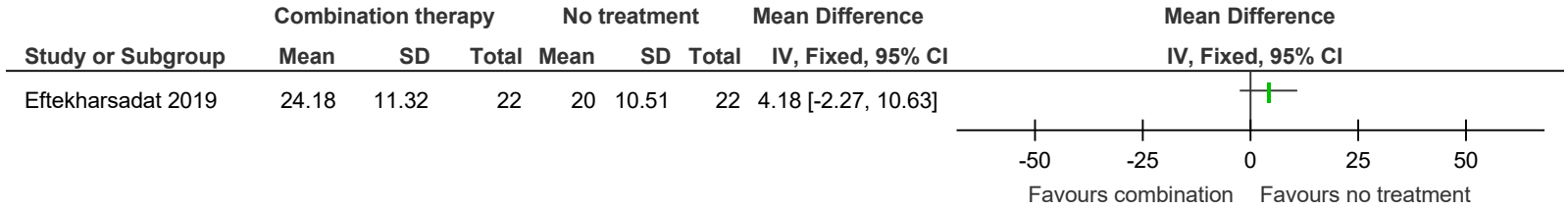
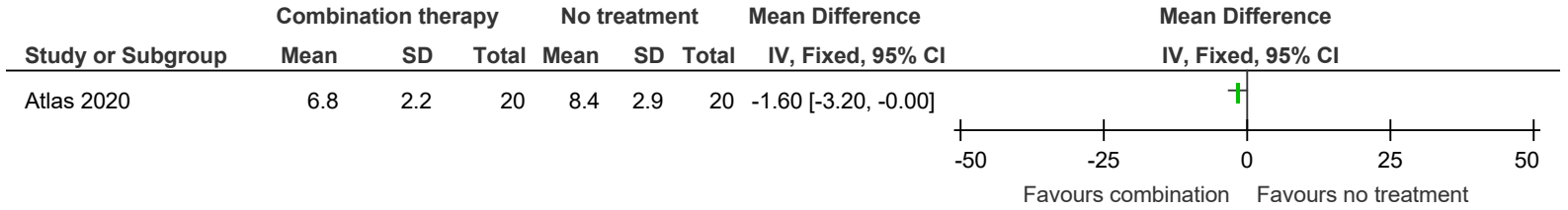


Figure 194: Psychological distress (BDI, 0-51, high is poor, final value) at ≤3 months



Appendix F – GRADE tables

F.1 Pulsed short-wave therapy compared to sham electrotherapy and no treatment

Table 66: Clinical evidence profile: pulsed short-wave therapy compared to sham electrotherapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	pulsed short-wave therapy	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
Quality of life (EQ-5D, KOOS, AIMS, 0-100, high is good, change score and final values) at <3 months (follow-up: mean 4 weeks; assessed with: EQ-5D, KOOS, AIMS; Scale from: 0 to 100)												
3	randomised trials	serious[a]	serious[b]	not serious	not serious	none	111	67	-	MD **2.73 higher** (3.37 lower to 8.83 higher)	⨁⨁◯◯ Low	CRITICAL
Quality of life (SF-36 physical component, 0-100, high is good, final value) at <3 months (follow-up: 4 weeks; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	randomised trials	not serious	not serious	not serious	serious[c]	none	30	33	-	MD **2.7 higher** (0.34 lower to 5.74 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Quality of life (SF-36 mental component, 0-100, high is good, final value) at <3 months (follow-up: 4 weeks; assessed with: SF-36 mental component; Scale from: 0 to 100)												
1	randomised trials	not serious	not serious	not serious	not serious	none	30	30	-	MD **0.2 higher** (1.92 lower to 2.32 higher)	⨁⨁⨁⨁ High	CRITICAL
Quality of life (KOOS, 0-100, high is good, final value) at >3 months (follow-up: 12 months; assessed with: KOOS; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	serious[c]	none	37	14	-	MD **3.4 higher** (5.26 lower to 12.06 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (SF-36 physical component, 0-100, high is good, change score) at >3 months (follow-up: 26 weeks; assessed with: SF-36 physical component; Scale from: 0 to 100)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	pulsed short-wave therapy	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	not serious	not serious	not serious	serious[c]	none	34	36	-	MD **1.6 lower** (4.64 lower to 1.44 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Quality of life (SF-36 mental component, 0-100, high is good, change score) at >3 months (follow-up: 26 weeks; assessed with: SF-36 mental component; Scale from: 0 to 100)												
1	randomised trials	not serious	not serious	not serious	not serious	none	34	36	-	MD **1.2 lower** (5.3 lower to 2.9 higher)	⨁⨁⨁⨁ High	CRITICAL
Pain (WOMAC [different scale ranges], high is poor, change scores) at <3 months (follow-up: mean 8 weeks; assessed with: WOMAC)												
4	randomised trials	serious[a]	very serious[b]	not serious	serious[c]	none	149	98	-	SMD **0.36 SD lower** (0.97 lower to 0.26 higher)	⨁◯◯◯ Very low	CRITICAL
Pain (KOOS, WOMAC, VAS, NRS [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 6 weeks; assessed with: KOOS, WOMAC, VAS, NRS)												
9	randomised trials	serious[a]	very serious[b]	not serious	serious[c]	none	244	200	-	SMD **0.67 SD lower** (1.12 lower to 0.21 lower)	⨁◯◯◯ Very low	CRITICAL
Pain (WOMAC [different scale ranges], high is poor, change scores) at >3 months (follow-up: mean 26 weeks; assessed with: WOMAC)												
2	randomised trials	not serious	not serious	not serious	not serious	none	66	67	-	SMD **0.01 SD higher** (0.49 lower to 0.5 higher)	⨁⨁⨁⨁ High	CRITICAL
Pain (KOOS, 0-100, high is good, final value) at >3 months (follow-up: 52 weeks; assessed with: KOOS; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	not serious	none	37	14	-	MD **24.6 higher** (16.63 higher to 32.57 higher)	⨁⨁◯◯ Low	CRITICAL
Physical function (WOMAC [different scale ranges], high is poor, change scores) at <3 months (follow-up: mean 8 weeks; assessed with: WOMAC)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	pulsed short-wave therapy	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
4	randomised trials	not serious	serious[b]	not serious	serious[c]	none	147	98	-	SMD **0.51 SD lower** (0.89 lower to 0.12 lower)	⨁⨁◯◯ Low	CRITICAL
Physical function (KOOS, WOMAC [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 6 weeks; assessed with: KOOS, WOMAC)												
5	randomised trials	serious[a]	serious[b]	not serious	serious[c]	none	171	132	-	SMD **0.52 SD lower** (0.97 lower to 0.06 lower)	⨁◯◯◯ Very low	CRITICAL
Physical function (WOMAC [different scale ranges], high is poor, change scores) at >3 months (follow-up: 26 weeks; assessed with: WOMAC)												
2	randomised trials	not serious	not serious	not serious	not serious	none	66	67	-	SMD **0.06 SD higher** (0.28 lower to 0.4 higher)	⨁⨁⨁⨁ High	CRITICAL
Physical function (KOOS, 0-100, high is good, final value) at >3 months (follow-up: 12 months; assessed with: KOOS; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	serious[c]	none	37	14	-	MD **19 higher** (8.09 higher to 29.91 higher)	⨁◯◯◯ Very low	CRITICAL
Psychological distress (GHQ, 0-90, high is poor, final value) at <3 months (follow-up: 12 weeks; assessed with: GHQ; Scale from: 0 to 90)												
1	randomised trials	very serious[a]	not serious	not serious	serious[c]	none	30	30	-	MD **3.48 higher** (3.98 lower to 10.94 higher)	⨁◯◯◯ Very low	IMPORTANT
Mild adverse events at <3 months (follow-up: mean 7 weeks)												
5	randomised trials	serious[a]	serious[d]	not serious	serious[e]	none	30/197 (15.2%)	21/142 (14.8%)	**RD 0.03** (-0.05 to 0.11)	**30 fewer per 1,000** (from 110 fewer to 50 more)	⨁◯◯◯ Very low	IMPORTANT

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	pulsed short-wave therapy	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
Moderate/major adverse events at <3 months (follow-up: 12 weeks)												
1	randomised trials	serious[a]	not serious	not serious	serious[e]	none	0/42 (0.0%)	0/41 (0.0%)	**RD 0.00** (-0.05 to 0.05)	**0 fewer per 1,000** (from 50 fewer to 50 more)	⨁⨁◯◯ Low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

c. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

d. Downgraded for heterogeneity due to conflicting number of events in different studies (zero events in one or more studies)

e. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

Table 67: Clinical evidence profile: pulsed short-wave therapy compared to no treatment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	pulsed short-wave therapy	no treatment	Relative (95% CI)	Absolute (95% CI)		
Quality of life (KOOS, 0-100, high is good, final value) at <3 months (follow-up: 3 weeks; assessed with: KOOS; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	59	32	-	MD **11.8 higher** (3.03 higher to 20.57 higher)	⨁◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	pulsed short-wave therapy	no treatment	Relative (95% CI)	Absolute (95% CI)		
Quality of life (SF-36 physical function, 0-100, high is good, change score) at <3 months (follow-up: 4 weeks; assessed with: SF-36 physical function; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **6.25 higher** (5.77 lower to 18.27 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (SF-36 bodily pain, 0-100, high is good, change score) at <3 months (follow-up: 4 weeks; assessed with: SF-36 bodily pain; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **2.5 lower** (16.2 lower to 11.2 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (SF-36 vitality, 0-100, high is good, change score) at <3 months (follow-up: 4 weeks; assessed with: SF-36 vitality; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **0.5 lower** (8.4 lower to 7.4 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (SF-36 general health, 0-100, high is good, change score) at <3 months (follow-up: 4 weeks; assessed with: SF-36 general health; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **1 lower** (10.54 lower to 8.54 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (SF-36 social function, 0-100, high is good, final value) at <3 months (follow-up: 4 weeks; assessed with: SF-36 social function; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **8.25 higher** (2.99 lower to 19.49 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (SF-36 physical function, 0-100, high is good, change score) at >3 months (follow-up: 16 weeks; assessed with: SF-36 physical function; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **7.25 higher** (5.07 lower to 19.57 higher)	⨁◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	pulsed short-wave therapy	no treatment	Relative (95% CI)	Absolute (95% CI)		
Quality of life (SF-36 bodily pain, 0-100, high is good, change score) at >3 months (follow-up: 16 weeks; assessed with: SF-36 bodily pain; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **12.4 lower** (29.24 lower to 4.44 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (SF-36 vitality, 0-100, high is good, change score) at >3 months (follow-up: 16 weeks; assessed with: SF-36 vitality; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **0.5 lower** (9.18 lower to 8.18 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (SF-36 general health, 0-100, high is good, change score) at >3 months (follow-up: 16 weeks; assessed with: SF-36 general health; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **4.75 lower** (15.36 lower to 5.86 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (SF-36 social function, 0-100, high is good, final value) at >3 months (follow-up: 16 weeks; assessed with: SF-36 social function; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **5.5 higher** (7.76 lower to 18.76 higher)	⨁◯◯◯ Very low	CRITICAL
Pain (WOMAC, VAS [different scale ranges], high is poor, change scores) at <3 months (follow-up: mean 6 weeks; assessed with: WOMAC, VAS)												
2	randomised trials	very serious[a]	not serious	not serious	not serious	none	40	40	-	SMD **0.07 SD lower** (0.5 lower to 0.37 higher)	⨁⨁◯◯ Low	CRITICAL
Pain (KOOS, WOMAC [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 6 weeks; assessed with: KOOS, WOMAC)												
2	randomised trials	very serious[a]	very serious[c]	not serious	very serious[b]	none	79	52	-	SMD **0.28 SD higher** (2.28 lower to 2.84 higher)	⨁◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	pulsed short-wave therapy	no treatment	Relative (95% CI)	Absolute (95% CI)		
Pain (WOMAC, 0-20, high is poor, change score) at >3 months (follow-up: 16 weeks; assessed with: WOMAC; Scale from: 0 to 20)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	20	20	-	MD **0.5 lower** (3.04 lower to 2.04 higher)	⨁◯◯◯ Very low	CRITICAL
Physical function (WOMAC, 0-68, high is poor, change score and final value) at <3 months (follow-up: mean 6 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
2	randomised trials	serious[a]	not serious	not serious	serious[b]	none	40	40	-	MD **2.2 lower** (4.05 lower to 0.35 lower)	⨁⨁◯◯ Low	CRITICAL
Physical function (KOOS, 0-100, high is good, final value) at <3 months (follow-up: 3 weeks; assessed with: KOOS; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	59	32	-	MD **14.2 higher** (6.45 higher to 21.95 higher)	⨁◯◯◯ Very low	CRITICAL
Physical function (WOMAC, 0-68, high is poor, change score) at >3 months (follow-up: 16 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **1.55 lower** (10 lower to 6.9 higher)	⨁◯◯◯ Very low	CRITICAL
Psychological distress (Beck depression score, 0-63, high is poor, change score) at <3 months (follow-up: 4 weeks; assessed with: Beck depression score; Scale from: 0 to 63)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **0.15 lower** (2.33 lower to 2.03 higher)	⨁◯◯◯ Very low	IMPORTANT
Psychological distress (GHQ, 0-90, high is poor, final value) at <3 months (follow-up: 12 weeks; assessed with: GHQ; Scale from: 0 to 90)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	30	30	-	MD **1.73 lower** (9.33 lower to 5.87 higher)	⨁◯◯◯ Very low	IMPORTANT
Psychological distress (Beck depression score, 0-63, high is poor, change score) at >3 months (follow-up: 16 weeks; assessed with: Beck depression score; Scale from: 0 to 63)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	pulsed short-wave therapy	no treatment	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **0.1 higher** (2.61 lower to 2.81 higher)	⨁◯◯◯ Very low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

c. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

F.2 Interferential therapy compared to pulsed short-wave therapy, laser therapy, sham electrotherapy and no treatment

