Recommended treatment doses for Low Level Laser Therapy

Laser class 3 B, 780 - 860nm GaAlAs Lasers. Continuous or pulsed, mean output: 5 - 500mW

Irradiation times should range between 20 and 300 seconds

Diagnoses

Tendinopathies	**Points or cm2**	**Joules 780 - 820nm**	**Notes**
Carpal-tunnel	2-3	8	Minimum 4 Joules per point
Lateral epicondylitis	1-2	4	Maximum 100mW/cm2
Biceps humeri c.l.	1-2	6	
Supraspinatus	2-3	8	Minimum 4 Joules per point
Infraspinatus	2-3	8	Minimum 4 Joules per point
Trochanter major	2-4	8	
Patellartendon	2-3	8	
Tract. Iliotibialis	1-2	4	Maximum 100mW/cm2
Achilles tendon	2-3	8	Maximum 100mW/cm2
Plantar fasciitis	2-3	8	Minimum 4 Joules per point
Arthritis	**Points or cm2**	**Joules**	
Finger PIP or MCP	1-2	4	
Wrist	2-4	8	
Humeroradial joint	1-2	4	
Elbow	2.4	8	
Glenohumeral joint	2-4	8	Minimum 4 Joules per point
Acromioclavicular	1-2	4	
Temporomandibular	1-2	4	
Cervical spine	4-12	16	Minimum 4 Joules per point
Lumbar spine	4-8	16	Minimum 4 Joules per point
Hip	2-4	12	Minimum 6 Joules per point
Knee medial	3-6	12	Minimum 4 Joules per point
Ankle	2-4	8	

Daily treatment for 2 weeks or treatment every other day for 3-4 weeks is recommended
Irradiation should cover most of the pathological tissue in the tendon/synovia.
Start with energy dose in table, then reduce by 30% when inflammation is under control
Therapeutic dose windows typically range from +/- 50% of given values, and doses outside these windows are inappropriate and should not be considered as Low Level Laser Therapy.
Recommended doses are for white/caucasian skin types based on results from clinical trials or extrapolation of study results with similar pathology and ultrasonographic tissue measurements.

Disclaimer

The list may be subject to change at any time when more research trials are being published. World Association of Laser Therapy is not responsible for the application of laser therapy in patients, which should be performed at the sole discretion and responsibility of the therapist.

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Recommended treatment doses for Low Level Laser Therapy

Laser class 3B, 904 nm GaAs Lasers
(Peak pulse output >1 Watt, mean output >5 mW and power density > 5mW/cm2)
Irradiation times should range between 30 and 600 seconds

Diagnoses	**Min. area/points**	**Min. total dose**	
Carpal-tunnel	2-3	4	Minimum 2 Joules per point
Lateral epicondylitis	2-3	2	Maximum 100mW/cm2
Biceps humeri cap.long.	2-3	2	
Supraspinatus	2-3	4	Minimum 2 Joules per point
Infraspinatus	2-3	4	Minimum 2 Joules per point
Trochanter major	2-3	2	
Patellartendon	2-3	2	
Tract. Iliotibialis	2-3	2	Maximum 100mW/cm2
Achilles tendon	2-3	2	Maximum 100mW/cm2
Plantar fasciitis	2-3	4	Minimum 2 Joules per point
Arthritis	**Points or cm2**	**Joules 904nm**	
Finger PIP or MCP	1-2	1	
Wrist	2-3	2	
Humeroradial joint	2-3	2	
Elbow	2-3	2	
Glenohumeral joint	2-3	2	Minimum 1 Joules per point
Acromioclavicular	2-3	2	
Temporomandibular	2-3	2	
Cervical spine	4	4	Minimum 1 Joules per point
Lumbar spine	4	4	Minimum 1 Joules per point
Hip	2	4	Minimum 2 Joules per point
Knee anteromedial	4-6	4	Minmum 1 Joules per point
Ankle	2-4	2	

Daily treatment for 2 weeks or treatment every other day for 3-4 weeks is recommended
Irradiation should cover most of the pathological tissue in the tendon/synovia.

Start with energy dose in table, then reduce by 30% when inflammation is under control
Therapeutic dose windows typically range from +/- 50% of given values, and doses outside these windows are inappropriate and should not be considered as Low Level Laser Therapy.
Recommended doses are for white/caucasian skin types based on results from clinical trials or extrapolation of study results with similar pathology and ultrasonographic tissue measurements.

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Effectiveness of Interferential Current Therapy in the Management of Musculoskeletal Pain: A Systematic Review and Meta-Analysis

Jorge P. Fuentes, Susan Armijo Olivo, David J. Magee, Douglas P. Gross

Background. Interferential current (IFC) is a common electrotherapeutic modality used to treat pain. Although IFC is widely used, the available information regarding its clinical efficacy is debatable.

Purpose. The aim of this systematic review and meta-analysis was to analyze the available information regarding the efficacy of IFC in the management of musculoskeletal pain.

Data Sources. Randomized controlled trials were obtained through a computerized search of bibliographic databases (ie, CINAHL, Cochrane Library, EMBASE, MEDLINE, PEDro, Scopus, and Web of Science) from 1950 to February 8, 2010.

Data Extraction. Two independent reviewers screened the abstracts found in the databases. Methodological quality was assessed using a compilation of items included in different scales related to rehabilitation research. The mean difference, with 95% confidence interval, was used to quantify the pooled effect. A chi-square test for heterogeneity was performed.

Data Synthesis. A total of 2,235 articles were found. Twenty studies fulfilled the inclusion criteria. Seven articles assessed the use of IFC on joint pain; 9 articles evaluated the use of IFC on muscle pain; 3 articles evaluated its use on soft tissue shoulder pain; and 1 article examined its use on postoperative pain. Three of the 20 studies were considered to be of high methodological quality, 14 studies were considered to be of moderate methodological quality, and 3 studies were considered to be of poor methodological quality. Fourteen studies were included in the meta-analysis.

Conclusion. Interferential current as a supplement to another intervention seems to be more effective for reducing pain than a control treatment at discharge and more effective than a placebo treatment at the 3-month follow-up. However, it is unknown whether the analgesic effect of IFC is superior to that of the concomitant interventions. Interferential current alone was not significantly better than placebo or other therapy at discharge or follow-up. Results must be considered with caution due to the low number of studies that used IFC alone. In addition, the heterogeneity across studies and methodological limitations prevent conclusive statements regarding analgesic efficacy.

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Successful management of musculoskeletal pain is a major challenge in clinical practice. One of the electrotherapeutic techniques used for managing musculoskeletal pain is interferential current therapy (IFC). The results of questionnaire surveys in England,[1] Canada,[2] and Australia[3,4] have shown that IFC is widely used by diverse clinicians throughout the world.

Interferential current therapy is the application of alternating medium-frequency current (4,000 Hz) amplitude modulated at low frequency (0–250 Hz).[5–7] A claimed advantage of IFC over low-frequency currents is its capacity to diminish the impedance offered by the skin.[6] Another advantage speculated for IFC is its ability to generate an amplitude-modulated frequency (AMF) parameter, which is a low-frequency current generated deep within the treatment area.[6,8–10] Several theoretical physiological mechanisms such as the "gate control" theory,[11] increased circulation, descending pain suppression, block of nerve conduction, and placebo have been proposed in the literature to support the analgesic effects of IFC.[5,8,12]

Despite IFC's widespread use, information about it is limited. A review of the literature reveals incomplete and controversial documentation regarding the scientific support of IFC in the management of musculoskeletal pain. For example, a systematic review about the use of electrotherapy for neck disorders[13] excluded the analysis of IFC. Moreover, much of the IFC information is not written in English,[10,14–22] and most articles appear to be based on case reports,[23–25] clinical studies not including a randomization process,[26,27] letters to the editor,[28,29] clinical notes,[30] experimental settings,[31–37] descriptive studies,[8,12,38,39] or experience in the field[40,41] instead of methodologically qualified studies.

Thus, the objective of this systematic review and meta-analysis was to determine the analgesic effectiveness of IFC compared with control, placebo, or other treatment modalities for decreasing pain in patients with painful musculoskeletal conditions.

Method

Search Strategy

Relevant studies of IFC in musculoskeletal pain management from 1950 to February 8, 2010, were obtained through an extensive computerized search of the following bibliographic databases: MEDLINE (1950 through week 4 of 2010), EMBASE (1988 through week 5 of 2010), CINAHL (1970 through February 8, 2010), Scopus (1970 through February 8, 2010), Cochrane Library (1991 through the first quarter of 2010), ISI Web of Science (1970 through February 8, 2010), and PEDro (Physiotherapy Evidence Database) (1970 through February 8, 2010). The key words "interferential," "interferential therapy," "interferential current," "musculoskeletal pain," "electrotherapy," "electroanalgesia," "muscle pain," "low back pain," "shoulder pain," "hip pain," "knee pain," "neck pain," "osteoarthritis pain," and "joint pain" were used in the search, including combinations of these words. For details regarding the search terms and combinations, see eAppendix 1 (available at ptjournal.apta.org). The literature search procedure was complemented by manually searching the bibliographies of the identified articles for key authors and journals.

Study Selection and Inclusion/Exclusion Criteria

Studies that met the following criteria were considered for inclusion: (1) randomized controlled trials (RCTs) from journal publications in the English language (because the clinical application of IFC often is based on its coadjutant effect, studies in which IFC was used as a cointervention also were included); (2) studies of male and female humans between 18 and 80 years of age; (3) studies of subjects clinically diagnosed with a painful musculoskeletal condition, such as muscle (eg, low back pain, neck pain), soft tissue (eg, tendinosis/tendinitis), or joint (eg, osteoarthritis) disorders; (4) regarding the type of interventions, all randomized comparisons of isolated or coadjutant IFC applications versus placebo, control, another physical therapy intervention, or another type of intervention; and (5) studies in which the outcome of interest was pain, as measured by the use of a visual analog scale (VAS) or numeric pain rating scale (NRS). Exclusion criteria for this study were: (1) studies based on animal data, (2) studies published in languages other than English, and (3) studies including subjects who were healthy in experimental settings.

Data Extraction and Quality Assessment

Two independent reviewers screened the abstracts of the publications found in the databases. The reviewers analyzed all articles initially selected by the abstract or title for the inclusion and exclusion criteria. Each criterion was graded on a yes/no basis. In case of discrepancies between reviewers regarding whether a particular article met a criterion, the ratings were compared and the

criterion forms were discussed until a consensus was reached.

A critical appraisal was conducted to determine the methodological quality of the final selected studies. We used 7 scales (ie, Delphi List, PEDro, Maastricht, Maastricht-Amsterdam List, Bizzini, van Tulder, and Jadad) commonly used in the physical therapy field to evaluate the methodological quality of the included studies, compiled in a set of 39 items.[42] These items were grouped into 5 categories: patient selection, blinding, intervention, outcomes, and statistics. Based on a recent systematic review,[42] no one scale effectively determines the overall methodological quality of individual studies. For this reason, we used all of them in a compiled fashion.

The articles were evaluated on the basis of only the information available in the articles using the critical appraisal sheet (eAppendix 2; available at ptjournal.apta.org). For each item listed on the critical appraisal sheet, a score of 1 was given when the item was included in the article, and a score of 0 was given when the item was not included or the information provided by the authors was not sufficient to make a clear statement. In cases where the study did not consider a particular item, the item was marked as not applicable on the critical appraisal sheet. The scoring for each study was calculated by dividing the number of items included by the number of applicable items. Finally, each study was graded as having low, moderate, or high methodological quality based on how many items from the critical appraisal were met. The cutoff was determined as follows: 0–0.40=low methodological quality, 0.41–0.70=moderate methodological quality, and 0.71–1.00=high methodological quality. This criterion was determined *a priori* to the quality assessment. Similar criteria for cutoffs have been used in correlational studies to determine reference values for quality of association or agreement.[43,44]

The critical appraisal was independently completed by the 2 reviewers, and the results were compared. At this stage, the intraclass correlation coefficient (ICC) was calculated using SPSS version 17 software* in order to determine the agreement between the reviewers for article grading. Any discrepancies were settled through discussion.

Data Synthesis and Analysis

Studies investigating similar outcomes and interventions and those providing clear quantitative data were grouped, evaluated for heterogeneity, and pooled, if possible. When combining outcome data was not possible, narrative, descriptive, and qualitative summaries were completed. In the present study, a meta-analysis was performed to quantify the pooled effect of IFC alone or as an adjunct treatment on pain intensity when compared with placebo, control group, or comparison intervention. Because the pooled effect was based on the results of the VAS or NRS, the mean difference was used to quantify the pooled effect. RevMan 5.0 software† was used to summarize the effects (ie, pooled mean differences) and construct the

* SPSS Inc, 233 S Wacker Dr, Chicago, IL 60606.

† Copenhagen, Denmark: The Nordic Cochrane Centre, The Cochrane Collaboration, 2008.

The Bottom Line

What do we already know about this topic?

Despite the widespread use of interferential current (IFC), information about its clinical effectiveness is limited and controversial. The pain-reducing effect of IFC, when applied alone or as part of a multimodal treatment plan to treat musculoskeletal pain, has not been determined.

What new information does this study offer?

The application of IFC as part of a multimodal treatment plan appears to produce a modest pain-relieving effect in a broad spectrum of acute and chronic musculoskeletal conditions when compared with no treatment or placebo. In addition, the potential long-term effects of IFC versus placebo observed at 3-month follow-up are of interest.

Interferential current alone was not significantly better than placebo and other interventions (ie, manual therapy, traction, or massage). However, heterogeneity across the included studies, along with methodological limitations identified in these studies, prevents conclusive statements regarding the analgesic efficacy of IFC.

If you're a patient, what might these findings mean for you?

If you are seeking pain treatment, IFC could be potentially effective in reducing musculoskeletal pain; however, its application should be included as part of a multimodal treatment plan.

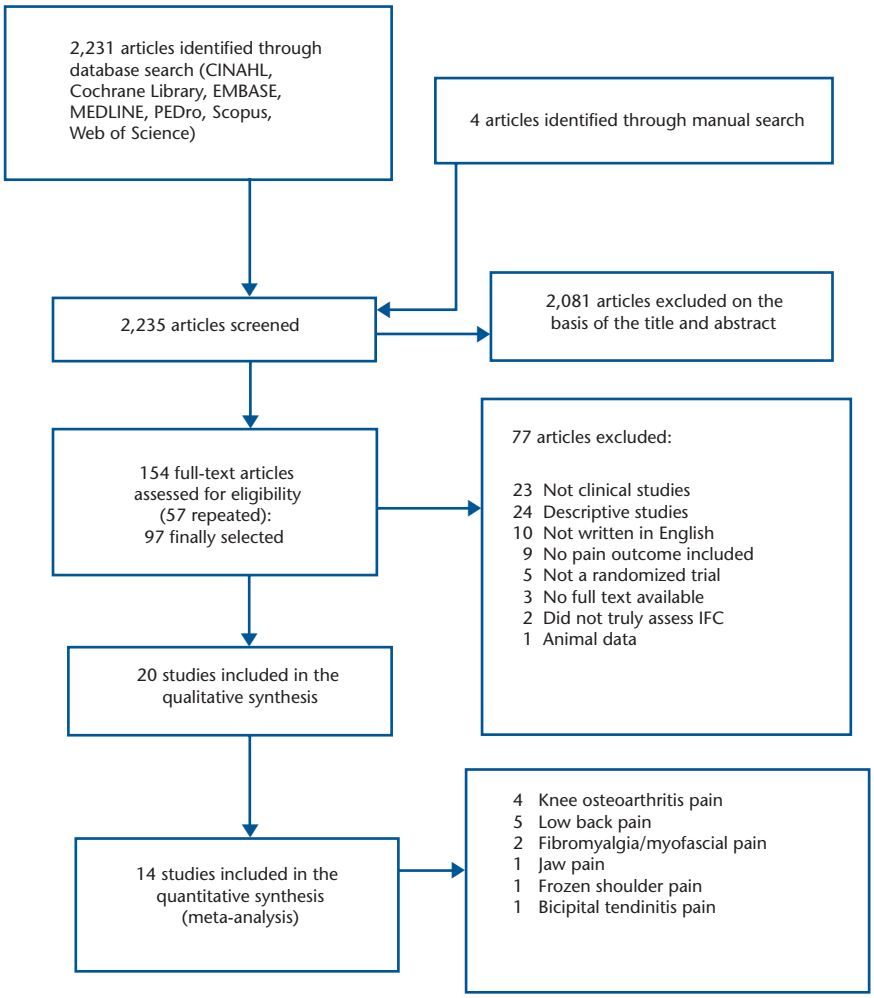

Figure 1.
Study screening process. IFC=interferential current therapy.

forest plots for all comparisons. For this analysis, the 95% confidence interval (CI) was used. A chi-square test for heterogeneity was performed ($P<.10$).[45] In the presence of clinical heterogeneity in the study population or intervention, the DerSimonian and Laird random-effects model of pooling was used based on the assumption of the presence of interstudy variability to provide a more conservative estimate of the true effect.[45,46] If there was relative homogeneity, a fixed-effects model was used to pool data.[45]

Results

A total of 2,235 articles were found in the database search. Of these, 154 were selected as potential studies of interest based on abstract review (Fig. 1). After full article review, only 20 studies were deemed to fulfill the initial selection criteria.[47–66] The kappa agreement between the reviewers in selecting articles after applying the inclusion and exclusion criteria was perfect at $\kappa=1.0$.

Seventy-seven studies were rejected after applying the inclusion and exclusion criteria. The primary reasons for exclusion from the study were: (1) the use of subjects who were healthy in an experimental setting[31–37,67–82]; (2) descriptive studies in the form of case reports, dissertations, or clinical notes,[8,12,23–25,30,38–41,69,83–96]; (3) studies not published in the English language[10,14–22]; (4) the absence of pain outcomes[97–105]; (5) randomized trial not used[26,27,106–108]; (6) use of a current other than IFC[109,110]; (7) use of animal data[111]; and (8) unavailability of the full text of the article.[112–114] At the end of the critical appraisal stage, there was an agreement of $\kappa=.83$ between the 2 raters. This ICC value is considered as "excellent" agreement according to the approach described by McDowell.[115]

Characteristics of the Studies

All 20 studies reviewed in detail were RCTs that examined the pain-reducing effectiveness of IFC. These studies analyzed the effects of IFC for several diagnoses considered to be either acute or chronic painful conditions. Only 6 articles (30%)[48,54,56,57,61,63] examined the clinical analgesic effectiveness of IFC as a single therapeutic modality. The rest of the articles included the application of IFC as a cointervention along with other therapeutic alternatives such as exercise,[47,49,53,58–60,62,64–66] shortwave diathermy,[51,59] hot packs,[55,60] ice,[58] myofascial release,[55] neuromuscular electrical stimulation,[52] infrared radiation,[51] and ultrasound.[50,60,62] Details of the studies' characteristics are shown in Table 1.

Methodological Quality of the Studies

The results of the critical appraisal for the selected studies are presented in Table 2. Three of the 20 studies were considered to be of high methodological quality, 14 studies were considered to be of moderate quality, and 3 studies were considered to be of poor quality. Even though the quality of most of the studies was rated as acceptable (17 studies were rated as being of moderate or high quality), there are some points regarding quality that need to be highlighted. Study flaws regarding patient selection were mainly related to description and appropriateness

Table 1.
Characteristics of the Studies[a]

Study	Country	Condition	Sample	Study Arms	Outcomes	Cointerventions	Follow-up	Treatment	Results	Strengths/Weaknesses
Quirk et al,[59] 1985	England	Knee OA	38	1. Active IFC + exercises 2. Active SWD + exercises 3. Exercises	ROM, pain (VAS), exercise endurance, maximum knee girth	Exercises	3 and 6 mo	• 12 patients in the IFC + exercise group, 12 patients in the SWD + exercise group, and 14 patients in the exercise group • Frequency of 0–100 Hz for 10 min and 130 Hz for 5 min, 3 times a week for 4 wk	• Significant improvement in groups 1, 2 and 3 ($P<.02$, $P<.05$, $P<.03$, respectively) • No significant difference among groups	• Randomized • Confounders not controlled • Reliability and validity of outcomes not reported • Small sample size • No control/placebo group included • Poor description of intervention
Adedoyin et al,[47] 2002	Nigeria	Knee OA	30	1. Active IFC 2. Placebo IFC	Pain (VAS)	Exercises	None	• 15 patients in IFC group and 15 patients in the placebo group • IFC: 4 electrodes (2 placed lateromedially and 2 placed anteroposteriorly), frequency of 100 Hz for the first 15 min and 80 Hz for the next 5 min, intensity (appreciable sensation) • Both groups had treatments and mobilization exercise twice a week for 4 wk	• Significant difference between initial and final pain rating in both groups ($P<.01$) • Significance difference between 2 groups after treatment ($P<.01$). Pain rating was found to be significantly better in the active IFC group than in the placebo group.	• Randomized • Clinicians blinded • Good control of confounders • Good description of intervention • Small sample size • Validity of outcomes not reported
Adedoyin et al,[49] 2005	Nigeria	Knee OA	51, 5 were excluded from the analysis	1. IFC + exercise 2. TENS + exercise 3. Exercise alone	Functional disability (WOMAC), pain (10-point pain rating scale)	Exercises	None	• 15 patients in the TENS + exercise group, 16 patients in the IFC + exercise group, and 15 patients in the exercise only group • IFC: 2 electrodes (either side of the knee longitudinally), frequency of 80 Hz continuous, intensity (strong tingling sensation), 20-min session, 2 sessions a week for 4 wk	• Significant time effect in WOMAC and pain scores ($P<.001$) • No significant difference between groups in WOMAC and pain scores ($P=.241$, $P=.813$) • All treatment protocols led to significant reductions in pain and improvement in function	• Randomized • Clinicians blinded • Sample size calculated *a priori* and adequate • Good description of intervention • Confounders not controlled • No control/placebo group included • Reliability of outcomes not reported
Defrin et al,[54] 2005	Israel	Knee OA	62	1. Active IFC noxious stimulus unadjusted 2. Active IFC noxious stimulus adjusted 3. Active IFC innocuous stimulus unadjusted 4. Active IFC innocuous stimulus adjusted 5. Placebo IFC 6. Control	Pain intensity (VAS), pain relief (0–100%), morning stiffness (10-cm line scale), active ROM (goniometer), electrically induced pain threshold (interferential current equipment)	None	None	• 11 patients in group 1, 11 patients in group 2, 12 patients in group 3, 11 patients in group 4, 9 patients in the placebo group, 8 patients in the control group • 2 electrodes (medial and lateral aspects of the knee); carrier current of 4,000 Hz, frequency between 30 and 60 Hz, intensity 30% above (noxious) or 30% below (innocuous) pain threshold, raise intensity (maintain sensation) for adjusted groups, 12 sessions every other day for 4 wk	• Significant improvement in groups 1 to 4 compared with the control group ($P<.001$) • Significantly larger decrease in noxious groups (1 and 2) for pain intensity ($P<.05$) and pain thresholds ($P<.01$) when compared with innocuous groups (3 and 4) • No significant difference between adjusted and unadjusted groups ($P=.47$)	• Randomized • Good description of intervention • Small sample size • Confounders not controlled • Reliability and validity of outcomes not reported • Control and placebo groups included

(Continued)

Table 1.
Continued

Study	Country	Condition	Sample	Study Arms	Outcomes	Cointerventions	Follow-up	Treatment	Results	Strengths/Weaknesses
Atamaz et al,[51] 2006	Turkey	Knee OA	85, 2 dropped out at discharge	1. Active IFC + IR + SWD 2. Intra-articular hyaluronan	Movement (ROM), pain (VAS), and function (SF-36, WOMAC, 15 min walking time)	IR and SWD	1, 3, 6, 9, and 12 mo	• 40 patients in the hyaluronan group (20 NaHA, 20 hylan) and 42 patients in the physical therapy group • Treatment applied 5 times a week for 3 wk with a series of IR, SWD, and interferential therapy	• Significant improvement in WOMAC, SF-36, and pain scores in both groups ($P<.05$) • Significant difference for pain at rest, pain on touch, and SF-36 in favor of physical therapy group at 1, 3, and 6 mo ($P<.05$) • Significant difference in WOMAC scores in favor of hyaluronan group ($P<.05$)	• Randomized • Clinicians blinded • Small sample size • No description of physical therapy interventions • Confounders not controlled • Reliability and validity of outcomes not reported • No control/placebo group included
Burch et al,[52] 2008	United States	Knee OA	116, 15 dropped out at discharge	1. IFC + NMES 2. Low-current intensity TENS	Pain and knee function (WOMAC), pain intensity (VAS), quality of life (VAS)	NMES	None	• 57 patients in the IFC + NMES group, 59 patients in the low-current TENS group • 15 min of true IFC (5 KHz with a beat sweep frequency of 1–150 Hz) followed by 20 min of NMES • 5 times a week for 8 wk	• IFC + NMES group reduced pain and increased function compared with low-current intensity TENS • The IFC + NMES group group had a significantly greater decrease in overall pain VAS ($P=.038$)	• Multicenter RCT • Clinicians blinded • Adherence tested • Sample size calculated *a priori* and appropriate • No true control/placebo group included • Confounders well controlled • Adverse effects reported • Reliability of outcomes not reported
Werners et al,[63] 1999	Germany	Chronic LBP	152, 20 were lost at 3-month follow-up	1. Active IFC 2. Lumbar traction + massage	Disability (Oswestry Disability Index), pain (VAS)	None	3 mo	• 74 patients in the IFC group and 73 patients in the traction group • 2 electrodes (placed paravertebrally in pain area), frequency of 30–60 Hz, six 10-min sessions over 14–21 d	• Significant improvement in both groups ($P<.05$) • No significant difference between groups	• Randomized • Sample size calculated *a priori* and appropriate • Confounders not controlled • Reliability and validity of outcomes not reported • No control/placebo group included
Hurley et al,[57] 2001	Northern Ireland	Acute LBP	60, 12 dropped out at 3-mo follow-up	1. Active IFC painful area + The Back Book 2. Active IFC spinal nerve + The Back Book 3. Control (The Back Book)	Pain (PRI), disability (RMDQ), generic health status (EQ-5D)	None	3 mo	• 18 patients in the painful area group, 22 patients in the spinal nerve group, and 20 patients in the control group • 2 electrodes, carrier frequency of 3,850 Hz, frequency of 140 Hz, 30 min • 2–3 treatment sessions weekly until discharge	• Significant improvement in pain severity, disability and health status for all groups at discharge ($P<.05$) and at follow-up ($P<.01$) • Significantly greater RMDQ score in spinal nerve group ($P=.042$)	• Randomized • Good description of treatment • Small sample size • Confounders not controlled • Clinical significance reported • Reliability and validity of outcomes not reported
Hurley et al,[56] 2004	Northern Ireland	Acute LBP	240, 82 lost at 12-mo follow-up	1. Active IFC 2. Manipulative therapy 3. IFC + manipulative therapy	Functional disability (RMDQ), pain (VAS, MPQ), quality of life (EQ-5D, SF-36), LBP (recurrence, work absenteeism, analgesic consumption, additional health care)	None	6 and 12 mo	• 52 patients in the MT group, 55 patients in the IFC group, and 51 patients in the MT + IFC group • 2 electrodes on spinal nerve root placement, carrier frequency of 3,850 Hz, frequency of 140 Hz, 30 min • 4 to 10 sessions over a period of 8 wk	• Significant improvement in all groups at discharge, 6 mo, and 12 mo ($P<.05$) • No significant difference between groups ($P>.05$)	• Randomized • Assessors blinded • Good description of treatment • Sample size calculated *a priori* and appropriate • Adverse effects reported • Clinical significance reported • No control/placebo group included • Reliability and validity of outcomes reported

(Continued)

Table 1.
Continued

Study	Country	Condition	Sample	Study Arms	Outcomes	Cointerventions	Follow-up	Treatment	Results	Strengths/Weaknesses
Lau et al,[66] 2008	Hong Kong	Acute LBP	110, 6 lost at 6-mo follow-up	1. IFC + medication + education + mobility and walking training 2. Walking training (control group)	Pain (NRS), satisfaction (Numeric Global Rating of Change Scale), disability (RMDQ)	Education, medication, mobility, and walking training	1, 3, and 6 mo	• 55 patients in the physical therapy group and 55 patients in the control group • 4 suction-type electrodes applied around the painful area, sweep frequency 70–130 Hz, intensity just below the pain threshold, 15 min • 1 or 2 sessions over a 24-hr period	• Significant decrease in pain (α=.025) and increase in satisfaction at discharge from the accident and emergency department • No significant difference between groups (α=.025) at 1, 3, and 6 mo follow-ups	• Randomized • Allocation adequate • Assessors blinded • Sample size calculated *a priori* • Intention-to-treat analysis included • High follow-up adherence • No placebo group included • Homogeneity of subjects uncertain
Adedoyin et al,[48] 2005	Nigeria	Chronic LBP	39	1. Active IFC swing pattern 1 integral 1 2. Active IFC swing pattern 6 integral 6 3. Active IFC swing pattern 6 wedge 6	Pain intensity (Verbal Semantic Differential Scale)	None	None	• 13 patients in the 1∫1 group, 13 patients in the 6∫6 group, 13 patients in the 6 wedge 6 groups • 2 electrodes (spinal nerve root correspondence to painful area), frequency of 100 Hz for burst group, sweep set between 50 and 100 Hz for the 6∫6 and the 6 wedge 6 groups, carrier frequency of 4,000 Hz in the channel, channel 2 set to fluctuate between 4,050 and 4,100 Hz • 2 treatment sessions daily for 2 times a week for 3 wk	• Significant decrease in pain over time (P<.001) • No significant effect between groups (P=.063)	• Randomized • Patients blinded • Good description of treatments • Small sample size • No control group • Confounders not controlled • Validity and reliability of outcomes not reported
Zambito et al,[65] 2006	Italy	Chronic LBP	120	1. Active IFC 2. Active horizontal therapy 3. Sham horizontal therapy	Functional questionnaire (Backill), pain (VAS), analgesic consumption	Exercise, analgesic medication	1 and 3 mo	• 45 patients in the active IFC group, 45 patients in the active horizontal therapy group, and 30 patients in the sham horizontal therapy group • 4 electrodes on a standard dermatomal pattern; frequency of 200 Hz, 10 min • 5 sessions weekly for 2 wk	• At discharge, significant and similar improvement in both the VAS and Backill score was reported in all 3 groups (P<.05) • The function and VAS scores continued to improve at 3 mo in the active groups compared with control (placebo) group (P<.01)	• Randomized • Sample size calculated *a priori* and adequate • Double blind approach • Validity and reliability of outcomes not reported • Moderate description of treatment
Zambito et al,[64] 2007	Italy	Chronic LBP	115	1. Active IFC 2. Active horizontal therapy 3. Sham horizontal therapy	Functional questionnaire (Backill), pain (VAS), analgesic consumption	Exercise, analgesic medication	1 and 3 mo	• 35 patients in the active IFC group, 35 patients in the active horizontal therapy group, and 35 patients in the sham horizontal therapy group • 4 electrodes on a standard dermatomal pattern, frequency of 200 Hz, 30 min • 5 sessions weekly for 2 wk	• At discharge, significant and similar improvement in both the VAS and Backill score was reported in the 3 groups (P<.01) • The function and pain scores continued to improve in the 2 active groups at weeks 6 and 14 compared with the control (placebo) group (P<.01)	• Randomized • Sample size calculated *a priori* and adequate • Double blind approach • Validity and reliability of outcomes not reported • Moderate description of treatment

(Continued)

Table 1.
Continued

Study	Country	Condition	Sample	Study Arms	Outcomes	Cointerventions	Follow-up	Treatment	Results	Strengths/Weaknesses
van der Heijden et al,[62] 1999	The Netherlands	Unspecified shoulder soft tissue condition	180, 1 dropped out at 12-mo follow-up	1. Active IFC + active US 2. No IFC + No US 3. Sham IFC + Sham US	Recovery, functional status (SDQ), chief complaint, pain (VAS), clinical status, ROM (goniometer)	Education and exercises	3, 6, 9, and 12 mo	• 34 patients in the active ET + active US group, 39 patients in the active ET + dummy US group, 39 patients in the dummy ET + active US group, 33 patients in the dummy ET + dummy US group, 35 patients in the no adjuvant group • 2 electrodes (1 in deltoid muscle region, 1 over homolateral erector trunci muscles), carrier frequency of 4,000 Hz, frequency of 60–100 Hz, intensity of electric paresthesia, 15 min, 12 sessions over 12 wk	• No significant difference between groups up to 12 mo follow-up (95% CI)	• Randomized • Patients and assessors blinded • Clinical significance reported • Sample size calculated *a priori* and adequate • Good description of treatment method
Taskaynatan et al,[60] 2007	Turkey	Bicipital tendinitis	47	1. IFC + US + hot packs + exercises 2. Steroid iophoresis + US + hot packs + exercises	Pain (VAS), ROM (goniometer), patient satisfaction (NRS), disability (function section of the Pennsylvania Shoulder Scale)	US+ hot packs + exercises	1 mo	• 21 patients in the IFC + US + hot packs + exercises group, 26 patients in the steroid iontophoresis + US + hot packs + exercises group • AMF frequency 0–100 Hz, 15 min, 15 sessions	• Statistical significant improvement at discharge and 1-mo follow-ups in the steroid iontophoresis group ($P<.05$) • Less dramatic improvement was reported for the IFC group at discharge and 1-mo follow-up ($P<.05$)	• Randomized • Assessors blinded • Poor description of interventions • Validity and reliability of outcomes not reported • Adverse effects reported • No dropouts reported
Cheing et al,[53] 2008	Hong Kong	Frozen shoulder	74, 4 dropped out at 8-mo follow-up	1. Active IFC 2. Active electro-acupuncture 3. Control	Shoulder function (Constant Murley Assessment Score), pain (VAS)	Exercise	1, 3, and 6 mo	• 24 patients in the IFC group, 25 patients in the electroacupuncture group, 25 patients in the control group • 4 suction-type electrodes around the shoulder in a coplanar arrangement, intensity just below the pain threshold, AMF swept frequency 80–120 Hz, 20 min • 10 sessions over 4 wk	• Both active groups showed a significant improvement at discharge and 6-mo follow-up for function and pain scores ($P<.001$) • No significant change was found in the control group, and no significant difference was found between the 2 active groups ($P>.05$)	• Randomized • Patients and assessors blinded • Reliability and validity of outcomes moderately reported • Good description of treatment protocols

(Continued)

Table 1.
Continued

Study	Country	Condition	Sample	Study Arms	Outcomes	Cointerventions	Follow-up	Treatment	Results	Strengths/Weaknesses
Hou et al,[55] 2002	Taiwan	Cervical myofascial pain	71	1. Hot pack, active ROM group 2. Hot pack, active ROM, ischemic compression group 3. Hot pack, active ROM, ischemic compression, TENS group 4. Hot pack, active ROM, stretch group 5. Hot pack, active ROM, stretch, TENS group 6. Hot pack, active ROM, IFC, myofascial release group	Index of change in pain threshold (algometer), pain tolerance (algometer), pain (VAS), and cervical ROM (goniometer)	Hot pack, active ROM, myofascial release	None	• 21 patients in the hot pack, active ROM group (B1); 13 patients in the hot pack, active ROM, ischemic compression group (B2); 9 patients in the hot pack, active ROM, ischemic compression, TENS group (B3); 10 patients in the hot pack, active ROM, stretch group (B4); 9 patients in the hot pack, active ROM, stretch, TENS group (B5); 9 patients in the hot pack, active ROM, IFC, myofascial release group (B6) • 4 electrodes; frequency of 100 Hz, carrier frequencies of 4,000 Hz and 4,100 Hz, 20 min	• Significant improvement in all groups ($P<.05$) • Groups B2, B3, B4, B5, and B6 had significantly larger improvement than group B1 ($P<.05$) • Groups B3, B5, and B6 had significantly larger improvement than group B2 ($P<.05$) • Group B6 had significantly larger improvement than group B4 ($P<.05$) • No significant difference among groups B3, B5, and B6	• Randomized • Good description of treatment • Sample size calculated *a priori* • No control/placebo group included • Reliability and validity of outcomes not reported
Almeida et al,[50] 2003	Brazil	Fibromyalgia	40, 23 dropped out	1. Active IFC + US 2. Placebo IFC + US	Pain (body map, VAS), tender points, (tender point threshold), polysomnography, sleep questionnaire	US	None	• 9 patients in the US + IFC group and 8 patients in the sham treatment group • Carrier frequency of 4,000 Hz, frequency of 100 Hz, intensity in the tactile sensation, 12 sessions for 4 wk	• Significant reduction in pain intensity and painful areas in the combined therapy group ($P<.001$) • No significant difference in sham treatment group	• Randomized • Investigator blinded • Small sample size • Very low adherence (missing data 57.5%) • Reliability and validity of measurement not reported
Taylor et al,[61] 1987	United States	Chronic jaw pain	40	1. Active IFC 2. Placebo IFC	Jaw pain (VAS), function (maximum vertical jaw opening)	None	None	• 20 patients in the IFC group and 20 patients in the placebo group • 4 electrodes (extraorally 1–1.5 cm in front of the tragus of ear), frequency of 90–100 Hz for 15 min and 40–90 Hz for 5 min, intensity (comfortable but not too strong), 3 treatments (24–72 hr between treatments)	• Significant improvement in both groups for pain and maximal vertical jaw opening • No significant difference between groups ($P<.05$)	• Randomization used • Patients blinded • Confounders not controlled • Reliability and validity of outcomes not reported • Small sample size • Good description of treatment
Jarit et al,[58] 2003	United States	Postoperative knee pain	87	1. Active IFC 2. Placebo IFC	Postoperative edema, pain (VAS), pain medication, ROM (goniometer)	Ice, exercises	None	• 28 patients in the ACL group (14 IFC and 14 placebo IFC), 34 patients in the meniscectomy group (17 IFC and 17 placebo IFC), 25 patients in the chondroplasty group (15 IFC and 10 placebo IFC) • 4 electrodes, frequency of 5–10 Hz in first 14 min, 80–150 Hz in second 14 min, 3 times daily for 7–9 wk	• Significantly less pain and greater ROM for the active IFC in all groups at all time points ($P<.05$)	• Randomized • Assessor blinded • Good description of treatment • Reliability and validity of outcomes not reported

[a] OA=osteoarthritis, IFC=interferential current therapy, SWD=shortwave diathermy, ROM=range of movement, VAS=visual analog scale, TENS=transcutaneous electrical nerve stimulation, WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index, IR=infrared radiation, SF-36=36-Item Short-Form Health Survey questionnaire, NMES=neuromuscular electrical stimulation, PRI=Pain Rating Index, RMDQ=Roland-Morris Disability Questionnaire, EQ-5D=EuroQol EQ-5D questionnaire, MT=manual therapy, MPQ=McGill Pain questionnaire, LBP=low back pain, US=ultrasound, SDQ=Shoulder Disability Questionnaire, ET=electrotherapy, CI=confidence interval, NRS=numeric rating scale, AMF=amplitude-modulated frequency, ACL=anterior cruciate ligament.

of the randomization procedure and concealment of allocation, with only 9 and 5 of the studies meeting these criteria, respectively. Items related to blinding were not achieved by the majority of the studies. Only 3 of the studies used a double-blinded design.

Testing subjects' adherence to intervention or having adequate adherence was another issue that was not accomplished by many studies (only 8 and 6 studies, respectively). Furthermore, adverse effects were reported in only 3 of the studies, and none of the studies provided details of the follow-up period.

Despite the fact that the adequate handling of dropouts is considered an important method used to prevent bias in data analysis, only 11 of the analyzed studies included information regarding the rate of withdrawals/dropouts. The outcome measures were not described well in terms of validity, reliability, or responsiveness.

Regarding statistical issues, it was uncertain whether sample size was adequate in 15 of the studies. Intention-to-treat analysis was used only in 11 of the studies. Finally, it also was unclear whether extraneous factors such as equipment calibration or medications during the study could affect the treatment responsiveness for IFC. For example, only 2 studies (10%) reported that the IFC equipment was calibrated during the study procedure.

IFC and Type of Pain Management

The effect of IFC has been studied predominantly in patients with chronic painful conditions (16 of 20 trials examined). These conditions included knee osteoarthritis,[47,49,51,52,54,59] chronic low back pain,[48,63–65] shoulder soft tissue pain,[53,60,62] fibromyalgia,[50] chronic jaw pain,[61] and myofascial syndrome pain.[55] In contrast, the analysis of IFC in acute pain included just 4 articles, 3 of them related to acute low back pain and 1 to postoperative knee pain.

Meta-analysis Results

Fourteen studies were included in the meta-analysis (Fig. 1),[47,49–56,60,61,63–66] with an overall sample size of 1,114 patients. Six studies were excluded for the following reasons: information regarding data variability (ie, mean and standard deviation) was not present,[58,59] the unit of variability included was different than the standard deviation (ie, interquartile range, median),[57,62] the comparison included in the trial was not relevant for the study's purpose,[48] and the interventions included in the trial were too heterogeneous[51] (ie, IFC, infrared radiation, shortwave diathermy, and 2 drugs [sodium hyaluronate and hylan G-F 20]).

The 14 selected studies were chosen because they provided complete information on the outcomes evaluated and homogeneity regarding outcome measures. Of these studies, 4 studies[54,56,61,63] addressed the analgesic effect of IFC alone and 10 studies[47,49,50,52,53,55,60,64–66] evaluated the effect of IFC applied as adjunct in a multimodal treatment protocol. In addition, of these 14 studies, 3 studies[53,54,66] compared the effectiveness of IFC with a control group, 6 studies[47,50,54,61,64,65] investigated IFC against placebo, and 7 studies[49,52,53,55,56,60,63] compared IFC with another intervention such as manual therapy or exercise.

Comparison 1: IFC Alone Versus Placebo Group on Pain Intensity at Discharge

Two studies[54,61] were included in this comparison. One study[54] measured outcomes at discharge after 4 weeks of therapy, and the other study[61] measured outcomes after 1 week of therapy. One trial[54] studied the effect of IFC on knee osteoarthritis, and the other trial[61] studied the effect of IFC on temporomandibular joint pain. One study[54] was rated of moderate methodological quality, and the other study[61] was rated of poor quality.[61] In this comparison, both studies had opposite results regarding the effectiveness of IFC when compared with a placebo group (Fig. 2). The pooled mean difference (MD) obtained for this analysis was 1.17 (95% CI=1.70–4.05). These results indicate that IFC alone was not significantly better than placebo at discharge.

Comparison 2: IFC Alone Versus Comparison Group on Pain Intensity at Discharge

Two studies[56,63] were included in this comparison. One study[63] measured outcomes at discharge after 2 to 3 weeks of treatment, and the other study[56] measured outcomes after 8 weeks. One trial[56] studied the effect of IFC on acute low back pain, and the other trial[63] studied the effect of IFC on chronic low back pain. Both studies were of moderate methodological quality. In this comparison, both studies agreed that IFC was not significantly better than manual therapy or traction and massage (Fig. 3). The pooled MD obtained for this analysis was −0.16 (95% CI=−0.62, 0.31). These results indicate that IFC alone was not significantly better than any of the comparisons at discharge from therapy.

Comparison 3: IFC as a Supplement to Another Treatment Versus Control Group on Pain Intensity at Discharge

Three studies[53,54,66] were included in this comparison. Two studies[53,54] used a 4-week discharge period, and one study[66] used a one-day discharge period. One trial[54] studied the effect of IFC on knee osteoarthritis, another trial[53] studied the effect of IFC on frozen shoulder, and the third tri-

Table 2.

Methodological Quality of the Studies[a]

Study	Item Scoring																																								Score/ Rating
	Patient Selection						Blinding						Interventions															Outcomes						Statistics						
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	
Adedoyin et al,[47] 2002	0	0	1	0	0	1	0	0	1	1	0	0	1	1	1	0	0	0	0	n/a	n/a	n/a	0	n/a	n/a	n/a	1	1	1	0	0	1	1	1	1	0	0	1	1	0.48 Moderate
Adedoyin et al,[48] 2005	1	1	1	0	0	1	0	0	0	1	0	0	1	n/a	0	0	0	0	0	0	0	0	0	n/a	n/a	n/a	1	1	1	0	0	0	1	1	1	0	0	1	0	0.37 Poor
Adedoyin et al,[49] 2005	1	1	1	0	0	1	0	0	1	1	0	0	1	0	1	1	1	0	0	1	1	1	0	n/a	n/a	n/a	1	1	1	1	0	0	1	0	1	1	1	1	0	0.61 Moderate
Almeida et al,[50] 2003	1	1	1	0	0	0	0	1	1	1	0	0	1	1	0	0	0	0	0	1	0	0	0	n/a	n/a	n/a	1	1	1	0	0	0	1	1	1	0	0	1	0	0.44 Moderate
Atamaz et al,[51] 2006	1	1	1	0	0	1	0	0	0	0	0	0	0	n/a	1	0	0	0	0	1	1	1	0	0	1	1	1	1	1	0	0	0	1	1	1	0	0	1	0	0.45 Moderate
Burch et al,[52] 2008	1	1	1	1	1	1	0	1	1	1	0	0	1	0	0	0	0	1	0	1	1	1	1	n/a	n/a	n/a	1	1	1	1	0	0	1	1	1	1	0	1	0	0.72 High
Cheing et al,[53] 2008	1	1	1	0	0	1	1	0	1	0	0	0	1	1	0	0	0	1	0	1	1	1	0	0	1	1	1	1	1	1	0	1	1	1	1	0	0	1	1	0.61 Moderate
Defrin et al,[54] 2005	1	1	1	0	0	0	0	0	0	0	0	0	1	1	1	1	1	0	0	0	0	0	0	n/a	n/a	n/a	1	1	1	0	0	0	1	1	1	0	0	1	0	0.42 Moderate
Hou et al,[55] 2002	1	1	1	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1	n/a	n/a	n/a	0	n/a	n/a	n/a	1	0	1	0	0	0	1	1	1	1	0	1	1	0.51 Moderate
Hurley et al,[56] 2004	1	1	1	1	1	1	0	0	0	0	0	0	1	0	1	0	1	1	1	1	0	1	1	0	1	1	1	0	1	1	0	1	1	1	1	1	0	1	1	0.66 Moderate
Hurley et al,[57] 2001	1	1	1	1	1	1	0	0	0	0	1	0	1	1	0	0	0	0	0	1	1	1	0	0	1	1	1	1	1	1	0	1	1	0	1	1	0	1	1	0.61 Moderate
Jarit et al,[58] 2003	1	1	1	0	0	1	0	1	1	1	1	0	1	1	1	0	1	1	0	0	0	0	0	0	1	1	1	1	1	0	0	0	1	0	1	0	0	1	0	0.54 Moderate
Lau et al,[66] 2008	1	1	1	1	1	0	0	1	1	0	0	0	1	0	1	0	1	1	1	1	1	1	0	0	1	1	1	1	1	0	0	1	1	1	1	1	1	1	1	0.72 High
Quirk et al,[59] 1985	1	1	1	0	0	1	0	0	0	0	0	0	0	0	1	0	1	0	1	1	1	0	0	0	1	1	1	0	0	0	0	0	1	0	0	0	0	1	0	0.36 Poor
Taskaynatan et al,[60] 2007	1	1	1	0	0	1	0	0	1	0	0	0	0	n/a	1	1	1	0	0	n/a	n/a	n/a	1	0	0	1	1	1	1	0	0	0	1	1	1	0	0	1	1	0.51 Moderate
Taylor et al,[61] 1987	1	1	1	1	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	n/a	n/a	n/a	0	n/a	n/a	n/a	1	1	1	0	0	0	1	1	1	0	0	1	0	0.39 Poor
van der Heijden et al,[62] 1999	1	1	1	1	0	1	0	1	1	1	0	0	1	n/a	1	1	1	1	1	1	1	1	0	0	1	1	1	1	1	1	1	0	1	1	1	1	0	1	1	0.78 High
Werners et al,[63] 1999	1	1	1	1	1	1	0	0	0	0	0	0	1	n/a	0	0	0	1	1	1	1	0	0	0	0	1	1	0	1	0	0	0	1	1	1	1	1	1	1	0.56 Moderate
Zambito et al,[64] 2007	1	1	1	1	0	0	1	1	1	1	0	0	1	1	1	1	1	0	0	n/a	n/a	n/a	0	0	1	1	1	0	1	0	0	0	1	1	1	1	1	1	1	0.67 Moderate
Zambito et al,[65] 2006	1	1	1	1	0	0	1	1	1	1	0	0	1	1	1	1	1	0	0	n/a	n/a	n/a	0	0	1	1	1	0	1	0	0	0	1	1	1	1	1	1	1	0.67 Moderate
Accomplished items	19	19	20	9	5	13	3	7	11	9	2	0	17	9	13	7	11	8	6	11	9	8	3	0	10	12	20	14	19	6	1	5	20	16	19	10	5	20	11	
Total percentage	95	95	100	45	25	68	15	35	55	45	10	0	85	60	65	35	55	40	30	79	64	57	15	0	83	100	100	70	95	30	5	25	100	80	95	50	25	100	55	

[a] 1=eligibility criteria; 2=described as randomized; 3=randomization performed; 4=randomization described as appropriate; 5=randomization concealed; 6=baseline comparability; 7=described as double blind; 8=blinding described an appropriate; 9=blinding of investigator/assessor; 10=blinding of subject/patient; 11=blinding of therapist; 12=blinding of the outcome (results); 13=treatment protocol adequately described for the treatment and control groups; 14=control and placebo adequate; 15=cointerventions avoided or comparable; 16=cointerventions reported for each group separately; 17=control for cointerventions in design; 18=testing of subject adherence; 19=adherence acceptable in all groups; 20=description of withdrawals and dropouts; 21=withdrawals/dropouts rate described and acceptable; 22=reasons for dropouts; 23=adverse effects described; 24=follow-up details reported; 25=follow-up period adequate; 26=short follow-up performed; 27=timing of outcomes comparable in all groups; 28=description of outcome measures; 29=relevant outcomes included; 30=validity reported for main outcome measure; 31=responsiveness reported for main outcome measure; 32=reliability reported for main outcome measure; 33=use of quantitative outcome measures; 34=descriptive measures reported for the main outcome; 35=appropriate statistical analysis included; 36=sample size calculated *a priori*; 37=adequate sample size; 38=sample size described for each group; 39=intention-to-treat analysis included; n/a=not applicable.