Table 68: Clinical evidence profile: interferential therapy compared to pulsed short-wave therapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	interferential therapy	pulsed short-wave therapy	Relative (95% CI)	Absolute (95% CI)		
Pain (WOMAC, 0-20, high is poor, final values) at <3 months (follow-up: mean 10 weeks; assessed with: WOMAC; Scale from: 0 to 20)												
2	randomised trials	serious[a]	not serious	not serious	not serious	none	51	52	-	MD **0.52 lower** (1.25 lower to 0.21 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Pain (WOMAC, 0-20, high is poor, final value) at >3 months (follow-up: 6 months; assessed with: WOMAC; Scale from: 0 to 20)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	interferential therapy	pulsed short-wave therapy	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	31	32	-	MD **1.1 lower** (2.93 lower to 0.73 higher)	⨁⨁◯◯ Low	CRITICAL
Physical function (WOMAC, 0-68, high is poor, final values) at <3 months (follow-up: mean 10 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
2	randomised trials	serious[a]	not serious	not serious	not serious	none	51	52	-	MD **0.88 lower** (2.6 lower to 0.84 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Physical function (WOMAC, 0-68, high is poor, final value) at >3 months (follow-up: 6 months; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	31	32	-	MD **1.4 lower** (7.42 lower to 4.62 higher)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; **MD:** mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 69: Clinical evidence profile: interferential therapy compared to laser therapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	interferential therapy	laser therapy	Relative (95% CI)	Absolute (95% CI)		
Pain (WOMAC, NRS [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 10 weeks; assessed with: WOMAC, NRS)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	interferential therapy	laser therapy	Relative (95% CI)	Absolute (95% CI)		
2	randomised trials	not serious	not serious	not serious	serious[a]	none	62	62	-	SMD **0.25 higher** (0.11 lower to 0.6 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Pain (NRS, 0-10, high is poor, final value) at >3 months (follow-up: 6 months; assessed with: NRS; Scale from: 0 to 10)												
1	randomised trials	not serious	not serious	not serious	serious[a]	none	42	42	-	MD **0.7 higher** (0.46 lower to 1.86 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Physical function (WOMAC, 0-68, high is poor, final value) at <3 months (follow-up: 8 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	serious[b]	not serious	not serious	serious[a]	none	20	20	-	MD **3 lower** (4.76 lower to 1.24 lower)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

Explanations

a. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

b. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Table 70: Clinical evidence profile: interferential therapy compared to sham electrotherapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	interferential therapy	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
Pain (WOMAC, 0-20, high is poor, change score and final value) at <3 months (follow-up: mean 11 weeks; assessed with: WOMAC; Scale from: 0 to 20)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	interferential therapy	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
3	randomised trials	serious[a]	very serious[b]	not serious	very serious[c]	none	96	70	-	MD **2.84 lower** (9.07 lower to 3.39 higher)	⨁◯◯◯ Very low	CRITICAL
Pain (NRS, 0-10, high is poor, final value) at <3 months (follow-up: 12 weeks; assessed with: NRS; Scale from: 0 to 10)												
1	randomised trials	not serious	not serious	not serious	serious[c]	none	42	42	-	MD **0.3 lower** (1.55 lower to 0.95 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Pain (WOMAC, 0-20, high is poor, change score) at >3 months (follow-up: 6 months; assessed with: WOMAC; Scale from: 0 to 20)												
1	randomised trials	serious[a]	not serious	not serious	serious[c]	none	31	35	-	MD **0.2 lower** (1.8 lower to 1.4 higher)	⨁⨁◯◯ Low	CRITICAL
Pain (NRS, 0-10, high is poor, final value) at >3 months (follow-up: 6 months; assessed with: NRS; Scale from: 0 to 10)												
1	randomised trials	not serious	not serious	not serious	serious[c]	none	42	42	-	MD **0.45 lower** (1.73 lower to 0.83 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Physical function (WOMAC, 0-68, high is poor, change score and final value) at <3 months (follow-up: mean 11 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
3	randomised trials	serious[a]	very serious[b]	not serious	very serious[c]	none	96	70	-	MD **10.88 lower** (28.56 lower to 6.8 higher)	⨁◯◯◯ Very low	CRITICAL
Physical function (WOMAC, 0-68, high is poor, change score) at >3 months (follow-up: 6 months; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	serious[a]	not serious	not serious	serious[c]	none	31	35	-	MD **3 higher** (1.94 lower to 7.94 higher)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; **MD:** mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

c. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 71: Clinical evidence profile: interferential therapy compared to no treatment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	interferential therapy	no treatment	Relative (95% CI)	Absolute (95% CI)		
Pain (WOMAC, 0-20, high is poor, final value) at <3 months (follow-up: 8 weeks; assessed with: WOMAC; Scale from: 0 to 20)												
1	randomised trials	serious[a]	not serious	not serious	not serious	none	20	20	-	MD **2 higher** (1.2 higher to 2.8 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Physical function (WOMAC, 0-68, high is poor, final value) at <3 months (follow-up: 8 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	20	20	-	MD **2.7 lower** (4.91 lower to 0.49 lower)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; **MD:** mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

F.3 Neuromuscular electrical stimulation compared to no treatment

Table 72: Clinical evidence profile: neuromuscular electrical stimulation compared to no treatment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	neuromuscular electrical stimulation	no treatment	Relative (95% CI)	Absolute (95% CI)		
Quality of life (SF-36 physical component, 0-100, high is good, final value) at <3 months (follow-up: 14 weeks; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	10	6	-	MD **20.23 lower** (38.83 lower to 1.63 lower)	⨁◯◯◯ Very low	CRITICAL
Quality of life (SF-36 mental component, 0-100, high is good, final value) at <3 months (follow-up: 14 weeks; assessed with: SF-36 mental component; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	10	6	-	MD **5.1 lower** (24.75 lower to 14.55 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (NHP pain, scale range unclear, high is poor, final value) at <3 months (follow-up: 2 weeks; assessed with: Nottingham Health Profile)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	21	17	-	MD **13.35 lower** (31.41 lower to 4.71 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (NHP physical mobility, scale range unclear, high is poor, final value) at <3 months (follow-up: 2 weeks; assessed with: Nottingham Health Profile)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	21	17	-	MD **4.67 higher** (10.03 lower to 19.37 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (NHP energy level, scale range unclear, high is poor, final value) at <3 months (follow-up: 2 weeks; assessed with: Nottingham Health Profile)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	21	17	-	MD **20.23 lower** (45.51 lower to 5.05 higher)	⨁◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	neuromuscular electrical stimulation	no treatment	Relative (95% CI)	Absolute (95% CI)		
Quality of life (NHP sleep, scale range unclear, high is poor, final value) at <3 months (follow-up: 2 weeks; assessed with: Nottingham Health Profile)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	21	17	-	MD **2.17 lower** (21.98 lower to 17.64 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (NHP social isolation, scale range unclear, high is poor, final value) at <3 months (follow-up: 2 weeks; assessed with: Nottingham Health Profile)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	21	17	-	MD **1.29 lower** (15.17 lower to 12.59 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (NHP total score, scale range unclear, high is poor, final value) at <3 months (follow-up: 2 weeks; assessed with: Nottingham Health Profile)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	21	17	-	MD **45.49 lower** (125.53 lower to 34.55 higher)	⨁◯◯◯ Very low	CRITICAL
Pain (WOMAC [different scale ranges], high is poor, change scores) at <3 months (follow-up: 7 weeks; assessed with: WOMAC)												
2	randomised trials	serious[a]	not serious	not serious	not serious	none	66	64	-	SMD **0.12 SD higher** (0.22 lower to 0.47 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Pain (WOMAC, VAS [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 7 weeks; assessed with: WOMAC, VAS)												
4	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	81	73	-	SMD **0.56 SD lower** (0.89 lower to 0.23 lower)	⨁◯◯◯ Very low	CRITICAL
Pain (WOMAC, 5-25, high is poor, change score) at >3 months (follow-up: 16 weeks; assessed with: WOMAC; Scale from: 5 to 25)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	neuromuscular electrical stimulation	no treatment	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	16	14	-	MD **1.94 lower** (4.04 lower to 0.16 higher)	⨁◯◯◯ Very low	CRITICAL
Pain (VAS, 0-10, high is poor, final value) at >3 months (follow-up: 18 weeks; assessed with: VAS; Scale from: 0 to 10)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	23	21	-	MD **1.9 lower** (3.29 lower to 0.51 lower)	⨁◯◯◯ Very low	CRITICAL
Physical function (WOMAC [different scale ranges], high is poor, change scores) at <3 months (follow-up: mean 7 weeks; assessed with: WOMAC)												
2	randomised trials	very serious[a]	serious[c]	not serious	very serious[b]	none	66	64	-	SMD **0.02 SD lower** (0.62 lower to 0.58 higher)	⨁◯◯◯ Very low	CRITICAL
Physical function (WOMAC, 0-68, high is poor, final values) at <3 months (follow-up: mean 8 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
2	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	31	23	-	MD **4.22 higher** (3.12 lower to 11.56 higher)	⨁◯◯◯ Very low	CRITICAL
Physical function (WOMAC, 17-85, high is poor, change score) at >3 months (follow-up: 16 weeks; assessed with: WOMAC; Scale from: 17 to 85)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	16	14	-	MD **9.92 lower** (17.34 lower to 2.5 lower)	⨁◯◯◯ Very low	CRITICAL
Mild adverse events at <3 months (follow-up: 8 weeks)												
1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	1/50 (2.0%)	0/50 (0.0%)	**Peto OR 7.39** (0.15 to 372.38)	**20 more per 1,000** (from 30 fewer to 70 more)[d]	⨁⨁◯◯ Low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

c. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

d. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

F.4 Extracorporeal shockwave therapy compared to sham electrotherapy and no treatment

Table 73: Clinical evidence profile: extracorporeal shockwave therapy compared to sham electrotherapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	extracorporeal shockwave therapy	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
Pain (WOMAC, 0-20, high is poor, change score and final values) at <3 months (follow-up: mean 12 weeks; assessed with: WOMAC; Scale from: 0 to 20)												
3	randomised trials	serious[a]	not serious	not serious	not serious	none	99	101	-	MD **2.99 lower** (3.57 lower to 2.42 lower)	⨁⨁⨁◯ Moderate	CRITICAL
Pain (VAS, 0-10, high is poor, change score and final value) at <3 months (follow-up: mean 4 weeks; assessed with: VAS; Scale from: 0 to 10)												
2	randomised trials	very serious[a]	serious[b]	not serious	serious[c]	none	84	23	-	MD **2.17 lower** (3.55 lower to 0.79 lower)	⨁◯◯◯ Very low	CRITICAL
Physical function (WOMAC, 0-68, high is poor, change score and final values) at <3 months (follow-up: mean 12 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
3	randomised trials	serious[a]	not serious	not serious	not serious	none	99	101	-	MD **9.06 lower** (11.11 lower to 7.02 lower)	⨁⨁⨁◯ Moderate	CRITICAL
Mild adverse events at <3 months (follow-up: 12 weeks)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	extracorporeal shockwave therapy	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	not serious	not serious	not serious	serious[c]	none	0/34 (0.0%)	2/36 (5.6%)	**Peto OR 0.14** (0.01 to 2.27)	**60 fewer per 1,000** (from 150 fewer to 30 more)[d]	⨁⨁⨁◯ Moderate	IMPORTANT
Moderate/major adverse events at <3 months (follow-up: 12 weeks)												
1	randomised trials	not serious	not serious	not serious	very serious[e]	none	0/32 (0.0%)	0/31 (0.0%)	**RD 0.00** (-0.06 to 0.06)	**0 fewer per 1,000** (from 60 fewer to 60 more)[d]	⨁⨁◯◯ Low	IMPORTANT