Study or Subgroup	IFC Alone			Placebo			Weight	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Defrin et al,[54] 2005	2.1	0.5	12	−0.5	0.7	9	51.4%	2.60 (2.06, 3.14)
Taylor et al,[61] 1987	1.75	1.96	20	2.08	1.53	20	48.6%	−0.33 (−1.42, 0.76)
Total (95% CI)			32			29	100.0%	1.17 (−1.70, 4.05)
Heterogeneity: tau^2=4.10, χ^2=22.33, *df*=1 (*P*<.00001), I^2=96%								
Test for overall effect: *z*=0.80 (*P*=.42)								

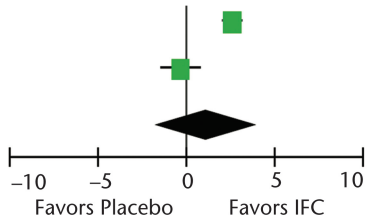

Figure 2.
Forest plot of comparison: interferential current therapy (IFC) alone versus placebo treatment on pain intensity at 1 week and 4 weeks (data presented as change scores). IV=inverse variance, 95% CI=95% confidence interval.

al[66] studied the effect of IFC on acute low back pain. Two studies included in this comparison were of moderate methodological quality,[53,54] and one study was considered to be of high quality.[66] In this comparison, the 3 studies tended to significantly favor IFC applied as a cointervention when compared with the control group (Fig. 4). The pooled MD obtained for this analysis was 2.45 (95% CI=1.69, 3.22). Thus, IFC applied as a cointervention was more than 2 points better, as measured with the VAS, in reducing pain intensity when compared with a control group in these conditions.

Comparison 4: IFC as a Supplement to Another Treatment Versus Placebo on Pain Intensity at Discharge

Five studies[47,50,54,64,65] were included in this comparison. Different times of discharge were used in the studies, ranging from 2 weeks[64,65] to 4 weeks.[47,50,54] Mean difference to pool the data was used. In addition, 95% CI and the random-effects model were chosen. In this comparison, 3 studies[47,50,54] of moderate quality tended to significantly favor IFC as a cointervention when compared with placebo. One study[64] of moderate methodological quality tended to significantly favor the placebo group. One study of moderate quality did not favor either IFC as a cointervention or placebo (Fig. 5, upper part).[65] The pooled MD obtained for this analysis was 1.60 (95% CI=−0.13, 3.34). This finding indicates that although IFC as a cointervention was statistically significantly better than a placebo at decreasing pain intensity at discharge in conditions such as osteoarthritis, chronic low back pain, and fibromyalgia, IFC tended to reduce pain in these conditions when compared with a placebo condition. In addition, the heterogeneity among studies was I^2=96%, which is considered substantial according to Cochrane group guidelines.[45] Therefore, these results should be interpreted with caution.

In this comparison, 2 studies[64,65] provided follow-up data (3 months). Thus, an analysis at the 3-month follow-up was performed (Fig. 5, lower part). The pooled MD obtained for this analysis was 1.85 (95% CI=1.47, 2.23). The 2 studies significantly favored IFC when compared with the placebo. This finding indicates that IFC as a cointervention was better than a placebo at decreasing pain intensity at the 3-month follow-up.

Study or Subgroup	IFC Alone			Comparison			Weight	Mean Difference IV, Random 95% CI
	Mean	SD	Total	Mean	SD	Total		
Hurley et al,[56] 2004	2.13	2.49	65	1.99	2.5	63	29.1%	0.14 (−0.72, 1.00)
Werners et al,[63] 1999	0.42	1.35	50	0.7	1.49	51	70.9%	−0.28 (−0.83, 0.27)
Total (95% CI)			115			114	100.0%	−0.16 (−0.62, 0.31)
Heterogeneity: tau^2=0.00, χ^2=0.64, *df*=1 (*P*=.42), I^2=0%								
Test for overall effect: *z*=0.66 (*P*=.51)								

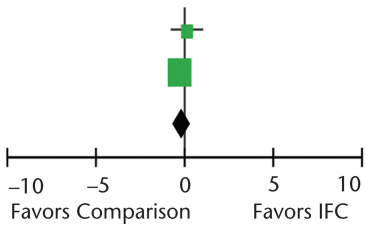

Figure 3.
Forest plot of comparison: interferential current therapy (IFC) alone versus comparison treatment on pain intensity at 3 weeks and 8 weeks (data presented as change scores). IV=inverse variance, 95% CI=95% confidence interval.

Study or Subgroup	IFC Therapy as Supplement Mean	SD	Total	Control Group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Cheing et al,[53] 2008	3.02	1.94	23	0.08	2.13	24	23.0%	2.94 (1.78, 4.10)
Defrin et al,[54] 2005	2.1	0.5	12	−0.7	0.7	8	38.9%	2.80 (2.24, 3.36)
Lau et al,[66] 2008	2.2	1.65	55	0.4	1.5	55	38.1%	1.80 (1.21, 2.39)
Total (95% CI)			90			87	100.0%	2.45 (1.69, 3.22)
Heterogeneity: tau^2=0.31; χ^2=6.76, *df*=2 (*P*=.03), I^2=70%								
Test for overall effect: *z*=6.28 (*P*<.00001)								

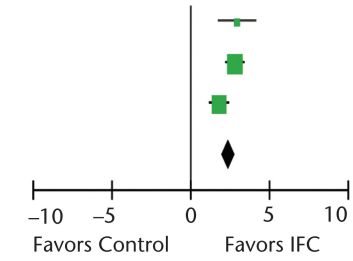

Figure 4.
Forest plot of comparison: interferential current therapy (IFC) as a supplemental treatment versus control treatment on pain intensity at 1 day and 4 weeks (data presented as change scores). IV=inverse variance, 95% CI=95% confidence interval.

Comparison 5: IFC as a Supplement to Another Treatment Versus Comparison on Pain Intensity at Discharge

Five studies[49,52,53,55,60] were included in this comparison (Fig. 6). Different times of discharge were used, ranging from 1 day[55] to 4 weeks[49,53,60] to 2 months.[52] Two studies[49,52] evaluated the effectiveness of IFC as a cointervention for knee osteoarthritis, 2 studies[53,60] evaluated the effectiveness of IFC as a cointervention for shoulder pain, and 1 study[55] evaluated the effectiveness of IFC as a cointervention for myofascial pain.

One study[55] compared IFC plus hot packs, active range of motion, and myofascial release with 5 different treatment modalities; thus, different analyses were run in order to deter-

Study or Subgroup	IFC Therapy as Supplement Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
3.1.1 Pain at discharge (1 week, 2 weeks, 4 weeks)								
Zambito et al,[64] 2007	1.9	0.78	35	2.6	1	35	21.5%	−0.70 (−1.12, −0.28)
Zambito et al,[65] 2006	1.8	1.27	45	1.7	1.65	30	21.0%	0.10 (−0.60, 0.80)
Adedoyin et al,[47] 2002	6.87	1.2	15	4.5	2.79	15	18.6%	2.37 (0.83, 3.91)
Defrin et al,[54] 2005	2.1	0.5	12	−0.5	0.7	9	21.3%	2.60 (2.06, 3.14)
Almeida et al,[50] 2003	4.2	2	9	0	1.82	8	17.6%	4.20 (2.38, 6.02)
Subtotal (95% CI)			116			97	100.0%	1.60 (−0.13, 3.34)
Heterogeneity: tau^2=3.59, χ^2=112.03, *df*=4 (*P*<.00001), I^2=96%								
Test for overall effect: *z*=1.81 (*P*=.07)								
3.1.2 Pain up to 3-month follow-up								
Zambito et al,[64] 2007	3.8	1.1	35	2	0.71	35	76.1%	1.80 (1.37, 2.23)
Zambito et al,[65] 2006	3.2	1.64	45	1.2	1.7	30	23.9%	2.00 (1.23, 2.77)
Subtotal (95% CI)			80			65	100.0%	1.85 (1.47, 2.23)
Heterogeneity: tau^2=0.00, χ^2=0.02, *df*=1 (*P*=.66), I^2=0%								
Test for overall effect: *z*=9.57 (*P*<.00001)								

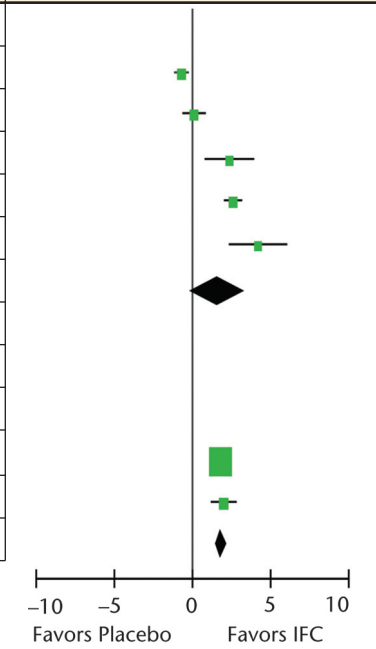

Figure 5.
Forest plot of comparison: interferential current therapy (IFC) as a supplemental treatment versus placebo treatment on pain intensity at 1-week, 2-week, 4-week, and 3-month follow-ups (data presented as change scores). IV=inverse variance, 95% CI=95% confidence interval.

Study or Subgroup	IFC as Supplement			Comparison			Weight	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Adedoyin et al,[49] 2005	5.07	1.39	16	4.74	1.14	15	20.1%	0.33 (−0.56, 1.22)
Burch et al,[52] 2008	2.79	1.32	53	2.32	1.54	53	23.1%	0.47 (−0.08, 1.02)
Cheing et al,[53] 2008	3.17	1.94	23	3.04	1.97	24	18.0%	0.13 (−0.99, 1.25)
Hou et al,[55] 2002 (B1)	3.34	1.14	9	0.77	1.8	21	18.5%	2.57 (1.50, 3.64)
Taskaynatan et al,[60] 2007	0.8	1.49	21	1.4	1.59	26	20.2%	−0.60 (−1.48, 0.28)
Total (95% CI)			122			139	100.0%	0.55 (−0.33, 1.44)

Heterogeneity: tau^2=0.80, χ^2=20.86, *df*=4 (*P*=.0003), I^2=81%

Test for overall effect: *z*=1.22 (*P*=.22)

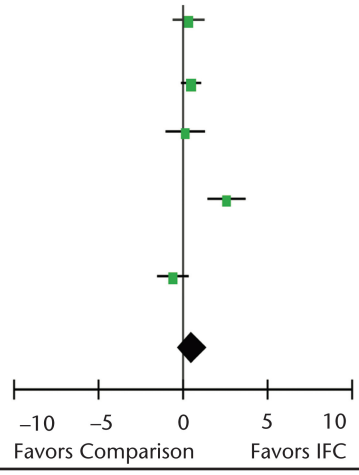

Figure 6.
Forest plot of comparison: interferential current therapy (IFC) as a supplemental treatment versus comparison treatment on pain intensity at 1 day, 2 weeks, 4 weeks, and 2 months (data presented as change scores). IV=inverse variance, 95% CI=95% confidence interval. B1=hot pack + active range of motion.

mine the effect of IFC as a cointervention when compared with all of these modalities (sensitivity analysis). We used the MD to pool the data. In addition, 95% CI and the random-effects model were chosen.

In this comparison, no clear trend favoring either IFC as a cointervention or the comparison treatments was observed for any of the analyses performed (Fig. 6). The pooled MD obtained for the various analyses was 0.55 (95% CI=−0.33, 1.44). The mean difference indicated that IFC as a cointervention was no better than other conventional interventions such as exercise, transcutaneous electrical nerve stimulation, or ultrasound plus hot packs at decreasing pain intensity at discharge.

Discussion

Analysis of the Analgesic Effect of IFC Alone

The results of this meta-analysis indicate that IFC applied alone as an intervention for musculoskeletal pain is not significantly better than placebo or comparison therapy (ie, manual therapy, traction, massage) at discharge from physical therapy treatment. However, few included studies (27%) examined the clinical analgesic effectiveness of IFC as a single therapeutic modality, and most did not focus on a specific musculoskeletal disorder. We also observed differences in length of treatment (ie, 1, 2, 3, and 8 weeks) and type of pain (ie, acute or chronic), indicating no consensus on optimal treatment parameters, which potentially contributed to the nonsignificance of the results.

Analysis of the Analgesic Effect of IFC as Part of a Multimodal Protocol (Cointerventions)

An important factor in this meta-analysis was the inclusion and analysis of studies including the application of IFC as a cointervention in a multimodal treatment protocol. This decision was clinically sound because IFC is used mainly as an adjunct treatment. The results of this study indicate that IFC as a cointervention is significantly better than control and placebo for reducing chronic musculoskeletal pain at discharge and at 3 months posttreatment, respectively. The pooled effect for IFC as a cointervention versus control was 2.45 on the VAS (95% CI=1.69, 3.22). According to some authors, this change is considered a clinically meaningful effect for acute painful conditions.[116–119] However, in chronic pain, a more stringent criterion seems to operate because a relative pain reduction of 50% or at least 3 cm on a VAS has been recommended for detecting a clinically successful pain reduction.[120,121]

In addition, when IFC as a cointervention was compared with placebo at discharge, there was no statistically significant difference between the groups. At 3-month follow-up, IFC as a cointervention obtained a better effect on the VAS, although less pronounced than when compared with a control group (pooled effect=1.85, 95% CI=1.47, 2.23). Thus, it seems that although IFC applied as a cointervention may have a modest analgesic effect, the magni-

tude of the effect is not large enough to be considered clinically relevant when compared with placebo or comparison interventions.

Because this is the first meta-analysis looking at the analgesic effect of IFC, direct comparisons cannot be made. In a previous study, Johnson and Martinson[122] concluded that transcutaneous electrical nerve stimulation, used mainly as an isolated intervention, provided significant pain relief when compared with a placebo intervention in a variety of chronic musculoskeletal conditions. Although methodological differences are present between both meta-analyses, some similarities such as the final sample sizes included, the focus on chronic musculoskeletal conditions, and clinical heterogeneity make the comparison between these 2 meta-analyses worth considering.

Some factors regarding IFC treatment may have accounted for the modest effect size observed. For example, although the stimulation of small-diameter fibers has been demonstrated to produce a more positive effect for chronic pain when compared with the stimulation of large-diameter fibers (Aβ),[54] the included studies, regardless of the type of pain, used stimulation parameters that were related mainly to the stimulation of Aβ fibers and the pain gate mechanism.[11,47–50,52,53,56–58,61,62] Although the stimulation of large-diameter fibers is acknowledged to produce a fast onset of analgesia, an important shortcoming is its brief analgesic effect.[123–125] Thus, it is plausible that in chronic pain, which was the dominant condition in this review, the effectiveness of IFC under these stimulation parameters may have been attenuated, resulting in a small effect in reported pain reduction. Further research is needed to evaluate the effect of noxious stimulation (eg, small-diameter fibers) on IFC effectiveness, especially in chronic pain.

Additionally, IFC has not been applied using a consistent treatment protocol. For example, similar AMF settings (≥80 Hz) were considered for treating either acute[56,57] or chronic[47,50,53,55,64,65] conditions. Moreover, under the same condition (eg, osteoarthritis), the authors inconsistently applied fixed AMF frequencies (ie, 80 Hz)[49] or sweep AMF frequencies (ie, 1–150 Hz, 30–60 Hz, 0–100 Hz).[52,54,59] Although experimental evidence has challenged the role of AMF as the main analgesic component of IFC,[36,37,85,126] inconsistency in the use of this parameter in clinical settings warrants consideration. Based on the current evidence, recommendations for optimal dosage when using IFC are not clear. It seems, however, that clinical evidence supports the fact that AMF should not be the most important parameter for clinical decision making. This fact has been corroborated by recent experimental evidence as well.[80] Instead, the use of a sensory level of intensity appears to be a consistent factor for the majority of the studies. Although some variations in the number of treatments and the treatment time exist, it seems that 10 to 20 minutes of application for 2 to 4 weeks with a total of 12 sessions is the most common treatment protocol for IFC.[47–51,53,54,59,60,62,64,65]

In this systematic review, 16 out of 20 studies evaluated the role of IFC in chronic rather than acute pain. Based on this fact, it seems that IFC has been applied more often in the management of chronic painful conditions. Interestingly, and apparently in contrast to current clinical practice in which IFC is used mostly for short-term pain relief, this meta-analysis provided information regarding potential positive long-term benefits from IFC.[64,65]

Adverse Effects

An important safety feature when applying electrotherapy modalities is the report of adverse effects. Although IFC is considered a safe modality, its application has been associated with local adverse effects such as blisters, burns, bruising, and swelling.[127,128] Interestingly, only 3 studies[52,56,60] included reports of adverse effects as a result of IFC treatment. Two studies[56,60] reported no complications, and one study[52] reported the presence of muscle soreness in one subject. Reporting adverse effects must be mandatory, not only for the safety of patients, but also for the professional integrity of therapists.

Methodological Elements Affecting Observed Effect

Even though the quality of the trials appraised generally was moderate, there are some methodological biases common to these studies that could have had an impact on the results. Selection bias could have existed, as only 9 trials reported appropriate randomization and only 5 trials reported concealment of allocation. Another potentially important bias was the lack of blinding, especially of the patients (9 studies) and assessors (11 studies). The outcome measure for this meta-analysis was pain, which is a subjective outcome and dependent on the subject's report. Trials without appropriate randomization, concealment of allocation, and blinding tend to report an inaccurate treatment effect compared with trials that include these features.[129–131]

Other potential biases that could have affected the observed effects were the lack of an appropriate sample size (only 5 of the trials reported adequate sample size) and the inappropriate handling of withdrawals and dropouts (only 11 trials used intention-to-treat analysis). Reporting clinical significance of results has become a relevant issue to dem-

onstrate the effectiveness of an intervention. Clinical significance provides the clinician with adequate information regarding the clinical impact of an intervention because it can identify when a meaningful change is produced.[132] Despite this message, the report of clinically meaningful changes in the present study was largely neglected, with only 3 studies including this component.[56,57,62]

The present study used a compilation of items from all of the scales used in the studies in the physical therapy literature. Although some of the scales used in physical therapy (ie, PEDro, Jadad) have been validated in some way, our recent analysis of health scales used to evaluate methodological quality determined that none of these scales are adequate for that use alone.[42] Therefore, it was decided that all of these scales would be used to assess methodological quality, and we used a compilation of items to provide a comprehensive and sensitive evaluation of the quality of individual trials. However, further research investigating methodological predictors for determining trial quality in physical therapy is needed.

Summary of Evidence

As an isolated treatment, IFC was not significantly better than placebo or other interventions. Conversely, when included in a multimodal treatment plan, IFC displayed a pain-relieving effect (VAS reduction of over 2 points) compared with a control condition.

Strengths

This meta-analysis is the first systematic investigation regarding the pain-reducing effectiveness of IFC on musculoskeletal pain. A comprehensive search was made of all the published research in this area over a wide range of years (1950–2010). In addition, authors were contacted in an attempt to have complete information about the selected studies. The 20 RCT articles included in this review covered a broad spectrum of acute and chronic musculoskeletal conditions. Interferential current therapy was analyzed as isolated intervention, as well as part of a multimodal treatment plan. In addition, the study provided multiple analyses, including the comparison between IFC and placebo, the comparison between IFC and control, and IFC contrasted to different types of interventions.

Limitations

Outcome level. A main limitation of this meta-analysis is the presence of clinical heterogeneity in the study population in most of the comparisons, casting some doubt on the validity of our results.

Study and review level. A potential limitation is the omission of non–English-language publications; however, English is considered the primary scientific language. It also has been reported that language-restricted meta-analyses only minimally overestimate treatment effects (~2% on average) compared with language-inclusive meta-analyses.[114] Therefore, language-restricted meta-analyses do not appear to lead to biased estimates of intervention effectiveness.[133,134] Applicability of results about the isolated effect of IFC on musculoskeletal pain also is limited, as only 4 studies addressed this issue. Another important limitation is that this study included only pain as an outcome measure. It would be important to know whether outcomes such as disability or function could have been modified by the application of IFC.

Conclusions

Implications for Practice

Interferential current therapy included in a multimodal treatment plan seems to produce a pain-relieving effect in acute and chronic musculoskeletal painful conditions compared with no treatment or placebo. Interferential current therapy combined with other interventions was shown to be more effective than placebo application at the 3-month follow-up in subjects with chronic low back pain. However, it is evident that under this scenario, the unique effect of IFC is confounded by the impact of other therapeutic interventions. Moreover, it is still unknown whether the analgesic effect of IFC is superior to that of these concomitant interventions.

When IFC is applied alone, its effect does not differ from placebo or other interventions (ie, manual therapy, traction, or massage). However, the small number of trials evaluating the isolated effect of IFC, heterogeneity across studies, and methodological limitations identified in these studies prevent conclusive statements regarding its analgesic efficacy.

Implications for Research

Because only 4 studies that evaluated the isolated effect of IFC were identified, and these studies had mixed results, further research examining this issue is needed, ideally in homogeneous clinical samples. Further research also is needed to study the effect of IFC on acute painful conditions. Also of interest would be the study of the effect of IFC in chronic conditions using a theoretical framework for the selection of parameters associated with suprasegmental analgesic mechanisms (ie, noxious stimulus) instead of sensory stimulation.

Mr Fuentes, Dr Armijo Olivo, and Dr Gross provided concept/idea/research design and writing. Mr Fuentes and Dr Armijo Olivo provided data collection and analysis. Mr Fuentes provided project management. Dr Magee and Dr Gross provided consultation (including review of manuscript before submission).

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ORIGINAL ARTICLE

Effects of Carrier Frequency of Interferential Current on Pressure Pain Threshold and Sensory Comfort in Humans

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Abstract

Objective: To assess the effect of carrier frequency of interferential current (IFC) on pressure pain threshold (PPT) and sensory comfort in healthy subjects.

Design: A double-blind randomized trial.

Setting: University research laboratory.

Participants: Healthy subjects (N = 150).

Interventions: Application of the IFC for 20 minutes and measures of PPT collected in the regions of the nondominant hand and forearm.

Main Outcomes Measures: We measured PPT and comfort at frequencies of 1kHz, 2kHz, 4kHz, 8kHz, and 10kHz.

Results: There was a significant increase in PPT in the 1-kHz group when compared with the 8-kHz and 10-kHz groups. There was a greater discomfort in the 1-kHz and 2-kHz groups.

Conclusions: IFC with a carrier frequency of 1kHz promotes a higher hypoalgesic response during and after stimulation than IFC with carrier frequencies of 8kHz and 10kHz. Carrier frequencies of 1kHz and 2kHz are perceived as more uncomfortable than carrier frequencies of 4kHz, 8kHz, and 10kHz.

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Interferential current (IFC) is a medium-frequency electrical current amplitude-modulated in low frequency, generated by the superimposition of 2 currents of medium-frequency slightly out of phase.[1,2] It is a type of electrotherapy that theoretically reaches deep tissues by means of the use of a carrier frequency in the kilohertz range with the aim of overcoming the electrical impedance offered by the skin.[1,3-8] Although this claim has been widely reported in the literature, it has been recently questioned because skin impedance to low-frequency pulsed currents depends on the phase duration, not the pulse frequency.[9-11] Moreover, some studies have failed to show differences in hypoalgesic response between IFC and low-frequency pulsed currents delivered by transcutaneous electrical nerve stimulation devices.[5,12,13] Nevertheless, IFC is one of the most common types of electrical current used in Canada[14] and England.[15]

Medium-frequency alternating currents (MFACs) are defined as currents in the frequency range of 1 to 10kHz and are often used in rehabilitation. IFC is a simple and noninvasive treatment often used to induce analgesia,[16] elicit muscle contractions,[17] and reduce edema.[2,18] Although some mechanisms of pain control with IFC have been proposed in the literature, the exact mechanism of action for this effect is still unknown.[5,19-21] The most popular theory used to explain IFC analgesia is the gate control theory of pain.[19,20]

Modern IFC equipment permits that the carrier frequency of the current can be adjusted in accordance with the therapeutic goal. It is claimed that the frequency of 2kHz is more appropriate to elicit muscle contractions and strengthening, whereas the frequency of 4kHz is ideal to generate hypoalgesia.[18,22] However, this information usually comes from electrotherapy textbooks and equipment manuals and not as results of scientific studies. Moreover, there are conflicts in the literature about the ideal

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parameters for electrical stimulation to be used with a minimum of sensory discomfort.[10,23,24]

When bursts of alternating current (AC) are applied transcutaneously, the threshold voltage for sensory nerve excitation decreases as the burst duration is increased.[1,10] This phenomenon of summation is known as "Gildemeister Effect." Thus, it is possible that a single long-duration burst results in multiple action potentials as a result of summation.[10,25-29] Therefore, the use of MFACs without modulation or with long-duration bursts can decrease the nerve fiber response due to the high number of action potentials and possibly cause synaptic fatigue.[10,22,29] Taking into consideration this neurophysiologic evidence, it is important to administer MFACs with short-duration bursts.

With IFC, burst duration can be defined as the time taken for a cycle of amplitude modulation (period) to occur (fig 1).[10,16,30] In IFC devices the only means of altering burst duration is by altering the amplitude-modulated frequency (AMF). Although experimental studies have failed to show the relevance of setting different AMF values for pain control,[20] it has been claimed that an AMF of 100Hz will produce the greatest analgesia.[18,31,32] Accordingly, an AMF of 100Hz is often used in studies assessing the hypoalgesic effects of IFC.[5,6,8,16,21,30,33]

When the AMF is set at 100Hz, the burst duration is 10 milliseconds, which has been found to be too long when compared with burst durations of 1 to 4 milliseconds, which are reported to be optimal for both sensory and motor stimulation by authors who measured sensory, motor, and pain-tolerance thresholds with MFAC in an experimental model in humans.[34,35] With this concern in mind, when analyzing a way of reducing the depolarization excess of nerve fibers during stimulation with IFC, we considered that carrier current frequency modification would decrease temporal summation and the number of action potentials and promote a higher hypoalgesic response. Therefore, the primary purpose of the present study was to assess the effect of the carrier frequency of IFC on pressure pain threshold (PPT) in healthy humans. A second purpose was to compare the sensory comfort during IFC application with different carrier frequencies.

Methods

Participants

A total of 150 healthy, pain-free participants (75 men, 75 women; age range, 18−35y) were recruited from the staff and students of the University of the City of Sao Paulo (table 1) after approval was obtained from the university's ethical committee. The sample size was calculated considering a difference of 100kPa between groups and an SD of 110kPa obtained from previous data on PPT and electrical stimulation.[11] At a significance level of .05 and power of 80%, it was calculated that 30 participants were required in each group, giving a total number of 150 participants for the study. Participants were screened and excluded if they had injury or nerve damage to the upper limbs, current pain, pregnancy, cancer, chronic illness, cardiac pacemaker, epilepsy, allergies to the electrodes, currently taking pain medication, skin conditions, or deficient skin sensation in the areas of electrode placement.[11,36,37] The participants were informed about the procedures to be used during the data collection and provided written informed consent. They were stratified by sex to ensure equal numbers of men and women in each group[36-39] and randomly allocated to 1 of 5 groups (n=30 per group): 1kHz, 2kHz, 4kHz, 8kHz, and 10kHz. Randomization was performed using the sequentially numbered, opaque sealed envelopes allocation concealment method.[38-41] The envelopes were stored in a secure cabinet that only the allocation investigator had access to and were opened immediately prior to intervention allocation. All participants completed the study.

List of abbreviations:

AC	alternating current
AMF	amplitude-modulated frequency
IFC	interferential current
MFAC	medium-frequency alternating current
PPT	pressure pain threshold

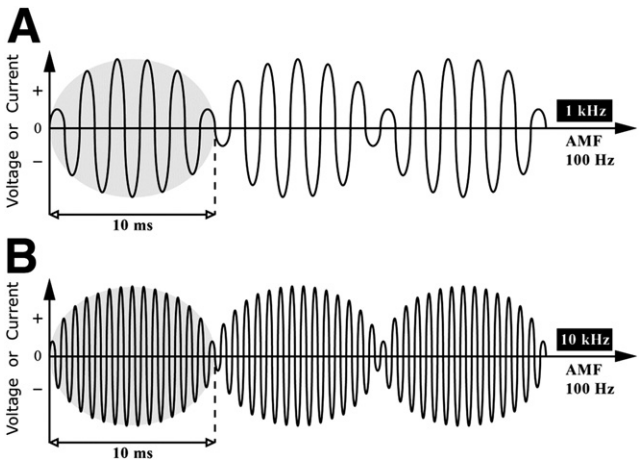

Fig 1 (A) An example of IFC with carrier frequency of 1kHz. This current is produced by the interference of 2 unmodulated MFACs. In this case, 1 current has a frequency of 1000Hz and another 1100Hz. The result is a burst-modulated AC with sinusoidal modulation and frequency of 1050Hz. The burst duration (period) is 10ms, and so the AMF is 100Hz. (B) Similarly, this current with a carrier frequency of 10kHz resulted from the interference of 1 current with 10,000Hz and another with 10,100Hz. The resulting frequency is 10,050Hz. Again, the burst duration is 10ms and the AMF is 100Hz; however, there are now more cycles of AC in each burst than in example A.

Participants' preparation

Participants' upper limbs were cleaned with soap and water prior to marking electrode placement and PPT recording sites using a marker. The electrode placement sites were marked out as described below. Two PPT recording sites were marked in the nondominant upper limb as follows: (1) 3 centimeter distal to the distal end of the anatomical snuff box in the midline of the belly of the first dorsal interosseous muscle and (2) on the anterior aspect of the forearm, 7.5 centimeter proximal to the distal wrist crease (figs 2A and B).[11,36] These sites of PPT measurements were chosen to examine the effects of IFC within the area of stimulation and in a distal area.[11,36,37] Participants were asked to remain seated in a comfortable upright position with the upper limb leaning on a table during all procedures.

Pressure pain threshold

PPT was recorded by a researcher who was blind to group allocation using a Kratos pressure algometer[a] (DDK 20). The

Table 1 Characteristics of the study participants

Characteristic	1kHz (n=30)	2kHz (n=30)	4kHz (n=30)	8kHz (n=30)	10kHz (n=30)
Sex					
Male	15 (50)	15 (50)	15 (50)	15 (50)	15 (50)
Female	15 (50)	15 (50)	15 (50)	15 (50)	15 (50)
Age (y), mean ± SD	24.53±0.87	25.53±1.04	22.47±0.81	28.57±0.90	29.17±0.91
BMI (kg/m^2), mean ± SD	23.99±0.64	24.62±0.61	23.88±0.83	24.44±0.85	23.86±0.54
Race					
White	19 (63.3)	19 (63.3)	22 (73.3)	20 (66.7)	21 (70)
African	9 (30)	5 (16.7)	5 (16.7)	10 (33.3)	7 (23.4)
Asian	2 (6.7)	3 (10)	1 (3.3)	ND	1 (3.3)
Other	ND	3 (10)	2 (6.7)	ND	1 (3.3)

NOTE. Values are mean ± SEM or n (%).
Abbreviations: BMI, body mass index; ND, no data.

algometer was calibrated prior to the beginning of the study by the manufacturer. The circular probe of the algometer (1cm^2 area) was placed perpendicular to the skin and applied at a constant rate (approximately 5N/s). Participants were asked to say "stop" when the sensation they were feeling changed from pressure to pain. Three measurements (in Newton) were taken from each recording site at each time point and the average used for data analysis. The pressure in kilopascal was calculated using the following formula: P [Pa] = F [N]/A [m^2], where P is the pressure, F is the applied force, and A is the area of the algometer probe.[11] Each participant had 2 practice trials on the dominant upper limb to ensure the participant understood the PPT measurement. At the 2 recording sites, PPT was recorded at 0, 10, 20, and 40 minutes (20min after treatment). During the study, PPT readings from the 2 recording sites were taken in a random order to avoid order bias.[11,36,42]

A preliminary reliability study was conducted by the PPT assessor by recording PPT from the 2 recording points described above from 10 healthy volunteers on 2 occasions, 48 hours apart. This reliability study demonstrated excellent overall between-session intrarater reliability for PPT measurements from the hand (.99) and from the forearm (.99).

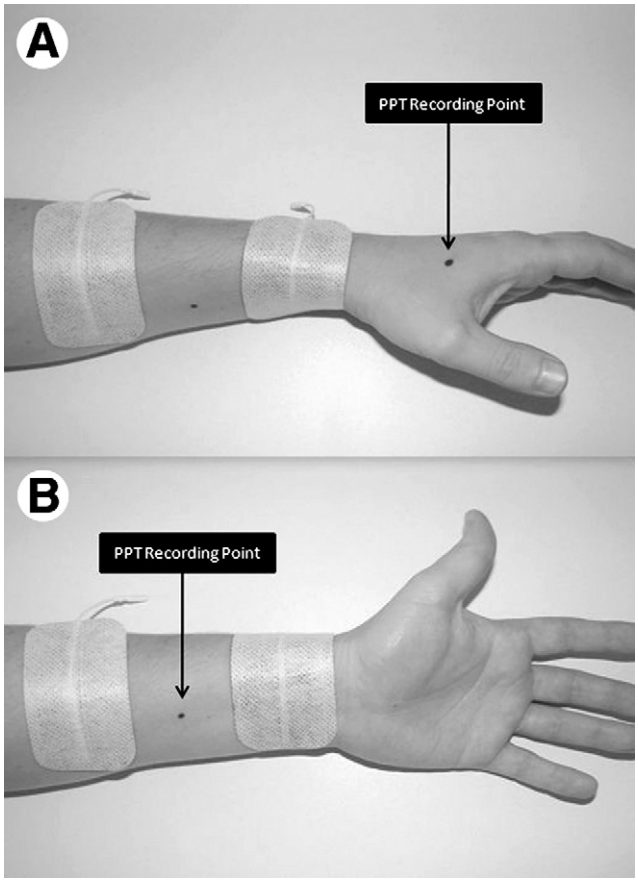

Fig 2 (A) Positioning of electrodes for IFC application and location of PPT recording point on the hand. (B) Positioning of electrodes for IFC application and PPT measurement site on the forearm.

IFC procedure

Two self-adhesive electrodes (50×90mm) (ValuTrode)[b] were placed on the lateral aspect of the forearm at the level of the distal wrist crease and the lateral aspect of the forearm, 10 centimeters proximal to the distal wrist crease (figs 2A and B).[11,36]

An electrical stimulator was provided by IBRAMED[c] and delivered premodulated IFC. This IFC device was modified exclusively for this study and is not commercially available. The unit was calibrated using a digital oscilloscope and 1-kΩ resistor before starting the study.

After the electrodes were positioned, the IFC parameters were adjusted by an investigator not involved in outcome assessments. The equipment was adjusted with the following parameters: carrier frequency according to group allocation and AMF=100Hz. After the parameters had been adjusted, the device display was covered to keep the outcome assessor blind to the participant's group allocation. The outcome assessor then recorded the PPTs (0min). After the measurement of the PPTs, the outcome assessor left the room and the current amplitude was increased until the participant reported a strong, but comfortable paresthesia. At 5-minute intervals, the participants were asked if the sensation had faded and the current amplitude was increased again until the participant reached the prior sensation.[11] In all groups, IFC was administered for 20 minutes.

Ten minutes from the beginning of IFC application PPT was recorded again followed by a discomfort measurement. Discomfort was assessed with a 10-centimeter visual analog scale where the far left end indicated "very comfortable" and the far right end indicated "very uncomfortable."[43] Both PPTs and discomfort measurements were repeated at the 20th minute. At the 40th minute (20min after treatment), only PPT was measured.

Current amplitude

The current amplitude required to reach sensory threshold and to promote a strong but comfortable paresthesia was recorded for all study groups throughout the treatment session.

Data analysis

Data were analyzed by a researcher who did not know the group allocation. The average of the 3 PPT scores recorded at each time point was used for analysis.

Descriptive statistics were calculated for all variables in the study. Shapiro-Wilk tests showed that the data were normally distributed. Therefore, we compared PPT between groups using a 3-way mixed analysis of covariance with group as between-subject factor, time and site as within-subject factors, and baseline PPT as covariate. The post hoc tests were based on estimates of multiple confidence intervals adjusted by Bonferroni correction. The variation of initial values (0min) of current amplitude at the end of treatment (20min) was calculated using the following equation: Current Amplitude Difference = Amplitude 20 minutes − Amplitude 0 minute. A 1-way analysis of variance and post hoc Tukey tests were used to compare discomfort and current amplitude between groups.

All analyses were performed using SPSS[d] (version 15.0). All tests were performed assuming a significance level of $P \leq .05$. Data are presented as mean ± SEM.

Results

PPT data

Data for the raw mean ± SEM PPT scores for all experimental groups at each time point are summarized in table 2.

Figure 3 summarizes the baseline-adjusted mean PPT ± SEM in the hand measurement site for all experimental groups. There was a significant hypoalgesic effect in the 1-kHz group when compared with 8-kHz and 10-kHz groups at 20 and 40 minutes ($P<.05$). There was no significant difference between any other groups ($P>.05$).

The baseline-adjusted mean ± SEM of PPT in the forearm over the 40 minutes are summarized in figure 4. Similar to the hand data, statistical analysis showed differences between the 1-kHz group when compared with the 8-kHz and 10-kHz groups at 20 and 40 minutes ($P<.05$). No significant differences were found between any other groups ($P>.05$).

Discomfort data

The discomfort scores measured with the visual analog scale at 10 and 20 minutes are presented in figure 5. One-way analysis of variance showed significant differences in both time points ($P<.0001$). Post hoc Tukey tests indicated a higher discomfort in the 1-kHz and 2-kHz groups than in the 4-kHz, 8-kHz, and 10-kHz groups.

Current amplitude

With regard to the amplitude of the current necessary to reach the sensory threshold, the groups presented significant differences ($P<.0001$). The 1-kHz and 2-kHz groups showed significant differences from the 4-kHz ($P<.0001$), 8-kHz ($P<.0001$), and 10-kHz ($P<.0001$) groups. The 4-kHz group showed significant differences from the 8-kHz ($P=.008$) and 10-kHz ($P=.001$) groups (fig 6). Table 3 summarizes the current amplitude applied in all experimental groups over time.

Figure 7 shows the current amplitude differences (Amplitude 20min − Amplitude 0min). Four-kilohertz, 8-kHz, and 10-kHz groups required a higher current amplitude increase over the treatment time than did the 1-kHz group ($P<.05$). Eight-kilohertz and 10-kHz groups also required a higher current amplitude increase than did the 2-kHz and 4-kHz groups ($P<.05$).

Discussion

To our knowledge, this is the first study conducted to investigate the effect of different carrier frequencies of IFC on PPTs and discomfort. In the present study, we showed that although low carrier frequencies were more uncomfortable they promoted a higher hypoalgesic response. Hans Nemec developed the IFC in the early 1950s with a carrier frequency of 4kHz, claiming that this particular frequency would be more comfortable for patients.[10,44] However, we have not found studies in the literature showing whether the frequency of 4kHz is really the most

Table 2 Mean ± SEM raw PPT scores for all time points, for each group for hand and forearm PPT measurements

			IFC Application		Post-IFC
	Group*	Baseline	10min	20min	40min
Hand	1kHz	328.55±38.24	391.43±47.26	431.34±51.98	377.07±48.65
	2kHz	319.85±38.28	372.56±47.97	395.31±51.45	348.80±38.29
	4kHz	274.70±35.00	314.96±36.18	336.77±36.00	315.11±40.58
	8kHz	227.55±17.21	244.89±16.64	263.44±18.61	240.43±18.95
	10kHz	210.86±11.52	226.88±12.11	237.15±8.47	213.12±11.94
Forearm	1kHz	402.91±36.92	454.75±45.46	490.20±47.92	457.19±48.10
	2kHz	415.22±45.68	457.99±50.55	472.53±49.56	444.52±46.09
	4kHz	391.67±38.66	417.30±37.36	426.90±35.53	424.27±42.35
	8kHz	298.47±15.94	318.55±15.76	334.46±18.07	309.44±17.13
	10kHz	288.52±13.38	303.62±11.60	311.76±10.92	283.67±10.80

NOTE. All values are expressed in kilopascal.
* n=30 per group.

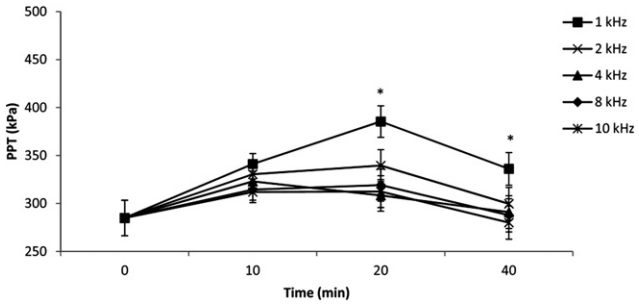

Fig 3 PPT data for hand measurements, for each experimental group (baseline-adjusted mean ± SEM). *Indicates significant difference ($P<.05$) from 8-kHz and 10-kHz groups.

comfortable and whether it produces a better hypoalgesic response than do other kilohertz-range frequencies. Manufacturers of electrotherapy devices produce commercial equipment of IFC with frequencies ranging from 1kHz to 10kHz.[30] The most often used frequencies are 2kHz for muscle contractions and 4kHz for pain control[20,22] despite the lack of evidence to support these claims.

In the current study, PPTs recorded from both hand and forearm showed a significantly higher hypoalgesic response in the 1-kHz group than in the 8-kHz and 10-kHz groups in the 20th and 40th minutes. A more pronounced hypoalgesic effect was observed when using lower carrier frequencies (1kHz), which may be explained on the basis of the decrease in summation and reduction in multiple firing. Long burst durations can lead to more summation and multiple nerve fires in each burst, causing fiber dropout due to neurotransmitter depletion (synapse fatigue), propagation failure, and/or nerve block, resulting in a lesser hypoalgesic effect.[24,29,45,46] In our study, the burst duration was always the same (10ms); however, we conclude that using lower carrier frequencies the number of cycles per burst decreases and summation consequently decreases, leading to a lesser nerve firing frequency.

High frequencies of AC can reduce the nerve response because successive stimuli fall within the relative or eventually absolute refractory period of the action potential, impairing nerve fiber repolarization.[18,22] The sensitivity of nerve fibers decreases, and a higher current intensity is needed to depolarize the nerve membrane. Prolonged stimulation with high frequencies causes the axon to cease conducting, and this phenomenon is known as Wedensky inhibition.[18] Bowman and McNeal[47] assessed the response of single alpha motoneurons for neural block, using

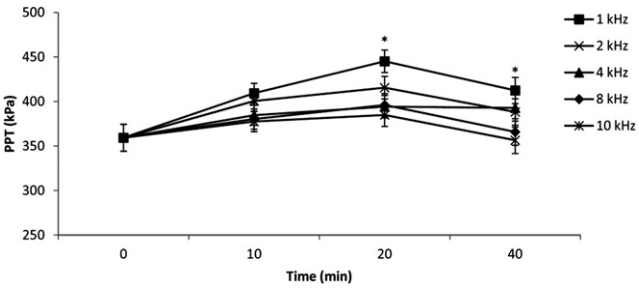

Fig 4 PPT data for forearm measurements, for each experimental group (baseline-adjusted mean ± SEM). *Indicates significant difference ($P<.05$) from 8-kHz and 10-kHz groups.

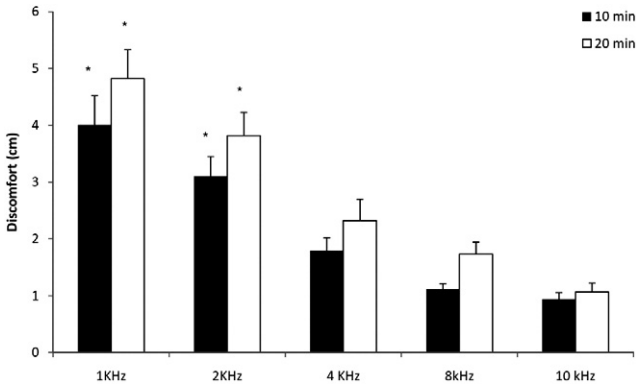

Fig 5 Mean ± SEM values of sensory discomfort measured by visual analog scale at the 10th and 20th minutes during IFC for each group (n = 30 per group). *Represents a statistically significant difference when compared with the 4-kHz, 8-kHz, and 10-kHz groups ($P<.05$).

frequencies between 100Hz and 10kHz, and they concluded that at higher AC frequencies (4kHz or more), the rate of decrease in activity was higher, with the firing frequency dropping to 0 in less than a second using stimulus intensities of 5 times the threshold.[10] Other studies have also demonstrated a neural conduction block using high-frequency ACs.[46,48] Accordingly, the use of frequencies of 8kHz and 10kHz could have impaired the neurophysiologic response of large-diameter (Aβ) afferent fibers, preventing them from activating the neural inhibitory circuits located in the posterior horn of the spinal cord (gate control theory of pain), decreasing the hypoalgesic response of IFC. Only 1 study compared 2 carrier frequencies of IFC (2kHz and 4kHz) and concluded that there was no difference in the hypoalgesic response in individuals with low back chronic pain.[49] Nevertheless, this is an unpowered study because only 7 patients were included in each group, which makes the identification of significant differences between groups difficult.

In the present study, we increased the current amplitude at 5-minute intervals over the treatment time in order to avoid

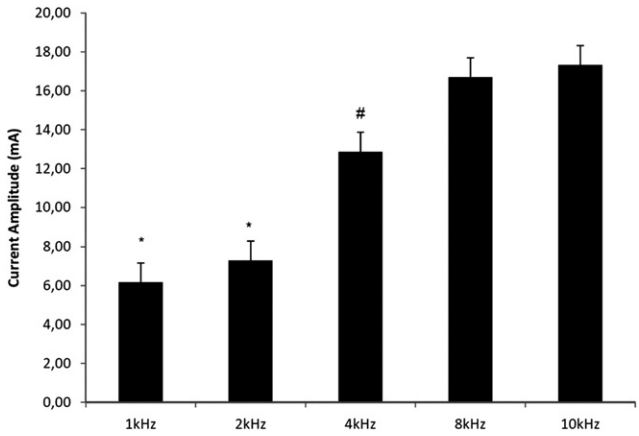

Fig 6 Mean ± SEM values of the amplitude of current required to achieve the sensory threshold for each group (n = 30 per group). *Represents a statistically significant difference when compared with the 4-kHz, 8-kHz, and 10-kHz groups. #Represents a statistically significant difference when compared with the 8-kHz and 10-kHz groups.