CI: confidence interval; **MD:** mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

c. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

d. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

e. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

Table 74:Clinical evidence profile: extracorporeal shockwave therapy compared to no treatment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	extracorporeal shockwave therapy	no treatment	Relative (95% CI)	Absolute (95% CI)		
Pain (WOMAC, VAS [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 10 weeks; assessed with: WOMAC, VAS)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	extracorporeal shockwave therapy	no treatment	Relative (95% CI)	Absolute (95% CI)		
2	randomised trials	serious[a]	not serious	not serious	serious[b]	none	31	42	-	SMD **0.43 SD higher** (0.05 lower to 0.91 higher)	⨁⨁◯◯ Low	CRITICAL
Physical function (WOMAC, 0-68, high is poor, final score) at <3 months (follow-up: 7 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	23	22	-	MD **10.74 higher** (3.67 higher to 17.81 higher)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

F.5 Laser therapy compared to pulsed short-wave therapy, neuromuscular electrical stimulation, sham electrotherapy and no treatment

Table 75: Clinical evidence profile: laser therapy compared with pulsed short-wave therapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	laser therapy	pulsed short-wave therapy	Relative (95% CI)	Absolute (95% CI)		
Pain (WOMAC, 0-20, high is poor, final value) at <3 months (follow-up: 8 weeks; assessed with: WOMAC; Scale from: 0 to 20)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	laser therapy	pulsed short-wave therapy	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	20	20	-	MD **0.85 lower** (1.62 lower to 0.08 lower)	⨁⨁◯◯ Low	CRITICAL
Physical function (WOMAC, 0-68, high is poor, final value) at <3 months (follow-up: 8 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	serious[a]	not serious	not serious	not serious	none	20	20	-	MD **3.2 higher** (1.84 higher to 4.56 higher)	⨁⨁⨁◯ Moderate	CRITICAL

CI: confidence interval; **MD:** mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 76: Clinical evidence profile: laser therapy compared with neuromuscular electrical stimulation

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	laser therapy	neuromuscular electrical stimulation	Relative (95% CI)	Absolute (95% CI)		
Pain (VAS, 0-10, high is poor, final value) at ≤3 months (follow up: 12 weeks; assessed with: VAS; Scale from: 0 to 10)												
1	randomised trials	very serious [a]	not serious	not serious	serious [b]	none	15	15	-	MD **0.7 higher** (0.22 higher to 1.18 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 77: Clinical evidence profile: laser therapy compared with sham electrotherapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	laser therapy	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
Quality of life (KOOS, NHP [different scale ranges], high is good, final values) at <3 months (follow-up: mean 8 weeks; assessed with: KOOS, NHP)												
2	randomised trials	not serious	not serious	not serious	not serious	none	65	62	-	SMD **0.08 SD higher** (0.27 lower to 0.43 higher)	⨁⨁⨁⨁ High	CRITICAL
Quality of life (SF-36 physical component, 0-50, high is good, change score) at <3 months (follow-up: 12 weeks; assessed with: SF-36 physical component; Scale from: 0 to 50)												
1	randomised trials	not serious	not serious	not serious	serious[a]	none	27	28	-	MD **2.3 lower** (5.97 lower to 1.37 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Quality of life (SF-36 mental component, 0-50, high is good, change score) at <3 months (follow-up: 12 weeks; assessed with: SF-36 mental component; Scale from: 0 to 50)												
1	randomised trials	not serious	not serious	not serious	serious[a]	none	27	28	-	MD **5.1 higher** (0.03 lower to 10.23 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Quality of life (SF-12 physical component, 0-100, high is good, final value) at <3 months (follow-up: 12 weeks; assessed with: SF-12 physical component; Scale from: 0 to 100)												
1	randomised trials	serious[b]	not serious	not serious	not serious	none	65	58	-	MD **0.8 lower** (4.28 lower to 2.68 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Quality of life (SF-12 mental component, 0-100, high is good, final value) at <3 months (follow-up: 12 weeks; assessed with: SF-12 mental component; Scale from: 0 to 100)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	laser therapy	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious[b]	not serious	not serious	not serious	none	65	58	-	MD **0.2 lower** (3.8 lower to 3.4 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Quality of life (SF-12 physical component, 0-100, high is good, final value) at >3 months (follow-up: 12 months; assessed with: SF-12 physical component; Scale from: 0 to 100)												
1	randomised trials	serious[b]	not serious	not serious	not serious	none	58	51	-	MD **0.6 higher** (3.18 lower to 4.38 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Quality of life (SF-12 mental component, 0-100, high is good, final value) at >3 months (follow-up: 12 months; assessed with: SF-12 mental component; Scale from: 0 to 100)												
1	randomised trials	serious[b]	not serious	not serious	not serious	none	58	51	-	MD **0.7 lower** (4.25 lower to 2.85 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Pain (WOMAC, AUSCAN, VAS [different scale ranges], high is poor, change scores) at <3 months (follow-up: mean 8 weeks; assessed with: WOMAC, AUSCAN, VAS)												
4	randomised trials	not serious	very serious[c]	not serious	serious[a]	none	193	135	-	SMD **0.96 SD lower** (2.09 lower to 0.18 higher)	⨁◯◯◯ Very low	CRITICAL
Pain (KOOS, WOMAC, VNPS, VAS [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 8 weeks; assessed with: KOOS, WOMAC, VNPS, VAS)												
14	randomised trials	serious[b]	serious[c]	not serious	serious[a]	none	452	370	-	SMD **0.31 SD lower** (0.55 lower to 0.06 lower)	⨁◯◯◯ Very low	CRITICAL
Pain (AUSCAN, 0-4, high is poor, change score) at >3 months (follow-up: 6 months; assessed with: AUSCAN; Scale from: 0 to 4)												
1	randomised trials	not serious	not serious	not serious	not serious	none	41	45	-	MD **0.06 lower** (0.39 lower to 0.27 higher)	⨁⨁⨁⨁ High	CRITICAL
Pain (WOMAC, NRS [different scale ranges], high is poor, final values) at >3 months (follow-up: mean 8 months; assessed with: WOMAC; Scale from: 0 to 20)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	laser therapy	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
3	randomised trials	serious[b]	not serious	not serious	not serious	none	120	113	-	SMD **0.12 SD lower** (0.38 lower to 0.14 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Physical function (WOMAC, AUSCAN [different scale ranges], high is poor, change score) at <3 months (follow-up: mean 12 weeks; assessed with: WOMAC, AUSCAN)												
2	randomised trials	not serious	not serious	not serious	not serious	none	68	73	-	SMD **0.15 SD lower** (0.48 lower to 0.19 higher)	⨁⨁⨁⨁ High	CRITICAL
Physical function (KOOS, WOMAC [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 8 weeks; assessed with: KOOS, WOMAC)												
8	randomised trials	serious[b]	very serious[c]	not serious	serious[a]	none	246	204	-	SMD **0.37 SD lower** (0.89 lower to 0.16 higher)	⨁◯◯◯ Very low	CRITICAL
Physical function (AUSCAN, 0-4, high is poor, change score) at >3 months (follow-up: 6 months; assessed with: AUSCAN; Scale from: 0 to 4)												
1	randomised trials	not serious	not serious	not serious	serious[a]	none	41	45	-	MD **0.07 lower** (0.4 lower to 0.26 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Physical function (WOMAC, 0-68, high is poor, final values) at >3 months (follow-up: 9 months; assessed with: WOMAC; Scale from: 0 to 68)												
2	randomised trials	serious[b]	not serious	not serious	not serious	none	78	71	-	MD **0.13 higher** (4.33 lower to 4.59 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Mild adverse events at <3 months (follow-up: mean 8 weeks)												
4	randomised trials	very serious[b]	serious[d]	not serious	very serious[e]	none	10/118 (8.5%)	6/109 (5.5%)	**RD 0.04** (-0.03 to 0.10)	**40 more per 1,000** (from 30 fewer to 100 more)	⨁◯◯◯ Very low	IMPORTANT

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	laser therapy	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
Mild adverse event at >3 months (follow-up: 6 months)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[e]	none	0/32 (0.0%)	0/34 (0.0%)	**RD 0.00** (-0.06 to 0.06)	**0 fewer per 1,000** (from 60 fewer to 60 more)	⨁◯◯◯ Very low	IMPORTANT
Moderate/major adverse events at <3 months (follow-up: 12 weeks)												
1	randomised trials	not serious	not serious	not serious	serious[a]	none	0/27 (0.0%)	2/28 (7.1%)	**Peto OR 0.14** (0.01 to 2.22)	**70 fewer per 1,000** (from 180 fewer to 40 more)[f]	⨁⨁⨁◯ Moderate	IMPORTANT

CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

Explanations

a. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

b. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

c. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

d. Downgraded for heterogeneity due to conflicting number of events in different studies (zero events in one or more studies)

e. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

f. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

Table 78: Clinical evidence profile: laser therapy compared with no treatment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	laser therapy	no treatment	Relative (95% CI)	Absolute (95% CI)		
Quality of life (SF-12 physical component, 0-100, high is good, final value) at <3 months (follow-up: 12 weeks; assessed with: SF-12 physical component; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	not serious	none	65	69	-	MD **0.1 lower** (3.52 lower to 3.32 higher)	⨁⨁◯◯ Low	CRITICAL
Quality of life (SF-12 mental component, 0-100, high is good, final value) at <3 months (follow-up: 12 weeks; assessed with: SF-12 mental component; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	65	69	-	MD **2.8 lower** (6.03 lower to 0.43 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (SF-12 physical component, 0-100, high is good, final value) at >3 months (follow-up: 12 weeks; assessed with: SF-12 physical component)												
1	randomised trials	very serious[a]	not serious	not serious	not serious	none	58	62	-	MD **0.1 lower** (3.93 lower to 3.73 higher)	⨁⨁◯◯ Low	CRITICAL
Quality of life (SF-12 mental component, 0-100, high is good, final value) at >3 months (follow-up: 12 weeks; assessed with: SF-12 mental component)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	58	62	-	MD **2.3 lower** (5.88 lower to 1.28 higher)	⨁◯◯◯ Very low	CRITICAL
Pain (WOMAC [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 10 weeks)												
4	randomised trials	very serious[a]	very serious[c]	not serious	serious[b]	none	138	141	-	SMD **0.39 SD higher** (0.2 lower to 0.98 higher)	⨁◯◯◯ Very low	CRITICAL
Pain (WOMAC, 0-20, high is poor, final value) at >3 months (follow-up: 12 months; assessed with: WOMAC; Scale from: 0 to 20)												
1	randomised trials	very serious[a]	not serious	not serious	not serious	none	58	62	-	MD **0.3 lower** (1.77 lower to 1.17 higher)	⨁⨁◯◯ Low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	laser therapy	no treatment	Relative (95% CI)	Absolute (95% CI)		
Physical function (WOMAC [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 10 weeks; assessed with: WOMAC)												
4	randomised trials	very serious[a]	very serious[c]	not serious	serious[b]	none	138	141	-	SMD **1 SD lower** (2.23 lower to 0.23 higher)	⨁◯◯◯ Very low	CRITICAL
Physical function (WOMAC, 0-68, high is poor, final value) at >3 months (follow-up: 12 months; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	very serious[a]	not serious	not serious	not serious	none	58	62	-	MD **1 higher** (3.78 lower to 5.78 higher)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

c. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

F.6 Transcutaneous electrical nerve stimulation compared to pulsed short-wave therapy, interferential therapy, sham electrotherapy and no treatment

Table 79: Clinical evidence profile: transcutaneous electrical nerve stimulation compared with pulsed short-wave therapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	transcutaneous electrical nerve stimulation	pulsed short-wave therapy	Relative (95% CI)	Absolute (95% CI)		
Pain (WOMAC, VAS [different scale ranges], high is poor, change score) at ≤3 months (follow up: mean 10 weeks; assessed with: WOMAC)												
2	randomised trials	serious [a]	not serious	not serious	serious [b]	none	57	52	-	SMD **0.24 SD higher** (0.14 lower to 0.61 higher)	⨁⨁◯◯ LOW	CRITICAL
Pain (WOMAC, 0-20, high is poor, change score) at >3 months (follow up: 6 months; assessed with: WOMAC; Scale from: 0 to 20)												
1	randomised trials	serious [a]	not serious	not serious	serious [b]	none	37	32	-	MD **1.5 higher** (0.21 lower to 3.21 higher)	⨁⨁◯◯ LOW	CRITICAL
Physical function (WOMAC, 0-68, high is poor, change score) at ≤3 months (follow up: 6 months; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	serious [a]	not serious	not serious	serious [b]	none	37	32	-	MD **2.7 higher** (2.99 lower to 8.39 higher)	⨁⨁◯◯ LOW	CRITICAL
Physical function (WOMAC, 0-68, high is poor, change score) at >3 months (follow up: 6 months; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	serious [a]	not serious	not serious	serious [b]	none	37	32	-	MD **0.4 higher** (5.49 lower to 6.29 higher)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **SMD:** Standardised mean difference; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 80: Clinical evidence profile: transcutaneous electrical nerve stimulation compared with interferential therapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	transcutaneous electrical nerve stimulation	interferential therapy	Relative (95% CI)	Absolute (95% CI)		
Pain (WOMAC, 0-20, high is poor, change score) at ≤3 months (follow up: mean 10 weeks; assessed with: WOMAC; Scale from: 0 to 20)												
2	randomised trials	serious [a]	serious [b]	not serious	serious [c]	none	90	83	-	MD **1.2 higher** (0.48 lower to 2.89 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Pain (WOMAC, 0-20, high is poor, change score) at >3 months (follow up: 6 months; assessed with: WOMAC; Scale from: 0 to 20)												
1	randomised trials	serious [a]	not serious	not serious	serious [c]	none	37	31	-	MD **0.3 higher** (1.39 lower to 1.99 higher)	⨁⨁◯◯ LOW	CRITICAL
Physical function (WOMAC, 0-68, high is poor, change score) at ≤3 months (follow up: mean 10 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
2	randomised trials	serious [a]	serious [b]	not serious	serious [c]	none	90	83	-	MD **3.68 higher** (1.69 lower to 9.06 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Physical function (WOMAC, 0-68, high is poor, change score) at >3 months (follow up: 6 months; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	serious [a]	not serious	not serious	serious [c]	none	37	31	-	MD **1 higher** (4.39 lower to 6.39 higher)	⨁⨁◯◯ LOW	CRITICAL
Mild adverse events at ≤3 months (follow up: 8 weeks)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	transcutaneous electrical nerve stimulation	interferential therapy	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious [a]	not serious	not serious	very serious [c]	none	9/59 (15.3%)	5/57 (8.8%)	**RR 1.74** (0.62 to 4.88)	**65 more per 1,000** (from 33 fewer to 340 more)	⨁◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **MD:** Mean difference; **RR:** Risk ratio

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

c. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 81: Clinical evidence profile: transcutaneous electrical nerve stimulation compared with sham electrotherapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	transcutaneous electrical nerve stimulation	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
Quality of life (SF-36 physical function, 0-1, high is good, final value) at <3 months (follow-up: 3 weeks; assessed with: SF-36 physical function; Scale from: 0 to 1)												
1	randomised trials	very serious[a]	not serious	not serious	not serious	none	20	20	-	MD **0.16 higher** (0.07 higher to 0.25 higher)	⨁⨁◯◯ Low	CRITICAL
Quality of life (SF-36 vitality, 0-1, high is good, final value) at <3 months (follow-up: 3 weeks; assessed with: SF-36 vitality; Scale from: 0 to 1)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **0.02 lower** (0.12 lower to 0.08 higher)	⨁◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	transcutaneous electrical nerve stimulation	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
Quality of life (SF-36 general health, 0-1, high is good, final value) at <3 months (follow-up: 3 weeks; assessed with: SF-36 general health; Scale from: 0 to 1)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	20	20	-	MD **0.06 higher** (0.02 lower to 0.14 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (SF-36 mental health, 0-1, high is good, final value) at <3 months (follow-up: 3 weeks; assessed with: SF-36 mental health; Scale from: 0 to 1)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **0.02 higher** (0.08 lower to 0.12 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (SF-36 social function, 0-1, high is good, final value) at <3 months (follow-up: 3 weeks; assessed with: SF-36 social function; Scale from: 0 to 1)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	20	20	-	MD **0.11 higher** (0.02 higher to 0.2 higher)	⨁◯◯◯ Very low	CRITICAL
Pain (WOMAC, 0-20, high is poor, change score) at <3 months (follow-up: 12 weeks; assessed with: WOMAC; Scale from: 0 to 20)												
1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	37	37	-	MD **0.8 lower** (2.26 lower to 0.66 higher)	⨁⨁◯◯ Low	CRITICAL
Pain (WOMAC, VAS [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 6 weeks; assessed with: WOMAC, VAS)												
5	randomised trials	serious[a]	serious[c]	not serious	serious[b]	none	213	148	-	SMD **0.32 SD lower** (0.76 lower to 0.13 higher)	⨁◯◯◯ Very low	CRITICAL
Pain (WOMAC, 0-20, high is poor, change score and final value) at >3 months (follow-up: mean 25 weeks; assessed with: WOMAC; Scale from: 0 to 20)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	transcutaneous electrical nerve stimulation	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
2	randomised trials	serious[a]	not serious	not serious	very serious[b]	none	110	111	-	MD **0.49 higher** (0.81 lower to 1.8 higher)	⨁◯◯◯ Very low	CRITICAL
Physical function (WOMAC, 0-68, high is poor, change score) at <3 months (follow-up: 12 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	37	37	-	MD **0.7 lower** (5.78 lower to 4.38 higher)	⨁⨁◯◯ Low	CRITICAL
Physical function (WOMAC [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 7 weeks; assessed with: WOMAC)												
4	randomised trials	serious[a]	serious[c]	not serious	serious[b]	none	175	138	-	SMD **0.17 SD lower** (0.52 lower to 0.18 higher)	⨁◯◯◯ Very low	CRITICAL
Physical function (WOMAC, 0-68, high is poor, change score and final value) at >3 months (follow-up: mean 25 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
2	randomised trials	serious[a]	not serious	not serious	not serious	none	110	111	-	MD **0.45 higher** (2.97 lower to 3.88 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Mild adverse events at <3 months (follow-up: 4 weeks)												
1	randomised trials	serious[a]	not serious	not serious	very serious[d]	none	0/12 (0.0%)	0/12 (0.0%)	**RD 0.00** (-0.15 to 0.15)	**0 fewer per 1,000** (from 150 fewer to 150 more)[e]	⨁◯◯◯ Very low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

c. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

d. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

e. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

Table 82: Clinical evidence profile: transcutaneous electrical nerve stimulation compared with no treatment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	transcutaneous electrical nerve stimulation	no treatment	Relative (95% CI)	Absolute (95% CI)		
Pain (VAS, 0-10, high is poor, change score) at <3 months (follow-up: 8 weeks; assessed with: VAS; Scale from: 0 to 10)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **0.05 lower** (0.52 lower to 0.42 higher)	⨁◯◯◯ Very low	CRITICAL
Pain (WOMAC [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 7 weeks; assessed with: WOMAC)												
3	randomised trials	very serious[a]	serious[c]	not serious	not serious	none	54	57	-	SMD **0 SD** (0.45 lower to 0.46 higher)	⨁◯◯◯ Very low	CRITICAL
Physical function (WOMAC [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 7 weeks; assessed with: WOMAC)												
3	randomised trials	very serious[a]	serious[c]	not serious	very serious[b]	none	54	57	-	SMD **0.08 SD higher** (0.53 lower to 0.68 higher)	⨁◯◯◯ Very low	CRITICAL
Mild adverse events at <3 months (follow-up: 4 weeks)												
1	randomised trials	serious[a]	not serious	not serious	very serious[d]	none	0/12 (0.0%)	0/12 (0.0%)	**RD 0.00** (-0.15 to 0.15)	**0 fewer per 1,000** (from 150 fewer to 150 more)[e]	⨁◯◯◯ Very low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

c. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

d. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

e. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

F.7 Ultrasound compared to pulsed short-wave therapy, neuromuscular electrical stimulation, transcutaneous electrical nerve stimulation, sham electrotherapy and no treatment

Table 83: Clinical evidence profile: ultrasound compared with pulsed short-wave therapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ultrasound	pulsed short-wave therapy	Relative (95% CI)	Absolute (95% CI)		
Pain (VAS, 0-10, high is poor, change score) at ≤3 months (follow up: 8 weeks; assessed with: VAS; Scale from: 0 to 10)												
1	randomised trials	very serious [a]	not serious	not serious	very serious [b]	none	20	20	-	MD **0.01 lower** (0.54 lower to 0.52 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 84: Clinical evidence profile: ultrasound compared with neuromuscular electrical stimulation

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ultrasound	neuromuscular electrical stimulation	Relative (95% CI)	Absolute (95% CI)		
Pain (WOMAC, 0-20, high is poor, final value) at ≤3 months (follow up: 3 weeks; assessed with: WOMAC; Scale from: 0 to 20)												
1	randomised trials	very serious [a]	not serious	not serious	serious [b]	none	30	30	-	MD **0.94 lower** (1.78 lower to 0.1 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months (follow up: 3 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	very serious [a]	not serious	not serious	serious [b]	none	30	30	-	MD **1.16 lower** (2.24 lower to 0.08 lower)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 85: Clinical evidence profile: ultrasound compared with transcutaneous electrical nerve stimulation