Table 3 Mean ± SEM current amplitude applied in all experimental groups over time

Group	Sensory Threshold	0min	5min	10min	15min	20min
1kHz	6.17±0.34	13.07±0.90	16.07±1.03	18.43±1.14	20.43±1.25	22.40±1.41
2kHz	7.30±0.42	15.33±1.10	18.97±1.27	21.87±1.42	24.77±1.61	27.10±1.78
4kHz	12.87±0.64	22.73±1.32	27.70±1.59	31.43±1.78	34.90±1.84	37.73±1.97
8kHz	16.70±1.06	29.53±2.99	36.30±3.14	42.90±3.54	48.00±3.74	51.97±3.85
10kHz	17.33±1.14	30.62±2.33	38.07±2.38	44.21±2.54	49.24±2.58	53.62±2.85

NOTE. All values are expressed in milliampere.

habituation, based on a previous study that showed the importance of this practice to obtain maximal hypoalgesia.[11] It is important to note that the increase necessary to maintain a strong but comfortable parasthesia over the 20 minutes of IFC application was greater at higher than lower frequencies as shown in figure 7. This finding reinforces the hypothesis of synapse fatigue, propagation failure, and/or nerve block with the use of IFC with higher frequencies.

Some previous studies designed to assess the effects of IFC with a carrier frequency of 4kHz have failed to show an increase on PPTs[13,50,51] in contrast with studies using low-frequency pulsed currents.[11,36,37,52-56] Nevertheless, Ward and Oliver[29] showed that an MFAC with a carrier frequency of 1kHz and a 4-millisecond burst duration was equally effective as a low-frequency pulsed current to increase cold pain threshold in healthy humans. Therefore, it is possible that IFC parameters commonly used in scientific studies and/or in physical therapy practice currently are suboptimal.

During the present study, each individual used a visual analog scale for the assessment of sensory discomfort related to the current. The carrier frequencies of 4kHz, 8kHz, and 10kHz presented a higher sensory comfort when compared with 1kHz and 2kHz. This result can be related to strength-duration curves.[57,58] A carrier frequency of 1kHz presents a phase duration of 500 microseconds, whereas a carrier frequency of 10kHz presents a phase duration of 50 microseconds. Thus, according to the strength-duration curves, longer phase durations would be more uncomfortable because there is less separation between sensory, motor, and pain responses; thus, they can reach the pain threshold with smaller current amplitudes.

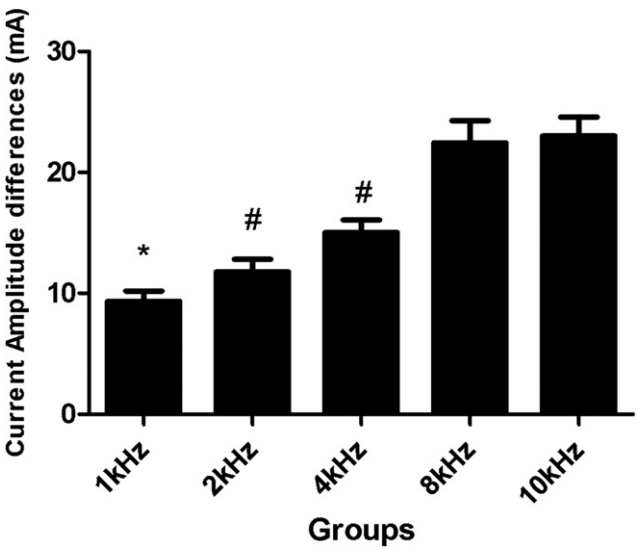

Fig 7 Mean ± SEM values of the differences of the amplitude of current (amplitude applied at 20min − amplitude necessary to promote a strong but comfortable paresthesia, applied at the beginning of treatment) for each group (n=30 per group). *Represents a statistically significant difference when compared with the 4-kHz, 8-kHz, and 10-kHz groups. #Represents a statistically significant difference when compared with the 8-kHz and 10-kHz groups.

Previous studies of electrical stimulation for pain control have shown that a strong intensity is required to promote higher hypoalgesia.[11,37,59-61] Olsen et al[61] compared the effects of low- and high-intensity transcutaneous electrical nerve stimulation for painful postpartum uterine contractions and verified that even though women receiving high-intensity transcutaneous electrical nerve stimulation experienced a greater discomfort during stimulation, they presented less pain than women in the low-intensity group. Thus, the greater discomfort observed when using lower frequencies (1 and 2kHz) in the present study may be related to a higher hypoalgesia.

With regard to the current amplitude we observed that to reach the sensory threshold in the groups using higher frequencies (8 and 10kHz) it was necessary to use higher amplitudes. This result can be explained by the fact that there is a decrease in phase duration as the frequency of the electrical current is increased. Again, as observed in strength-duration curves, a smaller phase duration needs a higher current amplitude to reach the excitatory response.[23,57,58] On the other hand, as the current frequency is increased, the electrical impedance of the skin decreases and facilitates the electrical stimulus reaching the nerve fiber. Thus, the threshold of activation of nerve fibers depends on the balance of the impedance of the skin and the sensitivity of nerve fibers.[23,62]

An interesting finding observed in the present study is that the hypoalgesic effects of IFC appear to be maximized after 20 minutes of treatment and are still significant 20 minutes post-treatment. This suggests that applying IFC for 10 minutes is less than optimal for pain control.

Study limitations

The present study has certain limitations that need to be taken into account. Some of the limitations include the generalizability of the results. Participants were pain-free; thus, future clinical studies should be performed to confirm these results in patients experiencing pain. In addition, we did not perform electrophysiologic tests to observe how nerve fibers would respond to each carrier frequency.

Conclusions

In summary, it can be concluded that IFC with a carrier frequency of 1kHz promotes a higher hypoalgesic response in an

experimental pain model during and after stimulation than IFC with a carrier frequency of 8kHz and 10kHz. Carrier frequencies of 1kHz and 2kHz are more uncomfortable than carrier frequencies of 4kHz, 8kHz, and 10kHz.

Suppliers

a. Neurovector; Industria Brasileira de Equipamentos Médicos Ltda., Av. Dr Carlos Burgos, 2800, Jd. Itália, Amparo, São Paulo, Brazil.
b. ValuTrode Electrodes; Axelgaard Manufacturing Co, Ltd, 520 Industrial Way, Fallbrook, CA 92028.
c. Algometer; Kratos Equipamentos, Rua Etiópia, 294, Bairro Rio Cotia, Cotia, São Paulo, Brazil.
d. SPSS, Inc, 233 S Wacker Dr, 11th Fl, Chicago, IL 60606.

Keywords

Electric stimulation therapy; Pain threshold; Physical therapy modalities; Rehabilitation

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BMC Musculoskeletal Disorders

RESEARCH ARTICLE Open Access

Effects of kinesiotherapy, ultrasound and electrotherapy in management of bilateral knee osteoarthritis: prospective clinical trial

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Abstract

Background: Although recent advances in knee osteoarthritis (OA) treatment and evaluation were achieved, to the best of our knowledge, few studies have evaluated the longitudinal effect of therapeutic modalities on the functional exercise capacity of patients with knee OA. The purpose was to investigate the effects of kinesiotherapy and electrotherapy on functional exercise capacity, evaluated using the six-minute walk test (6-MWT) in patients with bilateral knee OA. Secondary measurements included range of motion (ROM), severity of knee pain (VAS), and a measure of perceived health and physical function, evaluated using the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index.

Methods: A total of 40 women with bilateral knee OA were assigned to three groups: kinesiotherapy (KIN, $n = 16$), transcutaneous electrical nerve stimulation (TENS, $n = 12$), or ultrasound (US, $n = 10$). The groups underwent 12 weeks of intervention twice per week. The participants were subjected to the 6-MWT, ROM, VAS and WOMAC index. These tests were performed before and after the intervention. The study was focused on outpatients and was carried out at Universidade Estadual de Campinas, Brazil.

Results: At follow-up, the KIN and US groups had significantly higher 6-MWT distances (19.8 ± 21.7 and 14.1 ± 22.5%, respectively) compared with their respective pre-intervention values. All treatments were effective for reducing pain and improving the WOMAC index.

Conclusions: We demonstrated that the 6-MWT is a tool that can be used to evaluate improvements in the functional exercise capacity of patients submitted to a clinical intervention.

Keywords: Kinesiotherapy, Ultrasound, Electrotherapy, Knee osteoarthritis

Background

Osteoarthritis (OA) is a chronic and degenerative joint disease and is considered one of the most common musculoskeletal disorders [1,2]. Approximately 85% of the population near 65 years of age present radiographic evidences of OA [3]. The knees, hands, hips, spine, and feet include the joints most often affected by OA [4-6]. The main clinical symptoms related by patients with knee OA include pain, articular stiffness, crepitation, articular edema, joint deformities, articular instability, decrease in range of motion (ROM), physical activity limitations and muscle weakness [6,7]. For these reasons, several pharmacologic [8,9] and non-pharmacologic strategies [10-13] have been studied for relief of knee pain.

Physiotherapy is one of the professions that provide effective non-pharmacological interventions for people with knee OA [14] and procedures prescribed by physiotherapists are considered important and play a fundamental role in patient treatment. In this context, kinesiotherapy (KIN), which comprises different types of therapeutic exercises, such as stretching, strengthening (isotonic, isokinetic, and isometric) and aerobic exercise, [15] and electrotherapy are frequently used for the

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treatment of different musculoskeletal disorders [16-18]. The most common types of electrotherapy are ultrasound (US), a modality of treatment that uses sound waves to generate heat within a body part, and transcutaneous electrical nerve stimulation (TENS), a method of pain relief in which a special device transmits low-voltage electrical impulses through electrodes on the skin to an area of the body that is in pain [4].

Despite recent advances in OA treatment, few studies have evaluated the longitudinal effect of therapeutic modalities on the functional capacity of patients with knee OA, especially that functional capacity related to exercise performance. Lin et al. [19] described the results of a battery of physical function tests used to assess the physical function of older patients with clinical knee and/or hip OA. These tests included: walk a distance of 8 feet, ascend/descend 4 stairs, and stand and sit on a chair 5 times. The authors stated that these physical function tests are safe, practical, and may be useful in the evaluation of therapeutic interventions. French et al. [20] compared the responsiveness of three physical performance measures of function following physiotherapy for OA of the knee and found that the 6-min walk test (6-MWT) was more responsive in the assessment of physical performance than the timed-up-and-go test and the timed-stand test. In this context, the 6-MWT is a simple, safe and low-cost field test often used to evaluate chronic heart failure patients, chronic obstructive pulmonary disease patients, and the elderly to regularly assess functional exercise capacity and the effects of a rehabilitation/exercise program [21,22].

Therefore, the primary purpose of this study was to investigate the effects of 12 weeks of kinesiotherapy and electrotherapy on functional exercise capacity as evaluated by the 6-MWT. Secondary measurements included range of motion, severity of knee pain, and the measure of perceived health and physical function evaluated by the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index [23,24].

Methods

Participants

Patients with knee OA were recruited from a Rheumatology Clinic. These patients were initially contacted, evaluated, and informed about the objective and experimental procedures of the study. Of the 48 patients initially recruited, 40 patients completed all experimental procedures. Exclusion criteria included any rheumatic disease (with the exception of bilateral knee OA), unilateral knee OA, neurological disorders, cognitive limitations or history of cardiovascular, pulmonary or endocrinology disease. Inclusion criteria included female gender, a minimum of 45 years old, free from any other lower limb disease (except bilateral knee OA), able to perform physical exercise, not currently receiving physical therapy treatments for the knee OA condition, medication compliance (all patients were taking glucocorticoids at the time of study), and diagnosis of bilateral knee OA according to the American College of Rheumatology criteria [25]. The participants were randomly divided into three groups: kinesiotherapy (KIN, n = 16), transcutaneous electric nerve stimulation (TENS, n = 12), and ultrasound (US, n = 12). These physiotherapy interventions were performed twice per week for 12 weeks. The patient characteristics are presented in Table 1.

Experimental design

The study was organized in four successive phases: a basal medical and physical examination, the pre-intervention evaluations, the treatment period, and the post-intervention evaluations. The basal medical examination was performed three days before the beginning of the treatment period. The participants underwent a detailed medical examination (performed by a rheumatologist) and OA diagnostic evaluation (based on symptoms and conventional standing antero-posterior knee radiographs). In the two days before and after the treatment intervention, all of the participants performed

Table 1 Characteristics of the subjects

	Experimental groups		
	KIN (n = 16)	TENS (n = 12)	US (n = 12)
Age (yr)	59.6 ± 7.2	64.8 ± 7.0	62.8 ± 7.6
	(48 – 70)	(50 – 74)	(51 – 77)
Height (cm)	154.6 ± 6.1	153.4 ± 6.8	153.8 ± 6.0
	(146.0 – 166.0)	(143.0 – 165.0)	(141.0 – 163.0)
Body mass (kg)	71.1 ± 10.8	73.9 ± 13.7	71.3 ± 10.0
	(48.0 – 92.0)	(58.0 – 112.0)	(50.9 – 85.0)
Years diagnosed with osteoarthritis	5.6 ± 5.6	5.2 ± 6.8	4.8 ± 3.4
	(0.08 – 15)	(1 – 25)	(1 – 10)

Data expressed as mean ± S.D. (min – max).

follow-up evaluations in this order: perceived health and physical function by Western Ontario and MacMaster Universities Osteoarthritis Index (WOMAC) Questionnaire, pain by using a visual analogical scale (VAS), ROM by using a goniometer, and functional exercise capacity evaluated by the 6-MWT. Finally, the participants were submitted to 12 weeks of treatment intervention, twice per week, on non-consecutive days.

The participants were instructed to arrive at the laboratory in a rested and fully hydrated state, having not consumed caffeine in the previous 4 h, and to avoid strenuous exercise in the 48 h preceding a session. To minimize the effects of diurnal biological variation, all the tests were performed at the same time of day.

All experimental procedures were approved by the University Human Research Ethics Committee and conformed to the principles outlined in the Declaration of Helsinki. All participants signed informed consent forms prior to participating in the study.

Modes of physiotherapy treatment

The participants in each group participated in their respective treatment intervention for 12 weeks (24 sessions). All sessions were supervised by an experienced physical therapist. Missed sessions were compensated during the subsequent weeks so that the total number of sessions was completed.

The KIN protocol consisted of supervised stretching and isometric exercises for the entire lower limb. The stretching exercises were performed actively, using the static method. The participants were instructed to perform three bouts of 30 seconds each in each lower limb to the following muscles and in this order: calf, quadriceps, and hamstring muscles. The stretches were alternated for each limb. The static stretching exercises were performed until the maximal range of motion or pain threshold was reached. The isometric exercises consisted of three exercises using a conventional plastic ball (diameter of 20 cm) and one exercise using an elastic band (Rubber Band, Orange Color, Carci, Brazil) with extra strong resistance measuring 1.50 x 0.14 m. The participants were instructed to perform a total of 30 repetitions. Each repetition lasted 6 seconds with an interval of approximately 3 seconds. In the first exercise using the ball, the patients were placed in a supine position with knees flexed. The ball was positioned between the patient's knees, and the patient was instructed to press the knees against the ball to perform a maximal contraction. This exercise aimed to strengthen the adductor muscles. In the second exercise using the ball, the patients were placed in a supine position with one knee flexed and the other knee in full extension. With the ball placed under the ankle of the limb that was extended, the participants performed a maximal contraction against the ball. The patient alternated performing the exercise for each lower limb, and this exercise aimed to strengthen the quadriceps muscles. In the third exercise using the ball, the patient was positioned prone with both knees extended. The ball was placed under one ankle, and the patient was instructed to perform a maximal contraction against the ball. The patient alternated performing the exercise for each lower limb, and this exercise aimed to strengthen the hamstring muscles. Finally, in the fourth exercise, the patients were placed in a supine position with knees flexed. The knees were tied with an elastic band, and the patients were requested to perform a maximal abduction movement of the lower limbs. This exercise aimed to strengthen the abductor muscles. Each session lasted approximately 20 minutes.

The TENS was delivered by a transcutaneous electrical stimulator (Neurodyn II, Ibramed, Brazil) with two channels and four square, self-adhesive percutaneous electrodes measuring 5 x 5 cm. The TENS was applied using a frequency of 100 Hz, pulse width of 50 μs, 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. In the TENS protocol, 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. This group also performed the same stretching and isometric exercises for the lower limbs described for the KIN group. Each session lasted approximately 40 minutes.

The US protocol consisted of continuous ultrasonic waves of 1 MHz frequency and 0.8 W/cm [2] power, applied with a 5-cm diameter applicator (Sonic, 1–3 MHz, HTM, Brazil). The patients 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 edema. During the evaluation, we observed that some subjects exhibited evidence of edema. This group also performed the same stretching and isometric exercises for the lower limbs described for the KIN group. Each session lasted approximately 25 minutes.

Assessments

The participants were assessed at baseline and at the end of the treatment by an investigator who was blind to the randomization. The following assessments were performed: severity of pain, ROM for extension and flexion

of the knee, the 6-MWT, and the perceived health and physical function.

Severity of knee pain

Knee pain was assessed using a VAS. The VAS consists of a 10-cm line, with the left extreme indicating "no pain" or zero and the right extreme indicating "unbearable pain" or 10. The participants were asked to use the scale to indicate their current level of pain. Higher values suggest more intense pain. The values (in centimeters) were recorded for the statistical analysis.

Range of motion (ROM)

Knee flexion and extension ROM in degrees were measured bilaterally in a supine position according to Norkin and White [26]. To this end, the lateral femoral condyle was used as a landmark for the measurement of knee flexion and extension. The central pivot of a universal goniometer (CARCI, São Paulo, Brazil) was placed over the midpoint of the lateral joint margin, with the stationary arm of the universal goniometer aligned with the great trochanter. The moving arm of the goniometer was then aligned with the lateral malleolus with the neutral position taken as zero. For the knee flexion measurement, initially the hip was at zero degrees of extension, abduction, and adduction, but as the patients maximally flexed the knee, the hip also flexed. Thus, the examiner supported the lower limb and stabilized the femur to prevent rotation, abduction, and adduction of the hip. For the knee extension, the measurement was made with the lower limb extended. The previous precautions to prevent compensations (i.e., adduction, abduction, and rotation) were taken. The measurements were performed by two experienced physical therapists. Each knee and position (flexion or extension) was measured twice, and the higher angle was recorded for the statistical analysis.

The six-minute walking test (6-MWT)

The 6-MWT was performed to evaluate functional exercise capacity in a 100 m-long indoor hallway free of obstacles. The length of the corridor was marked every 1 m. The participants were instructed to walk at a self-selected regular pace to cover as much distance as they could during the allotted time. If necessary, slowing down and stopping to rest were allowed. At the end of each minute, the participants were given feedback on the elapsed time and standardized encouragement in the form of statements such as "you are doing well, keep it up" and "do your best." These technical aspects are in line with the American Thoracic Society recommendations for the 6-MWT [27]. The distance covered (in meters) was used for the statistical analysis. The test-retest reliability of the 6-MWT has been ascertained in patients with knee OA [28]. During the test, all the participants walked independently without using walking aids.

WOMAC Osteoarthritis Index

A disease-specific index of disability, the WOMAC Osteoarthritis Index, was used as a subjective measure of perceived health and physical function. The WOMAC Osteoarthritis Index is a three-part questionnaire that can be completed by the subject in approximately 10 minutes, consists of 24 questions and probes clinically important symptoms in the areas of pain (5 questions), stiffness (2 questions), and physical function (17 questions) for patients with OA of the hip and/or knee [23,24]. In the present study, we used a Likert scale version of the WOMAC that allows patients to make their responses on a five-point scale (0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = extreme). The higher the score achieved, the lower the level of perceived health and physical function. Scores were generated for the three dimensions of pain, stiffness and physical function by summing the coded responses. The patient should answer the questions to best describe their symptoms and difficulties from the past 72 hours [29]. Psychometric studies have shown moderate to high validity and reliability for the WOMAC questionnaire [30].

Statistical analysis

STATISTICA v 7.0 for Windows was used for the statistical analyses. All the variables presented normal distributions according to Kolmogorov-Smirnov tests. Two-way repeated-measure analyses of variance (ANOVA) were used to assess group (KIN *vs.* TENS *vs.* US) and time (before vs. after) differences in the variables measured. When significant group-by-time interactions were present, Tukey's post hoc procedures were used to identify the specific differences.

To describe the differences in related treatments, the effect sizes were calculated as the difference between the means divided by the pooled standard deviation. On the basis of Cohen's criteria (29), an effect size of ≥0.20 and <0.50 was considered small, ≥0.50 and <0.80 medium, and ≥0.80 large.

All the data are presented as the mean ± standard deviation (SD) (min – max). The results were determined to be statistically significant at $p < 0.05$.

Results

All the participants completed 24 treatment sessions. Table 2 presents the data with respect to the evaluation of right and left knee joint pain by VAS (cm) of the KIN, TENS and US groups. No significant differences were observed between the groups before the treatment period for the right and left knee (mean for all groups:

Table 2 Visual analog score (in centimeter) for both knees in each group before and after treatment

	Right Knee				Left Knee			
	Before	After	*P*	Effect size	Before	After	*P*	Effect size
KIN (n = 16)	6.9 ± 1.9 (5.0 – 10.0)	2.3 ± 2.7[a] (0.0 – 8.0)	0.0001	0.70	7.0 ± 2.1 (4.0 – 10.0)	2.4 ± 2.8[a] (0.0 – 7.0)	0.0008	0.68
TENS (n = 12)	8.0 ± 1.5 (6.0 – 10.0)	2.6 ± 2.9[a] (0.0 – 7.5)	0.0001	0.76	5.6 ± 2.7 (0.0 – 10.0)	2.3 ± 2.5[a] (0.0 – 9.0)	0.004	0.53
US (n = 12)	6.6 ± 3.0 (0.0 – 10.0)	4.5 ± 3.7[a] (0.0 – 10.0)	0.009	0.41	7.3 ± 2.3 (4.0 – 10.0)	3.8 ± 3.1 (0.0 – 7.0)	0.054	0.54

Data expressed as mean ± S.D. (min – max).
[a] different from before for the same group.

7.4 ± 1.9 cm) thus, there is no superiority in comparison between the different types of treatment. However, in the intra-group comparisons (before *vs.* after) a significant decrease was observed in the VAS for pain in all experimental groups and for both knees except for the left knee in the US group. No significant differences were observed between the groups for the right and left knee after the treatment period.

The data obtained from the evaluation of knee ROM are presented in Table 3. No significant differences were observed between the groups before the treatment period for the right and left knee in flexion and extension thus, there is no superiority in comparison between the different types of treatment. The protocols adopted by the present study did not cause improvements in flexion for either knee. For extension, increases in ROM were found in the KIN and TENS groups for both knees.

The WOMAC total scores and the score for each dimension were similar in all three groups at baseline except for the KIN group when compared with the US group (Table 4). Compared with the baseline, significant improvements were observed in each group at the end of the treatment. The improvement in the patients treated with US was significantly less pronounced than that in the patients from the KIN and TENS groups ($p < 0.05$).

The 6-MWT was completed by all the subjects without premature cessation and/or breaks. No symptoms or clinical complications occurred during the tests. The 6-MWT performances of the participants are shown in Table 5. No statistically significant differences between the groups were found at baseline. The distances completed and the walking speeds were significantly higher in the KIN (19.8%) and US (14.1%) groups when compared to the pre-treatment values. No statistically significant difference was found in the TENS group (8.9%). No statistically significant differences between the groups were found after the treatment period.