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ultrasound	transcutaneous electrical nerve stimulation	Relative (95% CI)	Absolute (95% CI)		
Pain (VAS, 0-10, high is poor, change score) at ≤3 months (follow up: 8 weeks; assessed with: VAS; Scale from: 0 to 10)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ultrasound	transcutaneous electrical nerve stimulation	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	very serious [a]	not serious	not serious	very serious [b]	none	20	20	-	MD **0.02 lower** (0.51 lower to 0.47 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Pain (WOMAC, 0-20, high is poor, final value) at ≤3 months (follow up: 8 weeks; assessed with: WOMAC; Scale from: 0 to 20)												
1	randomised trials	very serious [a]	not serious	not serious	serious [b]	none	12	12	-	MD **3 higher** (0.11 higher to 5.89 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Physical function (WOMAC, 0-68, high is poor, final value) at ≤3 months (follow up: 8 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	very serious [a]	not serious	not serious	serious [b]	none	12	12	-	MD **10.5 higher** (3.23 higher to 17.77 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 86: Clinical evidence profile: ultrasound compared with sham electrotherapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ultrasound	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
Quality of life (SF-36 physical function, 0-100, high is good, change score) at <3 months (follow-up: 13 weeks; assessed with: SF-36 physical function; Scale from: 0 to 100)												
1	randomised trials	not serious	not serious	not serious	not serious	none	49	48	-	MD **11.5 higher** (6.4 higher to 16.6 higher)	⨁⨁⨁⨁ High	CRITICAL
Quality of life (SF-36 bodily pain, 0-100, high is good, change score and final value) at <3 months (follow-up: mean 13 weeks; assessed with: SF-36 bodily pain; Scale from: 0 to 100)												
2	randomised trials	not serious	not serious	not serious	very serious[a]	none	87	66	-	MD **8.67 higher** (8.02 lower to 25.36 higher)	⨁⨁◯◯ Low	CRITICAL
Quality of life (SF-36 role physical, 0-100, high is good, change score) at <3 months (follow-up: 13 weeks; assessed with: SF-36 role physical; Scale from: 0 to 100)												
1	randomised trials	not serious	not serious	not serious	very serious[a]	none	49	48	-	MD **0.67 higher** (6.09 lower to 7.43 higher)	⨁⨁◯◯ Low	CRITICAL
Quality of life (SF-36 vitality, 0-100, high is good, change score) at <3 months (follow-up: 13 weeks; assessed with: SF-36 vitality; Scale from: 0 to 100)												
1	randomised trials	not serious	not serious	not serious	serious[a]	none	49	48	-	MD **5.72 higher** (1.36 higher to 10.08 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Quality of life (SF-36 general health, 0-100, high is good, change score and final value) at <3 months (follow-up: mean 13 weeks; assessed with: SF-36 general health; Scale from: 0 to 100)												
2	randomised trials	not serious	not serious	not serious	not serious	none	87	66	-	MD **7.30 higher** (7.57 lower to 22.17 higher)	⨁⨁◯◯ Low	CRITICAL
Quality of life (SF-36 mental health, 0-100, high is good, change score) at <3 months (follow-up: 13 weeks; assessed with: SF-36 mental health; Scale from: 0 to 100)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ultrasound	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	not serious	not serious	not serious	not serious	none	49	48	-	MD **0.6 higher** (1.78 lower to 2.98 higher)	⨁⨁⨁⨁ High	CRITICAL
Quality of life (SF-36 role emotional, 0-100, high is good, change score) at <3 months (follow-up: 13 weeks; assessed with: SF-36 role emotional; Scale from: 0 to 100)												
1	randomised trials	not serious	not serious	not serious	very serious[a]	none	49	48	-	MD **0.35 lower** (8.2 lower to 7.5 higher)	⨁⨁◯◯ Low	CRITICAL
Quality of life (SF-36 social function, 0-100, high is good, change score) at <3 months (follow-up: 13 weeks; assessed with: SF-36 social function; Scale from: 0 to 100)												
1	randomised trials	not serious	not serious	not serious	serious[a]	none	49	48	-	MD **6.75 higher** (0.27 higher to 13.23 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Quality of life (SF-36 physical component, 0-100, high is good, change score and final value) at <3 months (follow-up: mean 9 weeks; assessed with: SF-36 physical component; Scale from: 0 to 100)												
2	randomised trials	serious[b]	not serious	not serious	serious[a]	none	45	47	-	MD **1.75 higher** (1.57 lower to 5.06 higher)	⨁⨁◯◯ Low	CRITICAL
Quality of life (SF-36 mental component, 0-100, high is good, change score and final value) at <3 months (follow-up: mean 9 weeks; assessed with: SF-36 mental component; Scale from: 0 to 100)												
2	randomised trials	serious[b]	not serious	not serious	very serious[a]	none	45	47	-	MD **0.34 higher** (3.17 lower to 3.86 higher)	⨁◯◯◯ Very low	CRITICAL
Pain (WOMAC, VAS [different scale ranges], high is poor, change scores) at <3 months (follow-up: mean 6 weeks; assessed with: WOMAC, VAS)												
5	randomised trials	serious[b]	serious[c]	not serious	serious[a]	none	190	151	-	SMD **0.53 SD lower** (0.91 lower to 0.15 lower)	⨁◯◯◯ Very low	CRITICAL
Pain (WOMAC, VAS [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 8 weeks; assessed with: WOMAC, VAS)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ultrasound	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
8	randomised trials	serious[b]	very serious[c]	not serious	serious[a]	none	268	190	-	SMD **0.48 SD lower** (0.89 lower to 0.08 lower)	⨁◯◯◯ Very low	CRITICAL
Pain (VAS, 0-100, high is poor, change score) at >3 months (follow-up: 6 months; assessed with: VAS; Scale from: 0 to 100)												
1	randomised trials	serious[b]	not serious	not serious	serious[a]	none	40	20	-	MD **1.4 lower** (8.54 lower to 5.74 higher)	⨁⨁◯◯ Low	CRITICAL
Physical function (WOMAC [different scale ranges], high is poor, change scores) at <3 months (follow-up: mean 5 weeks; assessed with: WOMAC)												
4	randomised trials	serious[b]	not serious	not serious	serious[a]	none	141	103	-	SMD **0.41 SD lower** (0.67 lower to 0.15 lower)	⨁⨁◯◯ Low	CRITICAL
Physical function (WOMAC, 0-68, high is poor, final values) at <3 months (follow-up: mean 5 weeks; Scale from: 0 to 68)												
3	randomised trials	very serious[b]	not serious	not serious	not serious	none	85	82	-	MD **1.92 lower** (5.67 lower to 1.83 higher)	⨁⨁◯◯ Low	CRITICAL
Physical function (WOMAC, 0-68, high is poor, change score) at >3 months (follow-up: 6 months; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	serious[b]	not serious	not serious	serious[a]	none	40	20	-	MD **2.2 lower** (6.58 lower to 2.18 higher)	⨁⨁◯◯ Low	CRITICAL
Psychological distress (HADS anxiety, 0-21, high is poor, change score) at <3 months (follow-up: 3 weeks; assessed with: HADS anxiety; Scale from: 0 to 21)												
1	randomised trials	serious[b]	not serious	not serious	serious[a]	none	20	20	-	MD **0.45 lower** (1.93 lower to 1.03 higher)	⨁⨁◯◯ Low	IMPORTANT
Psychological distress (HADS depression, 0-21, high is poor, change score) at <3 months (follow-up: 3 weeks; assessed with: HADS depression; Scale from: 0 to 21)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ultrasound	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious[b]	not serious	not serious	serious[a]	none	20	20	-	MD **0.3 lower** (1.84 lower to 1.24 higher)	⨁⨁◯◯ Low	IMPORTANT
Mild adverse events at <3 months (follow-up: mean 5 weeks)												
5	randomised trials	serious[b]	serious[d]	not serious	very serious[e]	none	2/206 (1.0%)	4/124 (3.2%)	**RD -0.01** (-0.05 to 0.03)	**10 fewer per 1,000** (from 50 fewer to 30 more)[f]	⨁◯◯◯ Very low	IMPORTANT
Moderate/major adverse events at <3 months (follow-up: 14 weeks)												
1	randomised trials	not serious	not serious	not serious	very serious[e]	none	0/38 (0.0%)	0/18 (0.0%)	**RD 0.00** (-0.08 to 0.08)	**0 fewer per 1,000** (from 80 fewer to 80 more)[f]	⨁⨁◯◯ Low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

Explanations

a. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

b. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

c. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

d. Downgraded for heterogeneity due to conflicting number of events in different studies (zero events in one or more studies)

e. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

f. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

Table 87: Clinical evidence profile: ultrasound compared with no treatment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ultrasound	no treatment	Relative (95% CI)	Absolute (95% CI)		
Quality of life (SF-36 physical component, 0-100, high is poor, final value) at <3 months (follow-up: 12 weeks; assessed with: SF-36 physical component; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	15	15	-	MD **0** (4.22 lower to 4.22 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (SF-36 mental component, 0-100, high is poor, final value) at <3 months (follow-up: 12 weeks; assessed with: SF-36 mental component; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	15	15	-	MD **2.1 higher** (1.13 lower to 5.33 higher)	⨁◯◯◯ Very low	CRITICAL
Pain (VAS, 0-10, high is poor, change scores) at <3 months (follow-up: mean 8 weeks; assessed with: VAS; Scale from: 0 to 10)												
4	randomised trials	very serious[a]	very serious[c]	not serious	serious[b]	none	195	105	-	SMD **0.38 SD lower** (1.16 lower to 0.4 higher)	⨁◯◯◯ Very low	CRITICAL
Pain (WOMAC, VAS [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 10 weeks; assessed with: WOMAC, VAS)												
2	randomised trials	very serious[a]	very serious[c]	not serious	serious[b]	none	27	31	-	SMD **0.18 SD lower** (2.99 lower to 2.64 higher)	⨁◯◯◯ Very low	CRITICAL
Pain (VAS, 0-10, high is poor, final values) at >3 months (follow-up: 12 months; assessed with: VAS; Scale from: 0 to 10)												
2	randomised trials	very serious[a]	very serious[c]	not serious	very serious[b]	none	95	65	-	MD **0.21 lower** (2.36 lower to 1.95 higher)	⨁◯◯◯ Very low	CRITICAL
Physical function (WOMAC, 0-68, high is poor, change score and final value) at <3 months (follow-up: mean 8 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
2	randomised trials	very serious[a]	very serious[c]	not serious	serious[b]	none	92	36	-	MD **3.42 lower** (6.93 lower to 0.1 higher)	⨁◯◯◯ Very low	CRITICAL

CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

c. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

F.8 Combination therapy compared to interferential therapy, neuromuscular electrical stimulation, laser therapy,ultrasound, transcutaneous electrical nerve stimulation, sham electrotherapy and no treatment

Table 88: Clinical evidence profile: combination therapy compared with interferential therapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	combination therapy	interferential therapy	Relative (95% CI)	Absolute (95% CI)		
Pain (VAS, 0-10, high is poor, final value) at <3 months (follow-up: 3 months; assessed with: VAS; Scale from: 0 to 10)												
1	randomised trials	not serious	not serious	not serious	serious[a]	none	42	42	-	MD **1.1 lower** (2.33 lower to 0.13 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Pain (VAS, 0-10, high is poor, final value) at >3 months (follow-up: 6 months; assessed with: VAS; Scale from: 0 to 10)												
1	randomised trials	not serious	not serious	not serious	serious[a]	none	42	42	-	MD **1.15 lower** (2.25 lower to 0.05 lower)	⨁⨁⨁◯ Moderate	CRITICAL

CI: confidence interval; **MD:** mean difference

Explanations

a. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 89: Clinical evidence profile: combination therapy compared with neuromuscular electrical stimulation

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	combination therapy	neuromuscular electrical stimulation	Relative (95% CI)	Absolute (95% CI)		
Pain (VAS, 0-10, high is poor, final value) at ≤3 months (follow up: 12 weeks; assessed with: VAS; Scale from: 0 to 10)												
1	randomised trials	very serious [a]	not serious	not serious	serious [b]	none	14	15	-	MD **0.3 higher** (0.24 lower to 0.84 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 90: Clinical evidence profile: combination therapy compared with laser therapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	combination therapy	laser therapy	Relative (95% CI)	Absolute (95% CI)		
Pain (VAS, NRS, 0-10, high is poor, final values) at <3 months (follow-up: mean 12 weeks; assessed with: VAS, NRS; Scale from: 0 to 10)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	combination therapy	laser therapy	Relative (95% CI)	Absolute (95% CI)		
2	randomised trials	very serious[a]	not serious	not serious	not serious	none	56	57	-	MD **0.46 lower** (1.02 lower to 0.09 higher)	⨁⨁◯◯ Low	CRITICAL
Pain (NRS, 0-10, high is poor, final value) at >3 months (follow-up: 6 months; assessed with: NRS; Scale from: 0 to 10)												
1	randomised trials	not serious	not serious	not serious	serious[b]	none	42	42	-	MD **0.45 lower** (1.47 lower to 0.57 higher)	⨁⨁⨁◯ Moderate	CRITICAL

CI: confidence interval; **MD:** mean difference

Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 91: Clinical evidence profile: combination therapy compared with transcutaneous electrical nerve stimulation

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	combination therapy	transcutaneous electrical nerve stimulation	Relative (95% CI)	Absolute (95% CI)		
Quality of life (SF-36, 0-100, high is good, final value) at <3 months (follow-up: 3 weeks; assessed with: SF-36; Scale from: 0 to 100)												
1	randomised trials	not serious	not serious	serious[a]	very serious[b]	none	19	19	-	MD **0.46 higher** (9.12 lower to 10.04 higher)	⨁◯◯◯ Very low	CRITICAL
Pain (WOMAC, 0-20, high is poor, final value) at <3 months (follow-up: 3 weeks; assessed with: WOMAC; Scale from: 0 to 20)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	combination therapy	transcutaneous electrical nerve stimulation	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	not serious	not serious	not serious	serious[b]	none	19	19	-	MD **1.06 higher** (1.12 lower to 3.24 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Physical function (WOMAC, 0-68, high is poor, final value) at <3 months (follow-up: 3 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	not serious	not serious	not serious	serious[b]	none	19	19	-	MD **5.05 higher** (1.22 lower to 11.32 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Mild adverse events at <3 months (follow-up: 3 weeks)												
1	randomised trials	not serious	not serious	not serious	very serious[c]	none	0/20 (0.0%)	0/20 (0.0%)	**RD 0.00** (-0.09 to 0.09)	**0 fewer per 1,000** (from 90 fewer to 90 more)[d]	⨁⨁◯◯ Low	IMPORTANT
Moderate/major adverse events at <3 months (follow-up: 3 weeks)												
1	randomised trials	not serious	not serious	not serious	very serious[c]	none	0/20 (0.0%)	0/20 (0.0%)	**RD 0.00** (-0.09 to 0.09)	**0 fewer per 1,000** (from 90 fewer to 90 more)[d]	⨁⨁◯◯ Low	IMPORTANT

CI: confidence interval; **MD:** mean difference

Explanations

a. Downgraded by 1 increment due to outcome indirectness (reported the global score of SF-36 rather than subscales)

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

c. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

d. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

Table 92: Clinical evidence profile: combination therapy compared with ultrasound

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	combination therapy	ultrasound	Relative (95% CI)	Absolute (95% CI)		
Quality of life (SF-36 pain, 0-100, high is good, final value) at <3 months (follow-up: 14 weeks; assessed with: SF-36 pain; Scale from: 0 to 100)												
1	randomised trials	not serious	not serious	not serious	very serious[a]	none	15	38	-	MD **1.75 higher** (12.59 lower to 16.09 higher)	⨁⨁◯◯ Low	CRITICAL
Quality of life (SF-36 general health, 0-100, high is good, final value) at <3 months (follow-up: 14 weeks; assessed with: SF-36 general health; Scale from: 0 to 100)												
1	randomised trials	not serious	not serious	not serious	very serious[a]	none	15	38	-	MD **8.88 higher** (2.22 lower to 19.98 higher)	⨁⨁◯◯ Low	CRITICAL
Pain (VAS, 0-100, high is poor, change score and final value) at <3 months (follow-up: mean 8 weeks; assessed with: VAS; Scale from: 0 to 100)												
2	randomised trials	very serious[b]	not serious	not serious	very serious[a]	none	89	112	-	MD **0.65 higher** (10.88 lower to 12.19 higher)	⨁◯◯◯ Very low	CRITICAL
Mild adverse events at <3 months (follow-up: mean 8 weeks)												
2	randomised trials	serious[b]	serious[c]	not serious	very serious[d]	none	4/79 (5.1%)	3/106 (2.8%)	**RD 0.01** (-0.05 to 0.08)	**10 more per 1,000** (from 50 fewer to 80 more)[e]	⨁◯◯◯ Very low	IMPORTANT
Moderate/ major adverse events at < 3 months (follow-up: 14 weeks)												
1	randomised trials	not serious	not serious	not serious	very serious[d]	none	0/15 (0.0%)	0/38 (0.0%)	**RD 0.00** (-0.09 to 0.09)	**0 fewer per 1,000** (from 90 fewer to 90 more)[e]	⨁⨁◯◯ Low	IMPORTANT