Discussion

Knee OA is expected to be the fourth highest cause of disability in women and is responsible for the deterioration of quality of life and functional capacity [31]. A plethora of studies have investigated several aspects related to muscle function, such as strength [32] and aerobic capacity [33] as well as other clinical aspects such as pain [34], stiffness [35], ROM [36] and WOMAC index [37] in patients with OA. Despite these important advances, to our knowledge, few studies have investigated the effects of different types of non-pharmacological treatments on the functional exercise capacity of patients with OA. In this context, the 6-MWT is an excellent tool to evaluate the effect of therapy on the functional exercise capacity. In this study, we found that the KIN and US procedures improved the functional exercise capacity of patients with bilateral knee OA after the intervention period; however, we found no inter-group differences. Moreover, we also evaluated the effect of the treatment period on pain using the VAS and WOMAC index, and we found that the three interventions improved the pain. The

Table 3 Range of motion (in degrees) for both knees in each group before and after treatment

	Flexion						Extension					
	Right			Left			Right			Left		
	Before	After	*P*	Before	After	*P*	Before	After	*P*	Before	After	*P*
KIN	76 ± 9	73 ± 12	>0.77	74 ± 11	69 ± 12	>0.98	171 ± 6	177 ± 4[a]	0.0003	172 ± 5	178 ± 3[a]	0.001
(n = 16)	(56 – 90)	(55 – 90)		(50 – 90)	(55 – 87)		(160 – 180)	(168 – 180)		(161–180)	(170 – 180)	
TENS	79 ± 7	76 ± 10	>0.34	81 ± 12	79 ± 7	>0.44	172 ± 6	178 ± 3[a]	0.003	170 ± 8	176 ± 4[a]	0.002
(n = 12)	(68 – 90)	(59 – 90)		(50 – 90)	(65 – 89)		(160 – 180)	(170 – 180)		(150 – 180)	(168 – 180)	
US	81 ± 8	76 ± 7	>0.83	80 ± 8	75 ± 8	>0.39	171 ± 6	175 ± 7	0.21	172 ± 7	173 ± 7	0.47
(n = 12)	(67 – 90)	(66 – 87)		(67 – 90)	(56 – 86)		(165 – 180)	(156 – 180)		(160 – 180)	(160 – 180)	

Data are expressed as mean ± S.D (min – max).
[a] different from before for the same group.

Table 4 Scores for the WOMAC Index in each group before and after treatment

	Pain			Rigidity			Physical function			Total score			
	Before	After	P	Before	After	P	Before	After	P	Before	After	P	Effect size
KIN (n = 16)	8.9 ± 4.4 (1 – 18)	2.0 ± 2.3[a] (0 – 8)	0.0001	3.0 ± 2.1 (0 – 6)	0.4 ± 0.8[a] (0 – 2)	0.0001	25.6 ± 13.6[b] (6 – 48)	4.6 ± 5.9[ab] (0 – 21)	0.0001	37.5 ± 18.7[b] (7 – 69)	7.0 ± 8.1[ab] (0 – 28)	0.0001	0.73
TENS (n = 12)	10.7 ± 3.0 (4 – 15)	3.3 ± 2.9[a] (0 – 9)	0.0001	4.3 ± 1.9 (2 – 8)	0.8 ± 0.8[a] (0 – 2)	0.0001	31.8 ± 9.2 (16 – 50)	10.1 ± 8.3[ab] (0 – 25)	0.0001	46.8 ± 12.2 (22 – 69)	14.2 ± 11.0[ab] (0 – 35)	0.0001	0.81
US (n = 12)	10.1 ± 3.8 (4 – 16)	6.2 ± 4.2[a] (2 – 17)	0.01	4.4 ± 2.5 (0 – 8)	2.0 ± 1.9[a] (0 – 6)	0.004	38.3 ± 9.1 (22 – 51)	20.6 ± 9.8[a] (5 – 43)	0.0001	53.5 ± 12.2 (36 – 70)	28.8 ± 14.8[a] (8 – 66)	0.0002	0.67

Data are expressed as mean ± S.D. (min – max).
[a] different from before for the same group.
[b] different from US group at same time point.

difference in this study is that our sample is homogeneous because we recruited only women with bilateral knee OA.

Pain is one of the most common complaints and disabling symptoms in OA populations. In the present study, we evaluated the efficacy of different treatment modes on knee pain, measured using the VAS and the pain dimension of the WOMAC index. We found that pain in both knees decreased in all the experimental groups. This is not the first study to demonstrate the positive effects of non-pharmacologic management on knee pain in OA patients. The Cochrane group [38] systematically reviewed and combined the study results of 17 OA exercise studies (a total of 2562 participants). This group found that land-based exercise had a small-to-moderate beneficial effect on pain for people with symptomatic knee OA. Roddy et al. [39] reviewed 19 randomized clinical trials investigating the effects of land-based exercise for knee or hip OA. They concluded that both strengthening and aerobic exercises performed on land could reduce pain and improve the function and health status in patients with knee and hip OA. However, these authors stated that there was not enough evidence to support or recommend specific types of exercise.

Concerning the TENS, Rutjes et al. [5] conducted a systematic Cochrane review of transcutaneous electrostimulation vs. sham or no specific intervention on pain in individuals with knee OA. This systematic review found little evidence of a significant effect for electrostimulation compared to sham or no intervention on pain in knee OA. The authors attributed these results to the poor quality of the trials and the high degree of heterogeneity across the studies. Our results contradict this systematic review because we found an improvement in the pain index (VAS and pain dimension of the WOMAC index) in all the experimental groups. To evaluate the therapeutic effect of the TENS modalities, NG et al. [40] studied 24 patients and compared electroacupuncture treatment and TENS, using the same parameters for both (low frequency - 2 Hz, continuous mode, pulsation of 200 μs for 20 min of application, and a control group with only educational orientations on OA of the knee) and showed that either electroacupuncture treatment or TENS are effective in pain reduction because a prolonged analgesic effect was maintained in the two groups. Another study was performed with 62 patients between 50 and 75 years of age and presenting knee OA during a four-week period. These patients were divided into four treatment groups: TENS placebo group, TENS group, exercise group and TENS plus exercise group. The results showed no significance between the different types of treatment due to the protocol duration [41]. This treatment was similar to ours in the number of patients and the modalities used, such as the conventional TENS and the isometric exercises. However, the TENS parameters and the application time were different and, unlike our study, did not present

Table 5 Distance covered and percent change obtained in the six-minute walk test before and after treatment

	Before	After	Δ%	P	Effect size
KIN (n = 16)	333 ± 80	387 ± 59[a]	19.8 ± 21.7	0.003	–0.35
	(212 – 500)	(308 – 500)	(–6.1 – 74.5)		
TENS (n = 12)	330 ± 61	355 ± 65	8.9 ± 17.1	0.61	N/A
	(200 – 420)	(275 – 500)	(–22.9 – 37.5)		
US (n = 12)	318 ± 68	358 ± 77[a]	14.1 ± 22.5	0.04	–0.26
	(200 – 400)	(200 – 450)	(–6.3 – 80.0)		

Data are expressed as mean ± S.D. (min – max).
[a] different from before for the same group. N/A: not applicable.

significance in the protocols due to the short treatment duration. In our study, the three groups (KIN, TENS and US) showed significant differences after the treatment duration.

In regards to the US, Loyola-Sanchez et al. [42] conducted a meta-analysis of the efficacy of US for decreasing pain and improving physical function in people with knee OA. New evidence was found that shows that US can reduce pain by 21% compared to a control group.

Range of motion was another variable evaluated in the present study. We did not observe any difference due to the three modes of treatment used in this study. Our results agree with Tascioglu et al. [43] who compared the effectiveness of ultrasound (continuous versus pulsed) therapy versus placebo ultrasound in patients with knee OA and also found no differences in ROM. These authors also found improvements in the WOMAC index and functional capacity as evaluated by a 20-m walking test.

Finally, we were particular interested in evaluating the effect of KIN, US and TENS treatment on the 6-MWT performance of woman with bilateral knee OA. Several modalities are available for the objective evaluation of cardiorespiratory fitness. Some provide a very complete assessment of all the systems involved in exercise performance, whereas others provide basic information but are low-tech and easy to perform. The 6-MWT is a simple test that requires a hallway but no equipment or advanced training for the technicians. This test evaluates the global and integrated responses of all the systems involved during exercise, including the pulmonary, cardiovascular and muscular systems [22]. To help predict the total distance walked during the 6-MWT, Enright and Sherrill [44] established a reference equation that incorporates subject characteristics such as age, body mass and height. These subject characteristics were shown to be associated with the distance walked during the 6-MWT. When applying this reference equation to the current data, the results revealed that the KIN, US and TENS groups walked 74%, 79% and 85%, respectively, of the predicted values found by the Enright and Sherrill [44] equation in the pre-evaluation. These modest values demonstrate the low functional exercise capacity, and consequently low health status, of the patients evaluated in the present study. On average, our patients walked 328.8 m before the treatment. These values agree with Wang et al. [45] who compared the efficacy of aquatic exercises and land-based exercises for patients with knee OA. However, these values are lower than those reported by French et al. [20] (405.1 m). The difference most likely results from the poorer physical condition of our volunteers, as represented in the lower highest total score obtained for the WOMAC index compared with that in the study by French et al. [20] Additionally, the sample studied by French et al. [20] contained male participants with unilateral and bilateral knee OA. The difference in this study is that our sample is homogeneous because we recruited only women with bilateral knee OA.

The impact of health status on 6-MWT performance was investigated in 165 elderly people. The covered distance decreased significantly with increasing age and with worsening health status (corrected for age) [46]. Patients with dilated cardiomyopathy were also investigated, and the results demonstrated that the covered distance and peak oxygen uptake (cardiorespiratory fitness index) were closely correlated [47]. In addition, the authors found a correlation between the 6-MWT covered distance and the New York Heart Association functional class. Santana et al. [21] showed that in the healthy elderly, the 6-MWT can be used to evaluate improvements in functional exercise capacity after exercise training. However, the 6-MWT is not appropriate to evaluate improvements in the cardiorespiratory fitness of elderly healthy men who have undergone exercise training because this test lacks sufficient sensitivity. Particularly in OA, French et al. [20] studied the responsiveness of three physical performance measures of function following physiotherapy for knee OA and found that the 6-MWT was more responsive for the assessment of physical performance than the timed-up-and-go test and the timed-stand test.

Following 12 weeks of treatment procedures performed by the KIN and US groups, the distance covered in the 6-MWT increased by 19.8% and 14.1%, respectively. These improvements in functional exercise capacity indicate improvements in muscle strength and aerobic metabolism assuming that patients with knee OA are often physically deconditioned, interventions, as performed by current study, potentiate those muscle adaptations. Wang et al. [45] investigated the effects of aquatic exercises and land-based exercises for patients with knee OA and found that the 6-MWT performance increased by $19 \pm 7\%$ and $12 \pm 5\%$, respectively. These changes were similar to the results found in previous studies [45,48]. Although these articles have studied different treatment modes, the results presented here suggest an improvement in functional exercise capacity and, consequently, of the quality of life and ability to perform activities of daily living. In fact, this assertion is supported by the positive results on the WOMAC and VAS scores. This improvement in ability to perform physical effort is very important because physical exercise is considered a valuable tool to reduce the risk of cardiovascular and endocrine diseases and to improve bone and muscle conditioning. These medical conditions may affect patients with OA due to the high level of inactivity and body disuse found in these patients. Indeed, this

high level of inactivity can be demonstrated by the reduced aerobic capacity in patients with severe hip and knee OA compared to controls [49,50].

Study limitations

We assessed study outcomes only on pre- and post-tests, so we were not able to determine the outcomes of these interventions across time. The evaluation of parameters related to exercise physiology, such as the maximal oxygen uptake, economy of motion and anaerobic threshold, could provide additional information on the level of aerobic fitness of the subjects before and after the treatment period.

Conclusions

Many previous studies have compared one treatment protocol group with one control group and have concluded that the treatment made a difference, but there is no indication of how one program compares with other treatment protocols. Our study compared three popular non-pharmacological treatments. The main finding of this study was that the 6-MWT is a tool that can be used to evaluate improvements in the functional exercise capacity of patients submitted to a clinical intervention. Furthermore, the study results showed that KIN, TENS and US are effective for reducing pain and improving the WOMAC score and that KIN and US are effective for increasing the 6-MWT performance. Together, these results can be informative for both clinicians and patients with OA in selecting appropriate types of treatment based on their preferences and convenience.

The results of this study provide further evidence that patients with knee OA can achieve significant benefits from using KIN, TENS or US therapeutic procedures. The knowledge of function and disability for patients with knee OA, obtained through use of the 6-MWT, may help clinicians and physical therapists evaluate and develop rehabilitation programs to improve functional efficiency and capability for this population.

Endnotes

The authors Claudio Andre Barbosa de Lira and Ibsen Bellini Coimbra contributed equally to this work and may be cited in interchangeable order.

Abbreviations

6-MWT: 6-min walk test; KIN: Kinesiotherapy; OA: Osteoarthritis; ROM: Range of motion; TENS: Transcutaneous electrical nerve stimulation; US: Ultrasound; VAS: Visual analogical scale; WOMAC: Western Ontario and McMaster Universities.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

NCM: study concept and design; data acquisition, analysis, and interpretation; manuscript preparation and critical revision of the manuscript. RLV and MdSA: data analysis, interpretation, manuscript preparation, and critical revision of the manuscript. EdPM: data acquisition and critical revision of the manuscript. CABdL: study and conception, manuscript preparation, and critical revision of the manuscript. IBC: study and conception, manuscript preparation, and critical revision of the manuscript. All authors read and approved the final manuscript.

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Abstract *available in* English | Français

Background

Neck pain is common, disabling and costly. The effectiveness of electrotherapy as a physiotherapeutic option remains unclear. This is an update of a Cochrane review first published in 2005 and previously updated in 2009.

Objectives

This systematic review assessed the short, intermediate and long-term effects of electrotherapy on pain, function, disability, patient satisfaction, global perceived effect, and quality of life in adults with neck pain with and without radiculopathy or cervicogenic headache.

Search methods

We searched CENTRAL, MEDLINE, EMBASE, MANTIS, CINAHL, and ICL, without language restrictions, from their beginning to August 2012; handsearched relevant conference proceedings; and consulted content experts.

Selection criteria

Randomized controlled trials (RCTs), in any language, investigating the effects of electrotherapy used primarily as unimodal treatment for neck pain. Quasi-RCTs and controlled clinical trials were excluded.

Data collection and analysis

We used standard methodological procedures expected by The Cochrane Collaboration. We were unable to statistically pool any of the results, but we assessed the quality of the evidence using an adapted GRADE approach.

Main results

Twenty small trials (1239 people with neck pain) containing 38 comparisons were included. Analysis was limited by trials of varied quality, heterogeneous treatment subtypes and conflicting results. The main findings for reduction of neck pain by treatment with electrotherapeutic modalities were as follows.

Very low quality evidence determined that pulsed electromagnetic field therapy (PEMF) and repetitive magnetic stimulation (rMS) were more effective than placebo, while transcutaneous electrical nerve stimulation (TENS) showed inconsistent results.

Very low quality evidence determined that PEMF, rMS and TENS were more effective than placebo.

Low quality evidence (1 trial, 52 participants) determined that permanent magnets (necklace) were no more effective than placebo (standardized mean difference (SMD) 0.27, 95% CI -0.27 to 0.82, random-effects model).

Very low quality evidence showed that modulated galvanic current, iontophoresis and electric muscle stimulation (EMS) were not more effective than placebo.

There were four trials that reported on other outcomes such as function and global perceived effects, but none of the effects were of clinical importance. When TENS, iontophoresis and PEMF were compared to another treatment, very low quality evidence prevented us from suggesting any recommendations. No adverse side effects were reported in any of the included studies.

Authors' conclusions

We cannot make any definite statements on the efficacy and clinical usefulness of electrotherapy modalities for neck pain. Since the evidence is of low or very low quality, we are uncertain about the estimate of the effect. Further research is very likely to change both the estimate of effect and our confidence in the results. Current evidence for PEMF, rMS, and TENS shows that these modalities might be more effective than placebo. When compared to other interventions the quality of evidence was very low thus preventing further recommendations.

Funding bias should be considered, especially in PEMF studies. Galvanic current, iontophoresis, EMS, and a static magnetic field did not reduce pain or disability. Future trials on these interventions should have larger patient samples, include more precise standardization, and detail treatment characteristics.

Plain language summary *available in* English | Français | Hrvatski | தமிழ்

Electrotherapy for neck pain

Background

Neck pain is common, disabling and costly. Electrotherapy is an umbrella term that covers a number of therapies using electric current that aim to reduce pain and improve muscle tension and function.

Study characteristics

This updated review included 20 small trials (N = 1239). We included adults (> 18 years old) with acute whiplash or non-specific neck pain as well as chronic neck pain including degenerative changes, myofascial pain or headaches that stem from the neck. No index for severity of the disorders could be specified. The evidence was current to August 2012. The results of the trials could not be pooled because they examined different populations, types and doses of electrotherapy and comparison treatments, and measured slightly different outcomes.

Key results

We cannot make any definitive statements about the efficacy of electrotherapy for neck pain because of the low or very low quality of the evidence for each outcome, which in most cases was based on the results of only one trial.

For patients with acute neck pain, TENS possibly relieved pain better than electrical muscle stimulation, not as well as exercise and infrared light, and as well as manual therapy and ultrasound. There was no additional benefit when added to infrared light, hot packs and exercise, physiotherapy, or a combination of a neck collar, exercise and pain medication. For patients with acute whiplash, iontophoresis was no more effective than no treatment, interferential current, or a combination of traction, exercise and massage for relieving neck pain with headache.

For patients with chronic neck pain, TENS possibly relieved pain better than placebo and electrical muscle stimulation, not as well as exercise and infrared light, and possibly as well as manual therapy and ultrasound. Magnetic necklaces were no more effective than placebo for relieving pain; and there was no additional benefit when electrical muscle stimulation was added to either mobilisation or manipulation.

For patients with myofascial neck pain, TENS, FREMS (FREquency Modulated Neural Stimulation, a variation of TENS) and repetitive magnetic stimulation seemed to relieve pain better than placebo.

Quality of the evidence

About 70% of the trials were poorly conducted studies. The trials were very small, with a range of 16 to 336 participants. The data were sparse and imprecise, which suggests that results cannot be generalized to the broader population and contributes to the reduction in the quality of the evidence. Therefore, further research is very likely to change the results and our confidence in the results.

Authors' conclusions

Implications for practice

We cannot make any definitive statements on the efficacy and clinical usefulness of electrotherapy modalities for neck pain. Since the quality of the evidence is low or very low, we are uncertain about the estimates of the effect. Further research is very likely to change both the estimate of effect and our confidence in the results. Current evidence for rMS, TENS and PEMF shows that these modalities might be more effective than placebo but not other interventions, and funding bias has to be considered, especially in PEMF studies. Galvanic current, iontophoresis, electric muscle stimulation (EMS) and a static magnetic field did not reduce pain or disability.

Implications for research

Due to a lack of consensus on parameters, and the restricted quality of most of the publications, additional studies need to be done to confirm the results described in this review. Possible new trials examining these specific interventions should include more participants and correct the internal validity and reporting shortcomings found in earlier randomized controlled trials. They should include more precise standardization and description of treatment characteristics.

Summary of findings

Summary of findings for the main comparison. Summary of findings: EMS **Open in table viewer**

EMS + another treatment compared with that same treatment for neck pain

Patient or population: Patients with subacute/chronic neck pain with or without radicular symptoms and cervicogenic headache

Settings: Community USA

Intervention: Electrical Muscle Stimulation (EMS) + another treatment

Comparison: that same treatment

Outcomes	Effect	No of Participants (studies)	Quality of the evidence (GRADE)
Pain Intensity - intermediate-term follow-up (about 6 months)	One trial with factorial design (multiple treatment meta-analysis, I^2 = 0%) showed no difference in pain intensity (pooled SMD 0.09, 95% CI Random -0.15 to 0.33)	269 (1 study with factorial design of 4 independent comparisons)	⊕⊕⊖⊖ **low** Design: 0 Limitations: 0 Inconsistency: 0 Indirectness: 0 Imprecision: -1 Other: -1
Function **intermediate-term follow-up**	One trial with factorial design (multiple treatment meta-analysis, I^2 = 0%) showed no difference in pain intensity (pooled SMD 0.09, 95% CI Random -0.15 to 0.33)	269 (1 study with factorial design of 4 independent comparisons)	⊕⊕⊖⊖ **low** Design: 0 Limitations: 0 Inconsistency: 0 Indirectness: 0 Imprecision: -1 Other: -1
Global Perceived Effect	Not measured		

Satisfaction **intermediate-term follow-up**	One trial with factorial design (multiple treatment meta-analysis, $I^2 = 0\%$) showed no difference in pain intensity (pooled SMD 0.02, 95% CI Random -0.22 to 0.26)	269 (1 study with factorial design of 4 independent comparisons)	⊕⊕⊖⊖ **low** Design: 0 Limitations: 0 Inconsistency: 0 Indirectness: 0 Imprecision: -1 Other: -1
Quality of life	Not measured		
Adverse effects	No known study related adverse events		

Low quality:

1. Imprecision: Sparce EMS-related data (-1)

2. Other: 2x2x2 factorial design (8 groups; 3 of them with EMS plus another treatment; N= 336) No setting parameters for EMS; Treatment schedule unclear: " ...at least 1 treatment..." (manip / mob) No maximum, no average number of treatments reported (-1)

Summary of findings 2 Summary of findings: static magnetic field (necklace)

Summary of findings 2. Summary of findings: static magnetic field (necklace) **Open in table viewer**

Static magnetic field (necklace) compared with placebo for neck pain

Patient or population: Patients with chronic non-specific neck pain

Settings: Community USA - Rehabilitation Institute

Intervention: Static magnetic field (necklace)

Comparison: placebo

Outcomes	Effect	No of Participants (studies)	Quality of the evidence (GRADE)

Pain Intensity **immediate post-treatment (3 weeks)**	One trial showed **no difference** in pain intensity (SMD 0.27, 95% CI Random -0.27 to 0.82)	52 (1 study)	⊕⊕⊖⊖ **low** Design: 0 Limitations: 0 Inconsistency: 0 Indirectness: -1 Imprecision: -1 Other: 0
Function	Not measured		
Global Perceived Effect **immediate post-treatment (3 weeks)**	One trial showed **no difference** in global perceived effect (RR 0.85, 95% CI Random 0.48 to 1.50)	52 (1 study)	⊕⊕⊖⊖ **low** Design: 0 Limitations: 0 Inconsistency: 0 Indirectness: -1 Imprecision: -1 Other: 0
Satisfaction	Not measured		
Quality of life	Not measured		
Adverse effects	Not reported		

Low quality:

1. Imprecision: Sparce data (-1)

2. Directness: Single small trial (-1)

Background

For many years, electrotherapy has been commonly used as one of the physiotherapeutic options to treat neck pain. In contrast, little is known about its efficacy and efficiency. In our first review, published in 2005 (Kroeling 2005) and evaluating 11 publications, we found the evidence for all described modalities of electrotherapy either lacking, limited or conflicting. Our first update (Kroeling 2009) replaced the 2005 review and added seven recent publications, including studies on a new modality. Four studies (Ammer 1990; Chee 1986; Persson 2001; Provinciali 1996) that were included in the first review were excluded in the 2009 update, because studies of multimodal treatment were excluded; the unique contribution of the electrotherapy could not be identified. In our 2009 update (Kroeling 2009)18 small trials (1093 people with neck pain) were included. Analysis was limited by trials of varied quality, heterogeneous treatment subtypes and conflicting results.

Description of the condition

We studied neck pain that could be classified as either:

- non-specific mechanical neck pain, including whiplash associated disorders (WAD) category I and II (Spitzer 1987; Spitzer 1995), myofascial neck pain, and degenerative changes including osteoarthritis and cervical spondylosis (Schumacher 1993);
- cervicogenic headache (Olesen 1988; Olesen 1997; Sjaastad 1990; or
- neck disorders with radicular findings (Spitzer 1987; Spitzer 1995).

It can be classified as acute (less than 30 days), subacute (30 to 90 days) or chronic duration (longer than 90 days). Neck pain is typically provoked by neck movements and by physical examination provocation tests, and is located between the occiput to upper thoracic spine with the associated musculature.