CI: confidence interval; **MD:** mean difference

Explanations

a. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

b. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

c. Downgraded for heterogeneity due to conflicting number of events in different studies (zero events in one or more studies)

d. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

e. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

Table 93: Clinical evidence profile: combination therapy compared with sham electrotherapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	combination therapy	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
Quality of life (SF-36 pain, 0-100, high is good, final values) at <3 months (follow-up: 14 weeks; assessed with: SF-36 pain; Scale from: 0 to 100)												
1	randomised trials	not serious	not serious	not serious	very serious[a]	none	15	18	-	MD **0.85 higher** (14.04 lower to 15.74 higher)	⨁⨁◯◯ Low	CRITICAL
Quality of life (SF-36 general health, 0-100, high is good, final values) at <3 months (follow-up: 14 weeks; assessed with: SF-36 general health; Scale from: 0 to 100)												
1	randomised trials	not serious	not serious	not serious	very serious[a]	none	15	18	-	MD **7.74 higher** (4.55 lower to 20.03 higher)	⨁⨁◯◯ Low	CRITICAL
Pain (VAS, 0-100, high is poor, final value) at <3 months (follow-up: mean 13 weeks; assessed with: VAS; Scale from: 0 to 100)												
2	randomised trials	not serious	not serious	not serious	serious[a]	none	57	60	-	MD **16.04 lower** (24.97 lower to 7.11 lower)	⨁⨁⨁◯ Moderate	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	combination therapy	sham electrotherapy	Relative (95% CI)	Absolute (95% CI)		
Pain (VAS, 0-10, high is poor, final value) at >3 months (follow-up: 6 months; assessed with: VAS; Scale from: 0 to 10)												
1	randomised trials	not serious	not serious	not serious	not serious	none	42	42	-	MD **3 lower** (4.03 lower to 1.97 lower)	⨁⨁⨁⨁ High	CRITICAL
Mild adverse events at <3 months (follow-up: 14 weeks)												
1	randomised trials	not serious	not serious	not serious	very serious[b]	none	0/15 (0.0%)	0/18 (0.0%)	**RD 0.00** (-0.11 to 0.11)	**0 fewer per 1,000** (from 110 fewer to 110 more)[c]	⨁⨁◯◯ Low	IMPORTANT
Moderate/major adverse events at <3 months (follow-up: 14 weeks)												
1	randomised trials	not serious	not serious	not serious	very serious[b]	none	0/15 (0.0%)	0/18 (0.0%)	**RD 0.00** (-0.11 to 0.11)	**0 fewer per 1,000** (from 110 fewer to 110 more)[c]	⨁⨁◯◯ Low	IMPORTANT

CI: confidence interval; **MD:** mean difference

Explanations

a. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

b. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

c. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

Table 94: Clinical evidence profile: combination therapy compared with no treatment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	combination therapy	no treatment	Relative (95% CI)	Absolute (95% CI)		
Quality of life (SF-36 physical function, 0-100, high is good, final value) at <3 months (follow-up: 3 weeks; assessed with: SF-36 physical function; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	not serious	none	20	20	-	MD **24 higher** (15.51 higher to 32.49 higher)	⨁⨁◯◯ Low	CRITICAL
Quality of life (SF-36 pain, 0-100, high is good, final value) at <3 months (follow-up: 3 weeks; assessed with: SF-36 pain; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	20	20	-	MD **10.2 higher** (1.58 higher to 18.82 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (SF-36 role physical, 0-100, high is good, final value) at <3 months (follow-up: 3 weeks; assessed with: SF-36 role physical; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	not serious	none	20	20	-	MD **37.55 higher** (24.51 higher to 50.59 higher)	⨁⨁◯◯ Low	CRITICAL
Quality of life (SF-36 vitality, 0-100, high is good, final value) at <3 months (follow-up: 3 weeks; assessed with: SF-36 vitality; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	not serious	none	20	20	-	MD **22 higher** (13 higher to 31 higher)	⨁⨁◯◯ Low	CRITICAL
Quality of life (SF-36 general health, 0-100, high is good, final value) at <3 months (follow-up: 3 weeks; assessed with: SF-36 general health; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	20	20	-	MD **2.9 higher** (5.46 lower to 11.26 higher)	⨁◯◯◯ Very low	CRITICAL
Quality of life (SF-36 role emotion, 0-100, high is good, final value) at <3 months (follow-up: 3 weeks; assessed with: SF-36 role emotion; Scale from: 0 to 100)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	combination therapy	no treatment	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	very serious[a]	not serious	not serious	not serious	none	20	20	-	MD **31.8 higher** (17.64 higher to 45.96 higher)	⨁⨁◯◯ Low	CRITICAL
Quality of life (SF-36 mental health, 0-100, high is good, final value) at <3 months (follow-up: 3 weeks; assessed with: SF-36 mental health; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	not serious	none	20	20	-	MD **13 higher** (4.56 higher to 21.44 higher)	⨁⨁◯◯ Low	CRITICAL
Quality of life (SF-36 social function, 0-100, high is good, final value) at <3 months (follow-up: 3 weeks; assessed with: SF-36 social function; Scale from: 0 to 100)												
1	randomised trials	very serious[a]	not serious	not serious	not serious	none	20	20	-	MD **26.2 higher** (14.16 higher to 38.24 higher)	⨁⨁◯◯ Low	CRITICAL
Pain (WOMAC, NRS [different scale ranges], high is poor, final values) at <3 months (follow-up: mean 5 weeks; assessed with: WOMAC, NRS)												
2	randomised trials	serious[a]	very serious[c]	not serious	very serious[b]	none	42	42	-	SMD **0.59 SD lower** (2.69 lower to 1.52 higher)	⨁◯◯◯ Very low	CRITICAL
Physical function (WOMAC, 0-68, high is poor, final value) at <3 months (follow-up: 7 weeks; assessed with: WOMAC; Scale from: 0 to 68)												
1	randomised trials	serious[a]	not serious	not serious	serious[b]	none	22	22	-	MD **4.18 higher** (2.27 lower to 10.63 higher)	⨁⨁◯◯ Low	CRITICAL
Psychological distress (BDI, 0-51, high is poor, final value) at <3 months (follow-up: 3 weeks; assessed with: BDI; Scale from: 0 to 51)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	20	20	-	MD **1.6 lower** (3.2 lower to 0)	⨁◯◯◯ Very low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

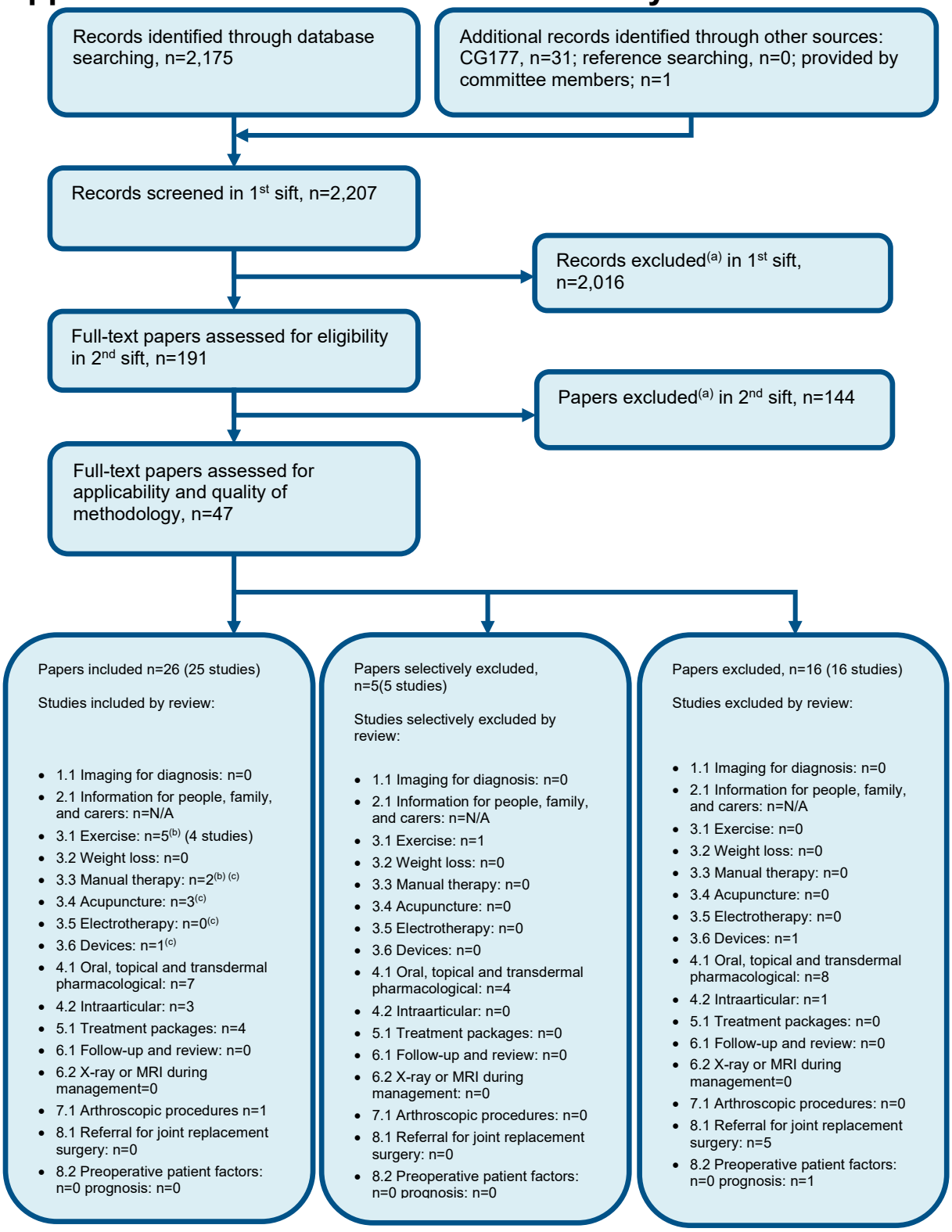
Explanations

a. Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

c. Downgraded by 1 or 2 increments because heterogeneity, unexplained by subgroup analysis

Appendix G – Economic evidence study selection



(a) Non-relevant population, intervention, comparison, design or setting; non-English language.
(b) Two articles identified were applicable to Q3.1 and Q3.3, for the purposes of this diagram they have been included under Q3.1 only.
(c) One article identified was applicable to Q3.3, Q3.4, Q3.5 and Q3.6, for the purposes of this diagram it has been included under Q3.3 only.