Description of the intervention

Electrotherapy is a treatment category and may include: direct current, iontophoresis, electrical nerve stimulation, electrical muscle stimulation, pulsed electromagnetic fields, repetitive magnetic stimulation, and permanent magnets. Their underpinning mechanisms vary and are described in the following section.

How the intervention might work

1) Galvanic current for pain control

Treatment by direct current (DC), so-called Galvanic current, reduces pain by inhibiting nociceptor activity (Cameron 1999). This effect is restricted to the area of current flow through the painful region. The main indication for Galvanic current is the treatment of acute radicular pain and inflammation of periarticular

structures such as tendons and ligaments. Because DC enhances the transport of ionised substances through the skin, it can also be used to promote resorption of topical treatments, especially anti-inflammatory drugs (iontophoresis).

2) Electrical nerve stimulation (ENS) or transcutaneous electrical nerve stimulation (TENS) for pain control

Alternating electrical current (AC) or modulated DC (so-called Galvanic stimulation), mostly in the form of rectangular impulses, may inhibit pain-related potentials at the spinal and supraspinal level, known as 'gate control'. This underpins all classical forms of stimulating electrotherapy (for example diadynamic current), as well as a modern form called TENS (including Ultra-Reiz). While Galvanic current efficacy is restricted to the area of current flow, analgesic effects of ENS can be observed in the whole segmental region, both ipsilateral and contralateral (Cameron 1999; Kroeling 1998; Stucki 2000; Stucki 2007; Walsh 1997).

3) Electrical muscle stimulation

Most characteristics of EMS are comparable to TENS. The critical difference is in the intensity, which leads to additional muscle contractions. Primary pain relief via gate control can be obtained by EMS, TENS or other forms of ENS (Hsueh 1997). Rhythmic muscle stimulation by modulated DC, AC or interferential current probably increases joint range of motion (ROM), re-educates muscles, retards muscle atrophy, and increases muscle strength. The circulation can be increased and muscle hypertension decreased, which may lead to secondary pain relief (Tan 1998).

4) Pulsed electromagnetic fields (PEMF) and permanent magnets

Electricity is always connected with both electrical and magnetic forces. Alternating or pulsed electromagnetic fields induce electric current within the tissue. Even though these currents are extremely small, we recognize PEMF and the application of permanent magnets as forms of electrotherapy. Their main therapeutic purpose is for enhancement of bone or tissue healing and pain reduction.

5) Repetitive magnetic stimulation

Repetitive magnetic stimulation (rMS), in contrast to PEMF therapy, is a rather new (mid-1980s) neurophysiologic technique that allows the transcutaneous induction of nerve stimulating electric currents. This technique requires extremely strong and sharp magnetic impulses (for example 15,000 amperes peak current; 2.5 T field strength; < 1 msec) applied by specially designed coils (< 10 cm) over the target area. Modern devices allow the repetition of up to 60 impulses per second. Mainly developed to study and influence brain functions, rMS also stimulates spinal chord fibres and peripheral nerves. Initial studies used

peripheral rMS for therapeutic reasons, such as in myofascial pain syndrome (Pujol 1998; Smania 2003; Smania 2005). Since the resulting small electric impulses are the nerve stimulating factor, rMS effects may be similar to TENS and EMS.

Why it is important to do this review

Neck disorders with episodic pain and functional limitation (Hogg-Johnson 2008) are common in the general population (Carroll 2008a; US Census Bureau 2012), in workers (Côté 2008) and in whiplash associated disorders (WAD) (Carroll 2008b). In a Canadian study, about 5% of cases revealed a clinically important disability (Côté 1998). There is a great impact on the work force; and 3% to 11% of claimants are off work each year (Côté 2008). Direct and indirect costs are substantive (Hogg-Johnson 2008). Chronic pain accounts for about USD 150 to USD 215 billion each year in economic loss (that is lost workdays, therapy, disability) (NRC 2001; US Census Bureau 1996). The annual expenditure on medical care for back and neck conditions adjusted for inflation per patient increased by 95%, from USD 487 in 1999 to USD 950 in 2008 (Davis 2012). Yet very little is known about the effectiveness of most of the numerous available treatments still. Two systematic reviews have been published subsequent to ours. Teasell 2010 investigated acute whiplash while Leaver 2010 reviewed non-specific neck pain. Neither review revealed any new data and agreed with our former update. There continues to be very little information on this topic. Therefore ongoing updates of this review are necessary.

Objectives

This systematic review assessed the short, intermediate and long-term effects of electrotherapy on pain, function, disability, patient satisfaction, global perceived effect, and quality of life in adults with neck pain with and without radiculopathy or cervicogenic headache.

Methods

Criteria for considering studies for this review

Types of studies

We included published randomized controlled trials (RCTs) in any language. Quasi-RCTs and controlled clinical trials (CCTs) were excluded.

Types of participants

The participants were adults, 18 years or older, who suffered from acute (less than 6 weeks), subacute (6 to 12 weeks) or chronic (longer than 12 weeks) neck pain categorized as:

- non-specific mechanical neck pain, including WAD category I and II (Spitzer 1987; Spitzer 1995), myofascial neck pain, and degenerative changes including osteoarthritis and cervical spondylosis (Schumacher 1993);
- cervicogenic headache (Olesen 1988; Olesen 1997; Sjaastad 1990; and
- neck disorders with radicular findings (Spitzer 1987; Spitzer 1995).

Studies were excluded if they investigated neck pain with definite or possible long tract signs, neck pain caused by other pathological entities (Schumacher 1993), headache that was not of cervical origin but was associated with the neck, co-existing headache when either the neck pain was not dominant or the headache was not provoked by neck movements or sustained neck postures, or 'mixed' headaches.

Types of interventions

All studies used at least one type of electrotherapy: direct current, iontophoresis, electrical nerve stimulation; electrical muscle stimulation; pulsed electromagnetic fields (PEMF), repetitive magnetic stimulation (rMS) and permanent magnets.

Interventions were contrasted against the following comparisons:

- electrotherapy versus sham or placebo (e.g. TENS versus sham TENS or sham ultrasound);
- electrotherapy plus another intervention versus that same intervention (e.g. TENS + exercise versus exercise);
- electrotherapy versus another intervention (e.g. TENS versus exercise);
- one type of electrotherapy versus another type (e.g. modulated versus continuous TENS).

Exclusion criteria

Other forms of high frequency electromagnetic fields, such as short wave diathermy, microwave, ultrasound and infrared light, were not considered in this review because their primary purpose is to cause therapeutic heat. Since electro-acupuncture is a special form of acupuncture, it was also excluded. Multimodal treatment approaches that included electrotherapy were excluded if the unique contribution of electrotherapy could not be determined.

Types of outcome measures

The outcomes of interest were pain relief (for example a Numerical Rating Scale), disability (for example Neck Disability Index), function (for example activities of daily living) including work-related outcomes (for example return to work, sick leave), patient satisfaction, global perceived effect and quality of life. Adverse events as well as costs of care were reported if available. The duration of follow-up was defined as:

- immediate post-treatment (within one day);
- short-term follow-up (closest to four weeks);
- intermediate-term follow-up (closest to six months); and
- long-term follow-up (closest to12 months).

Primary outcomes

The outcomes of interest were pain relief, disability, and function including work-related outcomes.

Secondary outcomes

Patient satisfaction, global perceived effect and quality of life.

Search methods for identification of studies

References of retrieved articles were independently screened by two review authors. Note that our systematic review methodological design is consistent with the Cochrane Back Group methods.

Electronic searches

A research librarian searched computerized bibliographic databases without language restrictions for medical, chiropractic, and allied health literature. The search for this review was part of a comprehensive search on physical medicine modalities. These databases were searched for this update from December 2008 to August 2012.

We searched the following databases: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (Ovid), EMBASE (Ovid), Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Manual Alternative and Natural Therapy (MANTIS). Subject headings (MeSH) and key words included anatomical terms (neck, neck muscles, cervical plexus, cervical vertebrae, atlanto-axial joint, atlanto-occipital joint, spinal nerve roots, brachial plexus); disorder and syndrome terms (arthritis, myofascial pain syndromes, fibromyalgia, spondylitis, spondylosis, spinal osteophytosis, spondylolisthesis, headache, whiplash injuries, cervical rib syndrome, torticollis, cervico-brachial neuralgia, radiculitis, polyradiculitis, polyradiculoneuritis, thoracic outlet syndrome); treatment terms (multimodal treatment, electric stimulation therapy, transcutaneous electric nerve stimulation, rehabilitation, ultrasonic therapy, phototherapy, lasers, physical

therapy, acupuncture, biofeedback, chiropractic, electric stimulation therapy); and methodological terms. See Appendix 1 for the full MEDLINE search strategy. We also searched trial registers such as ClinicalTrials.gov and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP).

Searching other resources

We communicated with identified content experts, searched conference proceedings of the World Confederation for Physical Therapy 2011 and International Federation of Orthopaedic and Manipulative Therapists 2008. In addition, we searched our own personal files for grey literature.

Data collection and analysis

Selection of studies

Two review authors independently conducted citation identification and study selection. All forms were pre-piloted. Each pair of review authors met for consensus and consulted a third author when there was persisting disagreement. Agreement (yes, unclear, no) was assessed for study selection using the quadratic weighted Kappa statistic, Cicchetti weights (Landis 1977).

Data extraction and management

Two review authors independently conducted data abstraction. Forms used were pre-piloted. Data were extracted on the methods (RCT type, number analysed, number randomized, intention-to-treat analysis), participants (disorder subtype, duration of disorder), interventions (treatment characteristics for the treatment and comparison groups, dosage and treatment parameters, co-intervention, treatment schedule), outcomes (baseline mean, reported results, point estimate with 95% confidence intervals (CI), power, side effects, costs of care) and notes (if authors were contacted or points of consideration related to the RCT). These factors are detailed in the 'Characteristics of included studies' table.

Assessment of risk of bias in included studies

We conducted the 'Risk of bias' assessment for RCTs using the criteria recommended by The Cochrane Collaboration (Higgins 2011) and the Cochrane Back Review Group (Furlan 2009) (see Appendix 2). At least two review authors independently assessed the risk of bias. A consensus team met to reach a final assessment. The following characteristics were assessed for risk of bias: randomisation; concealment of treatment allocation; blinding of patient, provider, and outcome assessor; incomplete data: withdrawals, dropout rate and intention-to-treat analysis; selective outcome reporting; other including similar at baseline, similar co-interventions, acceptable compliance, similar timing of assessment. A study with a low risk of bias was defined as having low risk of bias on six or more of these items and no fatal flaws.

Measures of treatment effect

Standardized mean differences (SMD) with 95% confidence intervals (95% CI) were calculated for continuous data while relative risks (RR) were calculated for dichotomous outcomes. We selected SMD over weighted mean difference (WMD) because we were looking across different interventions and most interventions used different outcome measures with different scales. For outcomes reported as medians, effect sizes were calculated using the formula by Kendal 1963 (p 237). When neither continuous nor dichotomous data were available, we extracted the findings and the statistical significance as reported by the author(s) in the original study.

In the absence of clear guidelines on the size of a clinically important effect, a commonly applied system by Cohen 1988 was used: small (0.20), medium (0.50) and large (0.80). A minimal clinically important difference between treatments for the purpose of the review was 10 points on a 100-point pain intensity scale (small: WMD < 10%; moderate: 10% ≤ WMD < 20%; large: 20% ≤ WMD of the visual analogue scale (VAS)). For the neck disability index, we used a minimum clinically important difference of 7/50 neck disability index units. It is noted that the minimal detectable change varies from 5/50 for non-complicated neck pain to 10/50 for cervical radiculopathy (MacDermid 2009). To translate effect measures into clinically meaningful terms and give the clinician a sense of the magnitude of the treatment effect, we calculated the number needed to treat (NNT) when the effect size was statistically significant (NNT: the number of patients a clinician needs to treat in order to achieve a clinically important improvement in one) (Gross 2002).

Unit of analysis issues

We performed one multiple treatment meta-analysis for the Hurwitz 2002 trial that used a factorial design. We used a random-effects model to allow for heterogeneity within each subgroup. An I^2 statistic was also computed for subgroup differences. The data in the subgroups were independent.

Dealing with missing data

Where data were not extractable primary authors were contacted. See the 'Characteristics of included studies' table, 'Notes' for details. Missing data from Hurwitz 2002 and Chiu 2005 were obtained in this manner. No other data were requested. Missing data that were greater than 10 years old were not requested.

Assessment of heterogeneity

Prior to calculation of a pooled effect measure, we assessed the reasonableness of pooling on clinical grounds. The possible sources of heterogeneity considered were: symptom duration (acute versus chronic); subtype of neck pain (for example WAD); intervention type (for example DC versus pulsed); characteristics of treatment (for example dosage, technique); and outcomes (pain relief, measures of function and disability, patient satisfaction, quality of life). We were unable to perform any of these calculations because the data were incompatible.

Assessment of reporting biases

Occurrences of reporting biases were noted in the text and 'Characteristics of included studies' tables, 'Notes' column. Our review search methods addressed language bias; no additional languages were selected for this review. Funding bias was possible in three trials (Sutbeyaz 2006; Thuile 2002; Trock 1994). One trial from Spain was judged to have serious flaws and high risks of bias which may represent reporting bias (Escortell-Mayor 2011).

Data synthesis

We assessed the quality of the body of the evidence using the GRADE approach, as recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) and adapted in the updated Cochrane Back Review Group (CBRG) method guidelines (Furlan 2009). Domains that may decrease the quality of the evidence are: 1) study design, 2) risk of bias, 3) inconsistency of results, 4) indirectness (not to generalize), 5) imprecision (insufficient data), and 6) other factors (for example reporting bias). The quality of the evidence was reduced by a level based on the performance of the studies against these five domains (see Appendix 3 for definitions of these domains). All plausible confounding factors were considered as were their potential effects on the demonstrated treatment responses and the treatment dose-response gradient (Atkins 2004). Levels of quality of evidence were defined as the following.

- High quality evidence: there are consistent findings among at least 75% of RCTs with low risk of bias; consistent, direct and precise data; and no known or suspected publication biases. Further research is unlikely to change either the estimate or our confidence in the results.
- Moderate quality evidence: one of the domains is not met. Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- Low quality evidence: two of the domains are not met. Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
- Very low quality evidence: three of the domains are not met. We are very uncertain about the results.
- No evidence: no RCTs were identified that addressed this outcome.

We also considered a number of factors to place the results into a larger clinical context: temporality, plausibility, strength of association, dose response, adverse events, and cost. Clinical relevance was addressed for individual trials and reported either in the 'Characteristics of included studies' table or in the text.

Subgroup analysis and investigation of heterogeneity

We had also planned to assess the influence of risk of bias (concealment of allocation, blinding of outcome assessor), duration (acute, subacute, chronic), and subtypes of the disorder (non-specific, WAD, degenerative change-related, radicular findings, cervicogenic headache), but again data were too sparse. Since a meta-analysis was not possible, sources of heterogeneity were not explored.

Sensitivity analysis

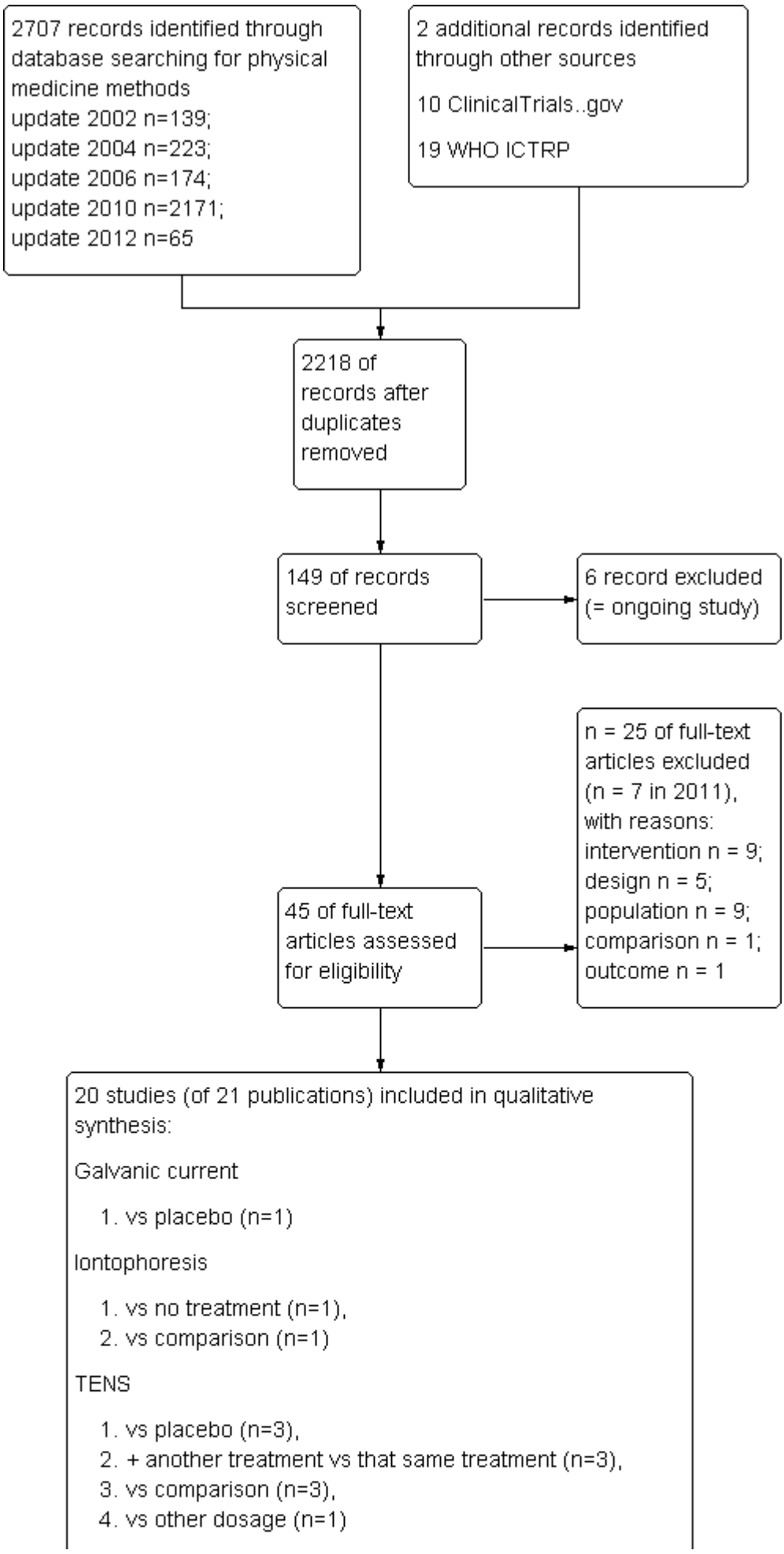
Sensitivity analysis or meta-regression for (1) symptom duration, (2) methodological quality, and (3) subtype of neck disorder were planned but were not carried out because we did not have enough data in any one category.

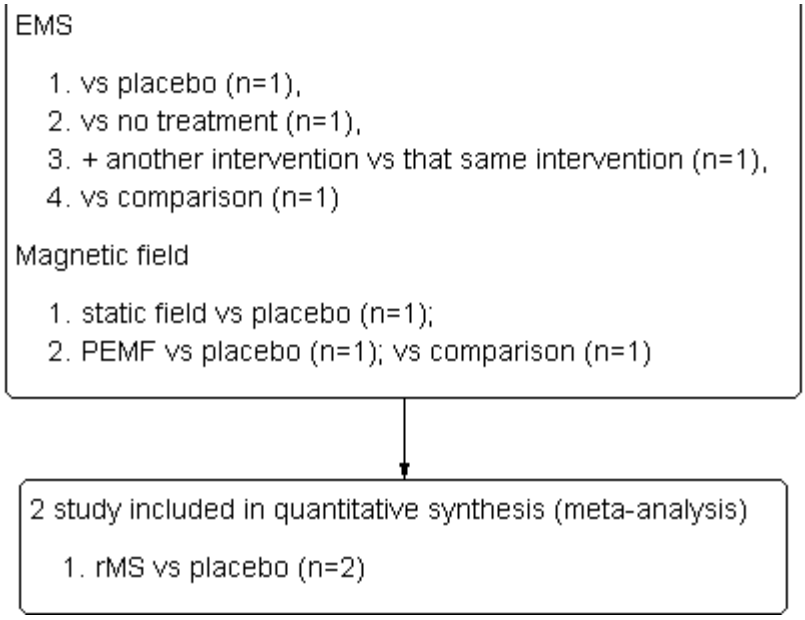
Results

Description of studies

Twenty trials (1239 participants) were selected (Figure 1). The duration of the disorder, disorder subtypes and electrotherapy subtypes were as follows.

Figure 1 **Open in figure viewer** | **Download as PowerPoint**


2707 records identified through database searching for physical medicine methods
update 2002 n=139;
update 2004 n=223;
update 2006 n=174;
update 2010 n=2171;
update 2012 n=65
2 additional records identified through other sources
10 ClinicalTrials..gov
19 WHO ICTRP
2218 of records after duplicates removed
149 of records screened
6 record excluded (= ongoing study)
45 of full-text articles assessed for eligibility
n = 25 of full-text articles excluded (n = 7 in 2011), with reasons:
intervention n = 9;
design n = 5;
population n = 9;
comparison n = 1;
outcome n = 1
20 studies (of 21 publications) included in qualitative synthesis:
Galvanic current
1. vs placebo (n=1)
Iontophoresis
1. vs no treatment (n=1),
2. vs comparison (n=1)
TENS
1. vs placebo (n=3),
2. + another treatment vs that same treatment (n=3),
3. vs comparison (n=3),
4. vs other dosage (n=1)



Study flow diagram.

- Acute whiplash associated disorders (WAD) with or without cervicogenic headache (n = 4): Fialka 1989, electrical muscle stimulation (EMS) and iontophoresis; Hendriks 1996, transcutaneous electric nerve stimulation (TENS); Foley-Nolan 1992, pulsed electromagnetic field (PEMF); Thuile 2002, PEMF.
- Acute non-specific neck pain (n = 1): Nordemar 1981, TENS.
- Chronic myofascial neck pain (n = 5): Farina 2004, TENS; Hsueh 1997, TENS; Hou 2002, TENS; Smania 2003, repetitive magnetic stimulation (rMS); Smania 2005, rMS.
- Chronic neck pain due to osteoarthritic cervical degenerative changes (n = 2): Trock 1994, PEMF; Sutbeyaz 2006, PEMF.
- Chronic non-specific neck pain (n = 5): Chiu 2005, TENS; Flynn 1987, TENS; Foley-Nolan 1990, PEMF; Hong 1982, static magnetic field; Philipson 1983, modulated galvanic current.
- Subacute or chronic neck pain with or without cervicogenic headache and radicular findings (n = 1): Hurwitz 2002, EMS.
- Subacute or chronic non-specific neck pain (n = 1): Escortell-Mayor 2011.

One trial was translated from Danish (Philipson 1983). Three further non-English trials (two French, one Italian) were subsequently excluded because they did not meet our criteria.

Six ongoing trials have been registered but not published (Triano 2009; Escortell 2011; Guayasamín 2013; Taniguchi 2010; Weintraub 2007).