Appendix H – Economic evidence tables

<table>
<tr><th>Study</th><th colspan="4">MacPherson 2017[145]</th></tr>
<tr><th>Study details</th><th>Population & interventions</th><th>Costs</th><th>Health outcomes</th><th>Cost effectiveness</th></tr>
<tr>
<td>Economic analysis: CUA (health outcome = QALYs)

Study design: Network meta-analysis based on a systematic review of 88 trials. Three different networks were used:
1. All trials
2. Subset of trials that were graded with a low risk of bias for allocation concealment
3. Same as point 2 but further restricting trials to those that reported outcomes</td>
<td>Population:
Patients reporting pain resulting from OA of the knee

Patient characteristics:
Mean age across all trials = 53-85
Male = NR

Intervention 1: Usual care (specific treatment not described)
Intervention 2: Static magnets
Intervention 3: Insoles
Intervention 4: TENS
Intervention 5: Braces
Intervention 6: Acupuncture</td>
<td>Total costs (mean per patient):
<u>All trials</u>
Intervention 1: £0
Intervention 2: £5
Intervention 3: £13
Intervention 4: £31
Intervention 5: £40
Intervention 6: £179
Intervention 7: £297
Intervention 8: £304
Intervention 9: £396
Intervention 10: £481
Intervention 11: £503
Intervention 12: £770
Intervention 13: £1,453

<u>Trials with adequate allocation concealment</u>
Intervention 1: £0
Intervention 2: £5</td>
<td>QALYs gained versus baseline (mean per patient):
<u>All trials</u>
Intervention 1: 0.000
Intervention 2: 0.001
Intervention 3: 0.001
Intervention 4: 0.011
Intervention 5: 0.001
Intervention 6: 0.014
Intervention 7: 0.005
Intervention 8: 0.008
Intervention 9: 0.011
Intervention 10: 0.005
Intervention 11: 0.007
Intervention 12: 0.033
Intervention 13: 0.007

<u>Trials with adequate allocation concealment</u>
Intervention 1: 0.000
Intervention 2: 0.000</td>
<td>Full incremental analysis[(c) (d)]:
<u>All trials</u>
<table>
<tr><th></th><th>Cost</th><th>QALYs</th><th>Inc. Cost</th><th>Inc. QALY</th><th>Cost per QALY</th><th>% most CE at £20 K</th></tr>
<tr><td>1</td><td>£0</td><td>0.000</td><td colspan="3">Baseline</td><td>0%</td></tr>
<tr><td>2</td><td>£5</td><td>0.001</td><td>£5</td><td>0.001</td><td>ED</td><td>22%</td></tr>
<tr><td>3</td><td>£13</td><td>0.001</td><td>£8</td><td>0.000</td><td>ED</td><td>0%</td></tr>
<tr><td>4</td><td>£31</td><td>0.011</td><td>£31</td><td>0.011</td><td>£2,690</td><td>49%</td></tr>
<tr><td>5</td><td>£40</td><td>0.001</td><td>£9</td><td>-0.01</td><td>D</td><td>6%</td></tr>
<tr><td>6</td><td>£179</td><td>0.014</td><td>£148</td><td>0.003</td><td>ED</td><td>6%</td></tr>
<tr><td>7</td><td>£297</td><td>0.005</td><td>£266</td><td>-0.006</td><td>D</td><td>0%</td></tr>
<tr><td>8</td><td>£304</td><td>0.008</td><td>£273</td><td>-0.003</td><td>D</td><td>0%</td></tr>
<tr><td>9</td><td>£396</td><td>0.011</td><td>£365</td><td>0.000</td><td>D</td><td>0%</td></tr>
<tr><td>10</td><td>£481</td><td>0.005</td><td>£450</td><td>-0.006</td><td>D</td><td>16%</td></tr>
<tr><td>11</td><td>£503</td><td>0.007</td><td>£472</td><td>-0.004</td><td>D</td><td>0%</td></tr>
<tr><td>12</td><td>£770</td><td>0.033</td><td>£739</td><td>0.022</td><td>£33,866</td><td>0%</td></tr>
<tr><td>13</td><td>£1,453</td><td>0.007</td><td>£683</td><td>-0.026</td><td>D</td><td>0%</td></tr>
</table>
</td>
</tr>
</table>

between 3 and 13 weeks.

Approach to analysis: QALY changes from the different networks of analysis were combined with treatment and non-treatment-related costs.

Perspective: UK NHS

Time horizon/ treatment duration: 8 weeks

Discounting: n/a

Intervention 7: Heat treatment
Intervention 8: Manual therapy
Intervention 9: PES
Intervention 10: NMES
Intervention 11: Laser light therapy
Intervention 12: Interferential therapy
Intervention 13: PEMF

Intervention 3: £13
Intervention 4: £30
Intervention 5: NR
Intervention 6: £192
Intervention 7: £214
Intervention 8: £276
Intervention 9: £410
Intervention 10: NR
Intervention 11: £288
Intervention 12: £1,179
Intervention 13: £577

<u>Trials with adequate allocation concealment and an end point reported at 3-13 weeks</u>

Intervention 1: £0
Intervention 2: £5
Intervention 3: £14
Intervention 4: £30
Intervention 5: NR
Intervention 6: £192
Intervention 7: £213
Intervention 8: £277
Intervention 9: £410
Intervention 10: NR
Intervention 11: £288
Intervention 12: £1,179
Intervention 13: £277

Intervention 3: 0.002
Intervention 4: 0.005
Intervention 5: NR
Intervention 6: 0.017
Intervention 7: 0.003
Intervention 8: 0.013
Intervention 9: 0.010
Intervention 10: NR
Intervention 11: 0.003
Intervention 12: 0.016
Intervention 13: 0.008

<u>Trials with adequate allocation concealment and an end point reported at 3-13 weeks</u>

Intervention 1: 0.000
Intervention 2: -0.001
Intervention 3: 0.004
Intervention 4: 0.006
Intervention 5: NR
Intervention 6: 0.017
Intervention 7: 0.002
Intervention 8: 0.018
Intervention 9: 0.010
Intervention 10: NR
Intervention 11: 0.003
Intervention 12: 0.017
Intervention 13: 0.007

<u>Trials with adequate allocation concealment</u>[(e)]

	Cost	QALYs	Inc. Cost	Inc. QALY	Cost per QALY	% most CE at £20 K
1	£0	0.000	Baseline			0%
2	£5	0.000	£5	0.000	D	26%
3	£13	0.002	£13	0.002	ED	4%
4	£30	0.005	£30	0.005	£6,142	15%
6	£192	0.017	£162	0.012	£13,502	47%
7	£214	0.003	£22	-0.014	D	0%
8	£276	0.013	£84	-0.004	D	7%
11	£288	0.003	£96	-0.014	D	0%
9	£410	0.010	£218	-0.007	D	0%
13	£577	0.008	£385	-0.009	D	0%
12	£1,179	0.016	£987	-0.001	D	0%

<u>Trials with adequate allocation concealment and an end point reported at 3-13 weeks</u>[(e)]

	Cost	QALYs	Inc. Cost	Inc. QALY	Cost per QALY	% most CE at £20 K
1	£0	0.000	Baseline			0%
2	£5	-0.001	£5	-0.001	D	17%
3	£14	0.004	£14	0.004	£3,540	13%
4	£30	0.006	£16	0.002	£9,750	25%
6	£192	0.017	£162	0.011	£14,275	25%

		For incremental analyses see cost effectiveness column **Currency & cost year:** 2011/12 UK pounds. **Cost components incorporated:** Physiotherapist's time to conduct weekly sessions, except for TENS, where patients self-administered after an initial physiotherapist visit. Changes in non-treatment-related visits to GPs and specialists arising from changes in EQ-5D score.	*For incremental analyses see cost effectiveness column*	7 £213 0.002 £21 -0.015 D 0% 8 £277 0.018 £85 0.001 £86,964 20% 13 £277 0.007 £0 -0.011 D 0% 11 £288 0.003 £11 -0.015 D 0% 9 £410 0.010 £133 -0.008 D 0% 12 £1,179 0.017 £902 -0.001 D 0% **Analysis of uncertainty:** TENS was the most cost-effective alternative at a £20K threshold when a linear relationship were assumed between EQ-5D treatment effect and session duration. When all the treatment benefit were assumed in the first 20/30 minutes of the session, interferential therapy was the most cost-effective option. In an analysis of all trials, TENS remained the most cost-effective option when the duration of treatment benefit were extended by 50%.

Data sources

Health outcomes: Study-level reported mean differences in pain as a measure of treatment effectiveness were standardised to the EQ-5D measure for each of the three network meta analyses. **Quality-of-life weights:** Generic EQ-5D quality-of-life scores were mapped from the SF-12 & SF-36 surveys, pain NRD, pain VAS and WOMAC scales. **Cost sources:** The cost to the NHS (physiotherapists time, GP and specialists' consultations) was obtained from the Personal Social Services Research Unit 2012. Equipment administered by physiotherapists (e.g., devices) were not included as the per-patient costs as these were expected to be small. **Resource use:** Estimates of resource use were based on consultations with clinical experts and published literature including trial data and NHS data. Treatment duration was based on a weighted average of the clinical trial data.

Comments

Source of funding: National Institute for Health Research (NIHR). **Limitations:** Unit costs taken from 2011/12 may not reflect current UK NHS practice. The time horizon was only 8 weeks. Adverse events and their downstream consequences were not considered. **Other:** Non-treatment-specific healthcare resource use was assumed to be a function of change in EQ-5D and was taken from the TOIB trial. TENS machine assumed to last for 1 year.

Overall applicability:[(a)] Partially applicable **Overall quality:**[(b)] Potentially serious limitations

Abbreviations: CE= cost effective; CI = confidence interval; CUA = cost-utility analysis; D= dominated; ED= extendedly dominated; EQ-5D = Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); GP= general practitioner; ICER = incremental cost-effectiveness ratio; Inc.= incremental; K= thousand; n/a = not applicable; NHS = National Health Service; NMES= neuromuscular electrical stimulation; NR = not reported; NRS = numeric rating scale; OA = Osteoarthritis; PEMF= pulsed electromagnetic field; PES= pulsed electrical stimulation; QALYs = quality-adjusted life years; SF-12 = short-form health survey 12 items; SF-36= short-form health survey 36 items; TENS= transcutaneous electrical nerve stimulation; UK= United Kingdom; VAS = visual analogue scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

(a) Directly applicable / Partially applicable / Not applicable

(b) Minor limitations /Potentially serious limitations / Very serious limitations

(c) Intervention number in order of least to most costly (in terms of cost)

(d) Full incremental analysis of available strategies: first strategies are ruled out that are dominated (another strategy is more effective and has lower costs) or subject to extended dominance (the strategy is more effective and more costly but the incremental cost effectiveness ratio is higher than the next most effective option and so it would never be the most cost effective option); incremental costs, incremental effects and incremental cost effectiveness ratios are calculated for the remaining strategies by comparing each to the next most effective option.

(e) Interventions 5 and 10 not available because these intervention did not provide information to network meta analyses.

Appendix I – Health economic model

No original economic modelling was undertaken.

Appendix J – Excluded studies

Clinical studies

Table 95: Studies excluded from the clinical review

Study	Exclusion reason
Abdel-aziem 2014[1]	Spinal osteoarthritis
Adedoyin 2002[2]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Adedoyin 2005[3]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Ahn 2017[4]	Incorrect interventions (transcranial direct current stimulation)
Al rashoud 2014[7]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Alcidi 2007[9]	Incorrect interventions (radiofrequency electromagnetic radiation)
Ali 2014[14]	Inappropriate comparison (comparing electrotherapy to manual therapy)
Akaltun 2021[5]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Ammar 2014[18]	Inappropriate comparison (comparing monochromatic infrared photo energy to low level laser therapy)
Ananias 2017[19]	Non-English language study
Angelova 2016[20]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Avendano-Coy 2020[23]	Systematic review, references checked
Ay 2009[24]	Inappropriate comparison (pulsed electromagnetic field therapy, TENS and hot pack compared to sham electromagnetic field therapy, TENS and hot pack)
Azizi, 2021[25]	Incorrect interventions (transcranial direct current stimulation)
Bagheri 2011[26]	Non-English language study
Bal 2007[28]	Non-English language study
Battisti 2004[30]	Inappropriate comparison (compared musically modulated electromagnetic field therapy to low frequency electromagnetic fields and simulated fields)
Beasley 2018[31]	Systematic review; references checked
Bertolucci 1995[32]	Not available
Bertolucci 1995[33]	Not available
Brosseau 2007[34]	Non-English language study
Burgess 2021[39]	Systematic review, references checked
Carlos 2012[43]	Non-English language study
Chang 2017[45]	Incorrect interventions (transcranial direct current stimulation)
Chaturvedi 2020[46]	Inappropriate intervention (transcranial direct current stimulation plus TENS)
Cheing 2002[48]	No usable outcomes (outcomes reported in a form that makes it not possible to interpret when compared to other studies)
Cheing 2003[49]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Cheing 2004[47]	No usable outcomes (reported only biomechanical outcomes which were not included in the protocol)

Study	Exclusion reason
Chen 2014[52]	People with conditions that may make them susceptible to osteoarthritis or often occur alongside osteoarthritis (including: crystal arthritis, inflammatory arthritis, septic arthritis, diseases of childhood that may predispose to osteoarthritis, medical conditions presenting with joint inflammation and malignancy).
Chen 2016[51]	Systematic review; references checked
Chen, 2019[50]	Systematic review; references checked
Chen 2019[53]	Systematic review; references checked
Cherian 2015[56]	Inappropriate comparison (standard care is not necessarily provided to both study arms)
Cherian 2016[54]	Inappropriate comparison (standard care is not necessarily provided to both study arms)
Cherian 2016[57]	Inappropriate comparison (standard care is not necessarily provided to both study arms)
Cherian 2016[55]	Inappropriate comparison (standard care is not necessarily provided to both study arms)
Cottingham 1985[59]	Not available
Cottingham 1985[60]	Not available
Da graca-tarrago 2016[62]	Incorrect interventions (electrical intramuscular stimulation)
De matos brunelli braghin 2019[64]	Same as study already included (De matos brunelli braghin 2018)
Dantas 2021[63]	Systematic review; references checked
De oliveira melo 2016[65]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Defrin 2005[67]	No usable outcomes (outcomes reported in subgroups not agreed in the protocol for this review)
Delkhosh 2018[68]	Non-English language study
Dincer 2008[70]	Non-English language study
Dundar 2016[72]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Durmus 2007[73]	Incorrect interventions. Inappropriate comparison (quadriceps electrical stimulation compared to exercise)
Elbadawy 2017[75]	Incorrect interventions (periosteal stimulation therapy compared to TENS)
Falconer 1992[77]	No usable outcomes (does not report outcomes as means and standard deviations [apart for pain where it is reported as a combined value for both study arms] and cannot be converted to produce this)
Fargas-babjak 1989[78]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Fischer 2005[81]	Non-English language study
Fischer 2006[82]	Non-English language study
Gaines 2004[85]	Incorrect interventions (treatment package)
Geler kulcu 2009[87]	Non-English language study
Goksen 2016[88]	Incorrect interventions (magnetic resonance therapy)
Grimmer 1992[89]	Less than minimum duration (<1 week)
He 2019[94]	Inappropriate comparison (real versus sham percutaneous electrical nerve stimulation)

Study	Exclusion reason
Hegedus 2009[95]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Hsieh 2012[99]	No usable outcomes (did not report outcomes stated in the protocol)
Hsieh 2020[98]	Systematic review; references checked
Huang 2015[103]	Systematic review; references checked
Imamura 2017[105]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Imoto 2013[106]	Inappropriate comparison (neuromuscular electrical stimulation and exercise compared to an educational leaflet)
Ip 2015[108]	Inappropriate comparison (low level laser therapy and physical therapy compared to physical therapy only)
Isik, 2020[109]	Incorrect interventions (dextrose prolotherapy plus short wave diathermy, dextrose prolotherapy plus sham)
Itoh 2008[110]	Inappropriate comparison (TENS and acupuncture compared to TENS only and a topical poultice)
Jacobson 2001[111]	Incorrect interventions (low amplitude low frequency magnetic fields)
Jensen 1991[112]	Incorrect study design (non-randomised study)
Jia, 2020[114]	Not in English language
Ji, 2019[113]	Incorrect population (femoral head necrosis) Incorrect study design (cohort)
Kamalakannan 2019[116]	Inappropriate comparison (proprioception training and conventional exercise versus interferential therapy)
Kapidzic 2011[117]	Abstract only
Katsnelson 2004[119]	Incorrect interventions (transcranial electrotherapy)
Kim 2009[123]	Non-English language study
Kim 2015[122]	Inappropriate comparison (medium energy extracorporeal shock wave therapy compared to low energy extracorporeal shock wave therapy)
Kolen 2012[125]	Inappropriate comparison (TENS compared to a different type of TENS)
Krauss 2011[127]	Protocol only
Kul'chitskaya 2015[128]	Non-English language study
Kulcu 2009[129]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Kumaran 2019[130]	Incorrect interventions (radiofrequency techniques)
Law 2004[133]	No usable outcomes (does not report outcomes specified in the protocol)
Lee 2004[134]	Non-English language study
Lewis 1984[136]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Lewis 1994[135]	Crossover trial
Lewith 1981[137]	Not available
Li 2013[138]	Systematic review is not relevant to review question or unclear PICO (Cochrane review investigating pulsed electromagnetic fields and pulsed electrical stimulation)
Iijima 2020[104]	Less than minimum duration

Study	Exclusion reason
Lizis 2017[139]	Inappropriate comparison (extracorporeal shockwave therapy compared to kinesiotherapy)
Lonauer 1986[140]	Abstract only
Lone 2003[141]	No usable outcomes (outcomes reported in subgroups not agreed in the protocol for this review)
Lue 2017[143]	Systematic review; references checked
Luz-santos 2017[144]	Protocol only
Madhusoodanan 2021[147]	Not relevant to the guideline condition (population without osteoarthritis)
Marini 2010[149]	Inappropriate comparison (low level laser therapy compared to NSAIDs)
Murat, 2019[156]	Inappropriate comparison (therapeutic ultrasound, TENS and hot pack versus different amounts of therapy)
Nazari 2019[158]	Inappropriate comparison (laser therapy compared to conventional physiotherapy and exercise)
Negm 2013[159]	Systematic review; references checked
Ng 2003[161]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Nicolakis 2002[162]	Not available
Obotiba 2022[163]	Inappropriate comparison (US versus MRI to detect OA)
Osiri 2000[164]	Cochrane review; references checked (different outcome measures being used than those stated in the protocol)
Ozdemir 2001[165]	Spinal osteoarthritis
Paolillo 2015[171]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Paolillo 2018[172]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Park 2021[173]	Inappropriate comparison
Peroz 2004[174]	Not review population (mixed temporomandibular joint disorders, the minority of which had osteoarthritis)
Pietrosimone 2010[177]	No usable outcomes (does not report outcomes specified in the protocol)
Pipitone 2001[180]	Non-English language study
Polat 2017[181]	Non-English language study
Quirk 1985[182]	Not available
Raj, 2019[183]	No usable outcomes (no relevant outcomes)
Rattanachaiyanont 2008[184]	Incorrect interventions (treatment package)
Rayegani 2017[185]	Systematic review; references checked
Rodriguez-merchan 2016[186]	Systematic review; references checked
Rosemffet 2004[187]	Inappropriate comparison (functional electrostimulation compared to physical training or the combination of the two)
Rutjes 2009[189]	Not available
Rutjes 2010[188]	Cochrane review; references checked (different outcome measures being used than those stated in the protocol)
Selfe 2008[191]	Incorrect interventions (noninvasive interactive neurostimulation)
Sener 2019[192]	No useable outcomes (microbiological outcomes only)
Shimoura 2019[194]	Less than minimum duration (<1 week)
Smith 1983[195]	Not available

Study	Exclusion reason
Song 2020[196]	Systematic review; references checked
Stange-rezende 2006[197]	Crossover study
Steinhilber 2017[199]	Incorrect interventions (supervised strength exercise compared to other exercise and no treatment)
Stelian 1992[200]	Not available
Strausholm 2019[198]	Systematic review; references checked
Sutbeyaz 2006[201]	Spinal osteoarthritis
Talbot 2003[202]	Incorrect interventions (treatment package)
Tan 2020[203]	Incorrect interventions (foot orthoses, flat shoe inserts, own shoes)
Tascioglu 2004[204]	Systematic review is not relevant to review question or unclear PICO (comparator varied from those in our protocol)
Tavares 2018[206]	Incorrect interventions (transcranial direct current stimulation). Protocol only
Taylor 1981[207]	Crossover study
Tok 2011[209]	Incorrect interventions. Inappropriate comparison (electrical stimulation and continuous passive movement compared to isometric exercise)
Tomruk sutbeyaz 2007[210]	Non-English language study
Trock 1994[212]	Spinal osteoarthritis
Usman 2019[214]	Incorrect intervention (infrared)
Vance 2012[215]	Less than minimum duration (<1 week)
Wang 2017[216]	Systematic review; references checked
Woods 2017[218]	Cost-effectiveness analysis only
Wu 2018[219]	Systematic review; references checked
Wyszynska 2018[221]	Systematic review; references checked
Yang 2011[222]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Yavuz 2013[223]	Non-English language study
Young 1991[226]	Not available
Youssef 2016[227]	No usable outcomes (does not report outcomes as means and standard deviations and cannot be converted to produce this)
Yuan 2016[228]	Incorrect interventions. Inappropriate comparison (pulsed radiofrequency treatment compared to intraarticular steroids)
Yuvarani 2018[230]	Not available
Zammit 2010[231]	Cochrane review; references checked (includes a variety of non-pharmacological therapies that are not directly related to this review)
Zeng 2014[232]	Systematic review; references checked
Zeng 2015[233]	Systematic review; references checked
Zhang 2016[234]	Systematic review; references checked
Zhang 2016[235]	Systematic review; references checked
Zhou 2018[239]	Systematic review; references checked

Health Economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2005 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

None.

Appendix K – Research recommendations – full details

K.1.1 Research recommendation

What is the clinical and cost effectiveness of extracorporeal shockwave therapy for managing osteoarthritis?

K.1.2 Why this is important

Many treatments have been proposed to help reduce osteoarthritis symptoms, such as pain and reduction in physical function. In this guideline, a lot of treatments have been found to be ineffective based on limited evidence. Electrotherapy was one of these treatments, where the evidence showed a significant amount of heterogeneity in the outcomes, which may be linked to inconsistency in the use of appropriate sham interventions and low quality study design (including trials with very few participants). Given this, the committee agreed that there was insufficient evidence of benefit from electrotherapy to recommend it in this guideline. However, the inconsistency in effect indicated that there is uncertainty in the efficacy, therefore further research may provide a clearer answer. In particular, extracorporeal shockwave therapy showed some evidence of benefit compared to sham. However, this was based on small trials, where the committee agreed that the sham therapy used as a comparator was likely to be an inadequate sham technique to ensure blinding and so did not consider the evidence as conclusive. Therefore, further research into this electrotherapy modality may help to elucidate the true effect.

K.1.3 Rationale for research recommendation

Importance to 'patients' or the population	Osteoarthritis symptoms can have a significant impact on the quality of life of a person with osteoarthritis. Establishing effective therapies that target pain relief is important for reducing this impact and may also help people to engage with recommended interventions that can have long term benefits, such as exercise. Having a clear answer as to the efficacy of extracorporeal shockwave therapy is important for ensuring the correct therapies are offered.
Relevance to NICE guidance	In this guideline, the committee concluded that there was insufficient evidence of benefit to recommend electrotherapy. This was based on inconsistent evidence with a large number of small, low quality studies being included in the analysis. Therefore, well conducted larger trials would be useful for giving a clear answer as to the benefits and harms of electrotherapy for people with osteoarthritis. In particular, extracorporeal shockwave therapy showed evidence of benefit when compared to sham therapy, but potential harms when compared to no treatment. The committee concluded that they were uncertain as to whether the sham therapy was effectively blinded due to the sensation felt from the intervention being applied. Therefore, a well conducted trial to compare against usual care would be useful to

	allow for a more robust assessment of the effectiveness of the intervention.
Relevance to the NHS	Electrotherapy devices are costly and if used widely in the NHS could have a significant cost and resource impact. In the case of extracorporeal shockwave therapy, a healthcare professional would be required to administer the therapy. Therefore, having a full assessment of the clinical and cost-effective would be important to help guide NHS decision making in the area.
National priorities	This is not a national priority area.
Current evidence base	The current evidence base for electrotherapy is mostly short-term studies with a small number of participants that shows wide variability in the effects of the interventions. There is often variation in how sham and control interventions are offered, with some of these sham procedures seeming potentially inadequate. The evidence for extracorporeal shockwave therapy showed benefits when compared to sham therapy, but a possible harm when compared to no treatment. However, the evidence when compared to no treatment was limited to one small study, and the evidence when compared to sham was potentially limited by the choice of sham used. Therefore, further research would be important to understanding the true effect of the intervention.
Equality considerations	The committee noted that the research identified in this review does not appear to represent the diverse population of people with osteoarthritis. They agreed that any further research should be representative of the population, including people from different family backgrounds, and socioeconomic backgrounds, disabled people, and people of different ages and genders. Future work should be done to consider the different experiences of people from diverse communities to ensure that the approach taken can be made equitable for everyone.

K.1.4 Modified PICO table

Population	Adults (age ≥16 years) with osteoarthritis affecting any joint
Intervention	Extracorporeal shockwave therapy
Comparator	Usual care (provided to both treatment arms, based on treatment usually received in a UK NHS context)
Outcome	Stratify by ≤/>3 months (longest time-point in each): • Health-related quality of life [validated patient-reported outcomes, continuous data prioritised]

	• Pain [validated patient-reported outcomes, continuous data prioritised] • Physical function [validated patient-reported outcomes, continuous data prioritised] • Psychological distress [validated patient-reported outcomes, continuous data prioritised] • Osteoarthritis flares [validated patient-reported outcomes, continuous data prioritised] • Mild adverse events [dichotomous data] • Moderate/major adverse events [dichotomous data]
Study design	Randomised controlled trial
Timeframe	Long term (at least 1 year)
Additional information	Adequately powered high quality randomised controlled trials. Trials with sufficient blinding, adequate randomisation methods and allocation concealment. Trials that can consider the potential treatment mediators to understand the mechanism of action further would be appreciated.