Excluded studies

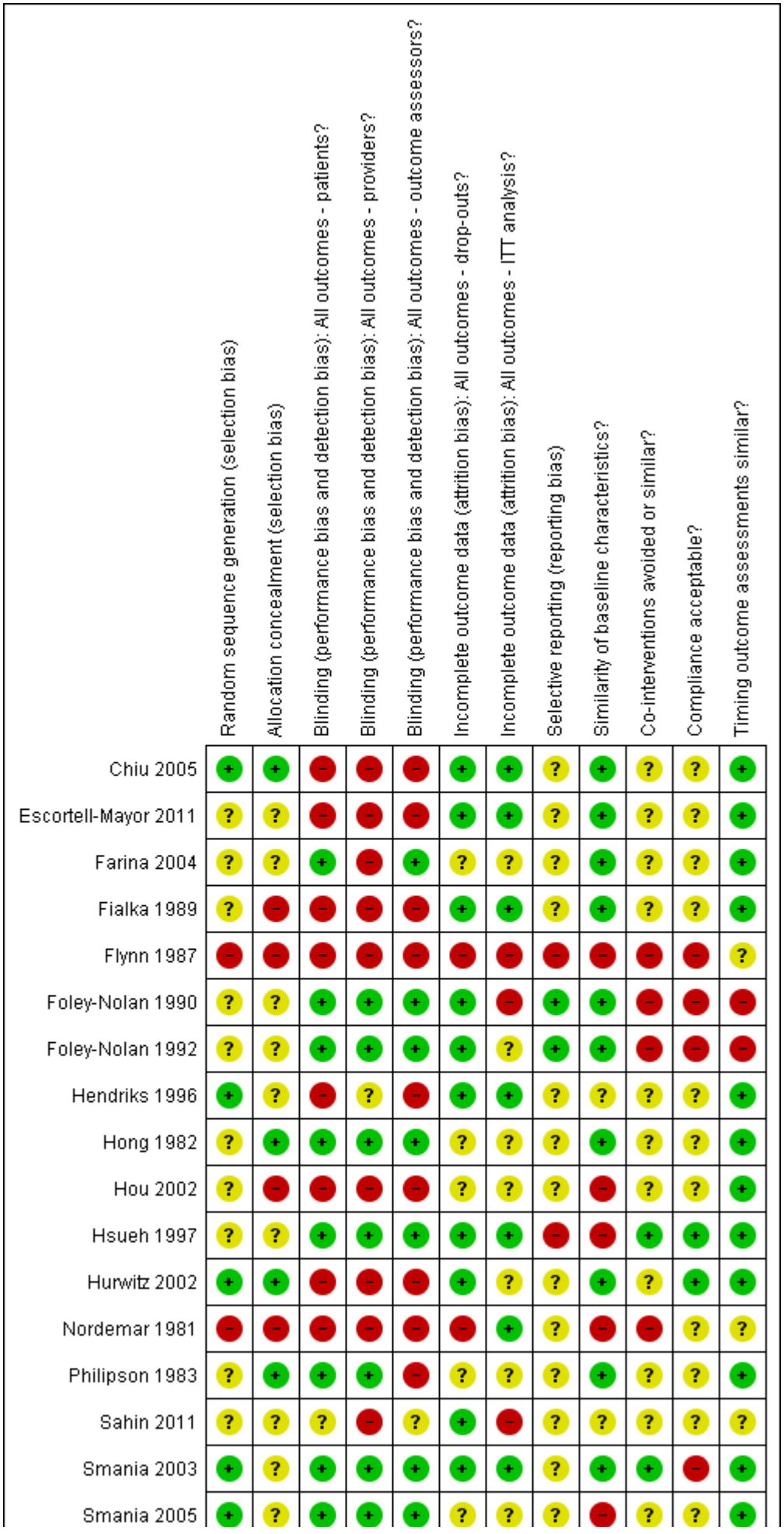
Twenty-five studies were excluded (n = 7 in 2011). The reasons were: the intervention (n = 9) (Ammer 1990; Fernadez-de-las Penas2004; Forestier 2007a; Forestier 2007b; Klaber-Moffett 2005; Persson 2001; Provinciali 1996; Vas 2006; Vikne 2007); population (n = 9) (Chen 2007; Coletta 1988; Gabis 2003; Hansson 1983; Jahanshahi 1991; Porzio 2000; Rigato 2002; Wang 2007; Wilson 1974); design (n = 5) (Chee 1986; Gonzales-Iglesias 2009; Lee 1997; Vitiello 2007; Yip 2007); comparison (n = 1) (Dusunceli 2009); outcome (n = 1) (Garrido-Elustondo 2010).

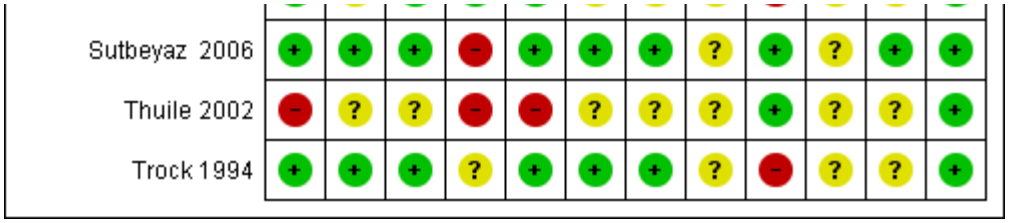
Risk of bias in included studies

Allocation

The allocation of concealment and reports on adequate randomisation were unclear in 60% of the trials (see also Figure 2).

Figure 2 **Open in figure viewer** | **Download as PowerPoint**


Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding (performance bias and detection bias): All outcomes - patients?
Blinding (performance bias and detection bias): All outcomes - providers?
Blinding (performance bias and detection bias): All outcomes - outcome assessors?
Incomplete outcome data (attrition bias): All outcomes - drop-outs?
Incomplete outcome data (attrition bias): All outcomes - ITT analysis?
Selective reporting (reporting bias)
Similarity of baseline characteristics?
Co-interventions avoided or similar?
Compliance acceptable?
Timing outcome assessments similar?
Chiu 2005
Escortell-Mayor 2011
Farina 2004
Fialka 1989
Flynn 1987
Foley-Nolan 1990
Foley-Nolan 1992
Hendriks 1996
Hong 1982
Hou 2002
Hsueh 1997
Hurwitz 2002
Nordemar 1981
Philipson 1983
Sahin 2011
Smania 2003
Smania 2005



Risk of bias summary: review authors' judgements about each item for each included study.

Blinding

There was no clear reporting of blinding of patients (50%), providers (60%) or observers (60%).

Incomplete outcome data

In 50% of the trials there was attrition bias, when considering both dropouts (30%) and intention-to-treat (ITT) analysis (50%).

Selective reporting

Selective reporting was present or unclear in 80% of the trials.

Other potential sources of bias

In Trock 1994 their research support was listed as Bio-Magnetic Systems, Inc. (co-author Markoll was the principle shareholder of Bio-Magnetic Sytems; Markoll and Trock were sentenced in 2001 for billing unapproved electromagnetic therapy (see FDA report: http://www.fda.gov/ora/about/enf_story/archive/2001/ch6/oci6.htm).

Effects of interventions

See: **Summary of findings for the main comparison** Summary of findings: EMS; **Summary of findings 2** Summary of findings: static magnetic field (necklace)

Galvanic current

1. Modulated Galvanic current versus placebo

One study with a high risk of bias (Philipson 1983) assessed the effects of 'diadynamic' modulated Galvanic current (50 or 100 Hz) against placebo for patients with chronic pain in trigger points of the neck and shoulders.

Pain relief

No difference (RR 0.69, 95% CI 0.39 to 1.24, random-effects model) between the groups was found after a one-week treatment.

Global perceived effect

No difference between the groups was noted immediately post-treatment.

Conclusion: there was very low quality evidence of no difference in pain or global perceived effect when diadynamic modulated Galvanic current was evaluated at immediate post-treatment.

Iontophoresis

1. Iontophoresis versus no treatment

One study with a high risk of bias (Fialka 1989) assessed the effects of iontophoresis (DC combined with diclofenac gel) compared to no treatment for patients with acute WAD pain with or without cervicogenic headache.

Pain relief:

No difference between the groups was determined after a five-week treatment.

Cervicogenic headache

No difference (RR 0.66, 95% CI 0.28 to 1.57, random-effects model) between the groups was reported after a five-week treatment.

Conclusion: very low quality evidence suggested that iontophoresis when compared to no treatment improved pain and headache for patients with acute WAD with or without cervicogenic headache.

2. Iontophoresis versus comparison

One study with a high risk of bias (Fialka 1989) assessed the effects of iontophoresis (DC combined with diclofenac gel, same as above) against two other treatments: a) interferential current, and b) multimodal treatment (traction + therapeutic exercise + massage) for patients with acute WAD.

Pain relief

No difference between the groups was determined after a five-week treatment period.

Cervicogenic headache

No difference between the groups was reported after five weeks of treatment.

Conclusion: there was very low quality evidence that iontophoresis improved pain or headache when contrasted against either interferential or a multimodal approach for acute WAD or cervicogenic headache.

Transcutaneous electrical nerve stimulation (TENS)

1. TENS versus placebo (sham control)

Two studies with low risk of bias (Hsueh 1997; Smania 2005) and two with high risk of bias (Flynn 1987; Sahin 2011) compared TENS to sham controls for patients with chronic neck pain.

Pain relief

All four trials reported immediate post-treatment pain relief favouring TENS. The results varied and they could not be combined since they assessed outcomes of very different treatment schedules. One trial also reported short-term pain relief, but our calculations did not support that (SMD -0.52, 95% CI -1.24 to 0.20, random-effects model) (Smania 2005).

Conclusion: there was very low quality evidence (four trials with sparse and non-generalizable data; group sizes between 7 and 22 participants) showing varied results for TENS therapy, with different frequencies and treatment schedules, immediately post-treatment for patients with chronic neck pain.

2. TENS plus another treatment versus that same treatment

Three studies with high risk of bias utilized TENS (80 to 100 Hz) for individuals with chronic neck pain (Chiu 2005), myofascial neck pain (Hou 2002), and acute neck pain (Nordemar 1981). Another trial assessed TENS (Ultra-Reiz, 143 Hz) for patients with acute WAD (Hendriks 1996). In these trials, TENS was added to other interventions received by both comparison groups (Chiu 2005: Infrared; Hou 2002: hot pack, exercises; Nordemar 1981: neck collar, exercises, analgesic; Hendriks 1996: standard physiotherapy).

Pain relief

Three trials reported no benefit of TENS at post-treatment (Hou 2002), short (Nordemar 1981) and intermediate-term (Chiu 2005) follow-up. One trial (Hendriks 1996) favoured Ultra-Reiz for pain relief in the short term. Due to different dosage parameters, data were not pooled.

Conclusion: there was very low quality evidence (two trials with group sizes between 10 and 13, one with no blinding and different treatment regimens) that the addition of TENS had no additional significant effect on pain relief in patients with acute to chronic neck pain, and that Ultra-Reiz reduced pain for patients with acute WAD (one trial, 2 X 8 participants).

3. TENS versus comparison

Three studies with high risk of bias compared TENS to EMS (Hsueh 1997), ultrasound (Flynn 1987) and manual therapy (Nordemar 1981) for treatment of acute and chronic neck pain. One study with high risk of bias (Escortell-Mayor 2011) compared TENS to manual therapy for subacute and chronic neck pain.

Pain relief

TENS seemed superior to EMS (Hsueh 1997), but there was little or no difference between TENS and manual therapy (Nordemar 1981; Escortell-Mayor 2011) or ultrasound (Flynn 1987).

Conclusion: there was very low quality evidence (trials with group sizes between 7 and 43 participants, sparse and non-generalizable data) that TENS may relieve pain better than EMS, but there was little or no difference between the effects of TENS and manual therapy (low quality evidence) or ultrasound (very low quality evidence) for patients with acute or chronic neck pain. Due to different comparative treatments, the results of the trials could not be pooled.

4. TENS versus TENS (with different parameters)

One study with a low risk of bias (Farina 2004) examined the effects of TENS (100 Hz) against FREMS (a frequency and intensity varying TENS modification, 1 to 40 Hz) for chronic myofascial pain. Another study with high risk of bias (Sahin 2011) compared conventional TENS (100 Hz) with both acupuncture like (AL)-TENS (4 Hz) and burst-mode (Burst)-TENS (100 Hz, 2 Hz) for chronic myofascial pain.

Pain relief

TENS and FREMS were both reported to be significantly effective for pain relief (VAS) after one week of treatment, and at one and three-month follow-up (Farina 2004). Conventional TENS showed no significant difference over AL-TENS or Burst-TENS after three weeks of treatment (Sahin 2011).

Conclusion: there was very low quality evidence (one trial, 19 + 21 participants; insufficient data reported) that FREMS and TENS were similarly effective for the treatment of chronic myofascial neck pain. There was very low quality evidence (one trial, two comparisons with 37 participants) that conventional TENS was similar to Burst-TENS or AL-TENS for chronic myofascial pain immediately post-treatment.

Electrical Muscle Stimulation (EMS)

1. EMS versus placebo (sham control)

One trial with a low risk of bias (Hsueh 1997) studied the effects of a single EMS treatment (20 minutes,10 Hz) for chronic neck pain with cervical trigger points compared to sham control.

Pain relief

No difference for pain intensity and pressure threshold was found.

Conclusion: there was very low quality evidence (one trial, 22 + 18 participants) that a single treatment of EMS had no effect on trigger point tenderness compared to placebo treatment in patients with chronic neck pain.

2. EMS (interferential current) versus no treatment

One study with a high risk of bias described the effect of EMS (stereodynamic 50 Hz interferential current) (Fialka 1989) for acute WAD versus no treatment.

Pain relief

No difference between treated and untreated control patients was found for neck pain relief and headache.

Conclusion: there was very low quality evidence (one trial, 2 x 15 participants) that EMS neither reduced neck pain nor cervicogenic headache in patients with acute WAD, compared to no treatment.

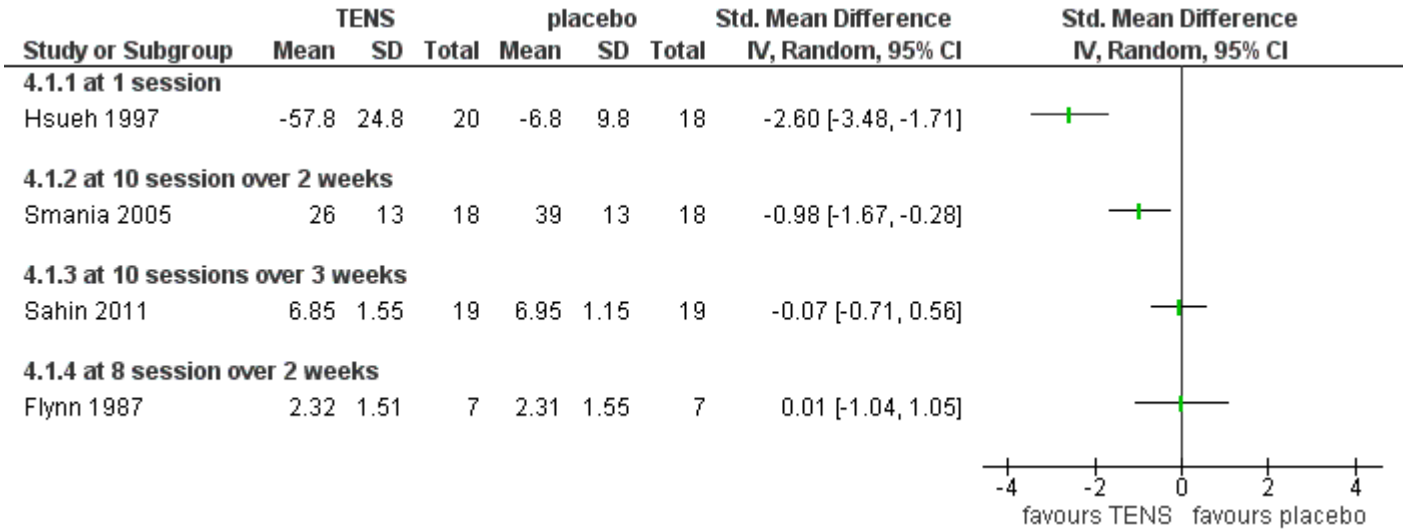
3. EMS plus another treatment versus the same treatment

One 2 x 2 x 2 factorial design study with a low risk of bias (Hurwitz 2002) compared the effects of additional EMS on two independent groups with mobilisation and two independent groups with manipulation (each arm with or without moist heat) for patients with subacute to chronic neck pain with and without cervicogenic headache or radicular symptoms.

Pain relief

No differences between the groups were found at post-treatment, short-term and intermediate-term follow-up (Figure 3). A multiple treatment meta-analysis from one factorial design of independent groups was pooled (SMD 0.09, 95% CI -0.15 to 0.33, random-effects model) with an I^2 of 0% at intermediate-term follow-up (Figure 4).

Figure 3 Open in figure viewer | Download as PowerPoint



Forest plot of comparison: 4 TENS versus placebo or sham, outcome: 4.1 pain intensity at post-treatment.

Figure 4

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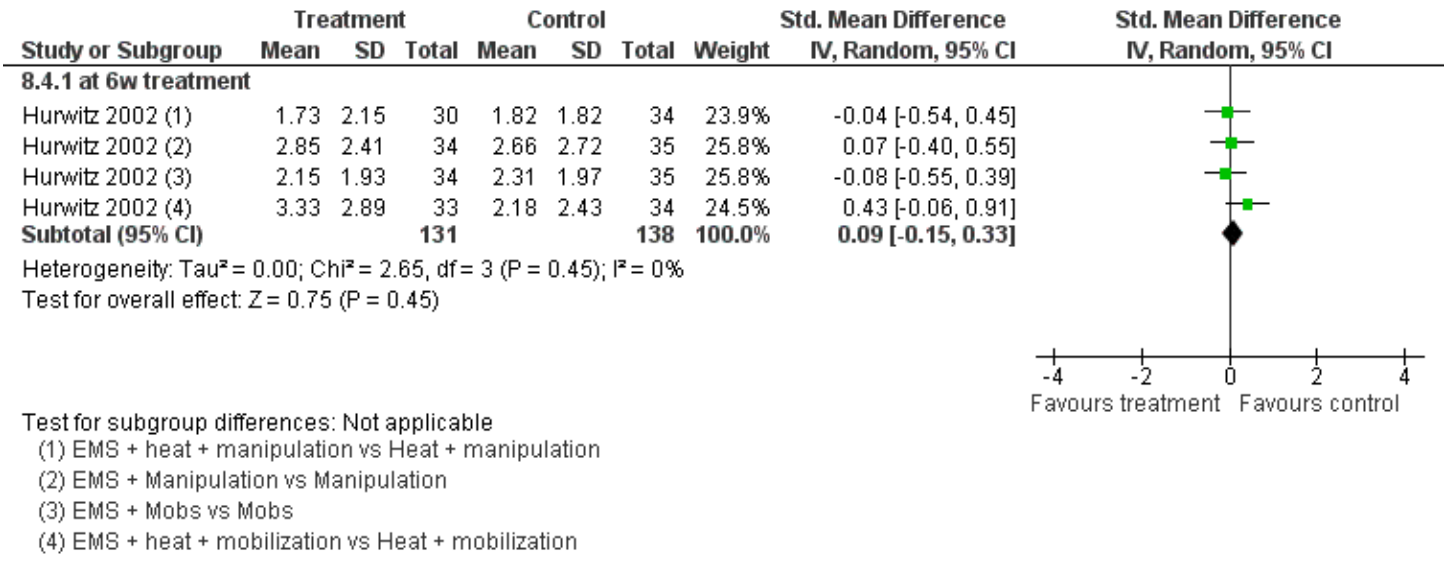

Forest plot of comparison: 8 EMS + another intervention versus that same intervention, outcome: 8.4 pain intensity at IT (6-month) follow-up.

Function

No differences between the groups were found (pooled SMD 0.09, 95% CI -0.15 to 0.33, random-effects model; I^2 = 0%) at post-treatment, short-term and intermediate-term follow-up (Figure 5).

Figure 5

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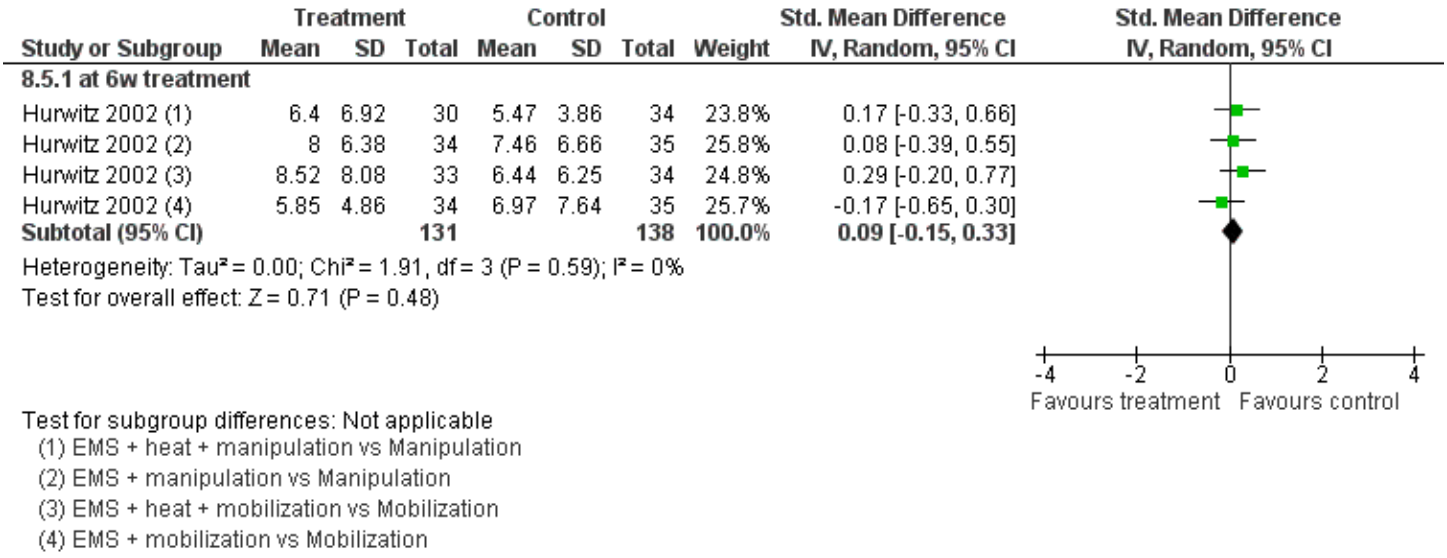
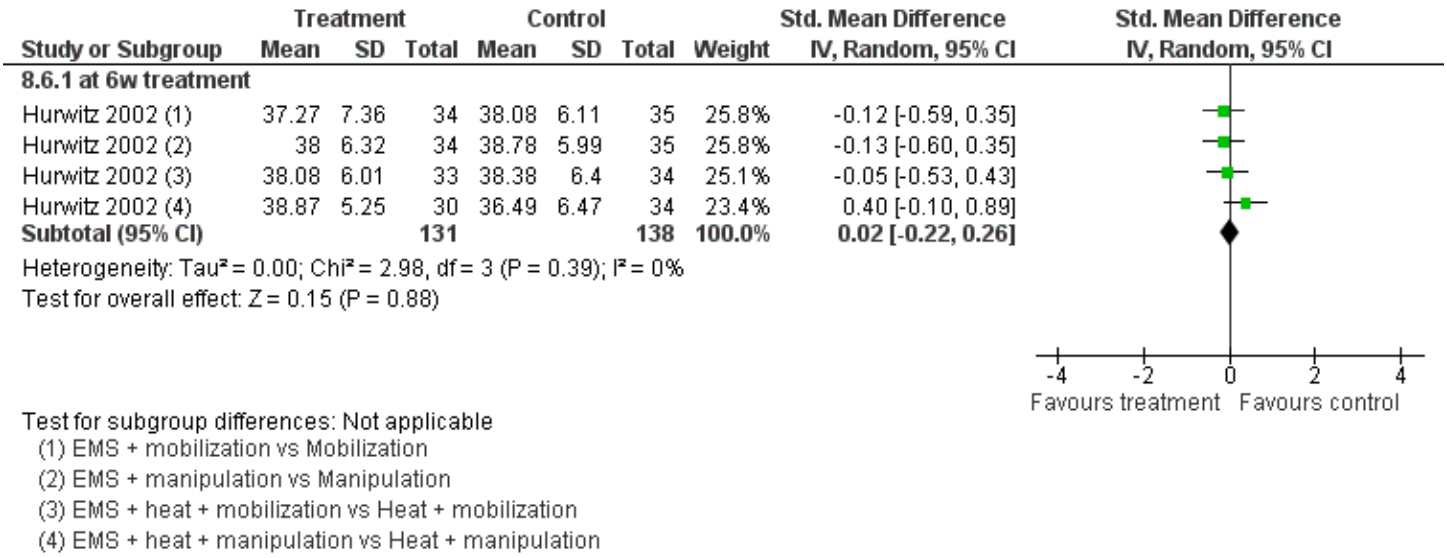


Forest plot of comparison: 8 EMS + another intervention versus that same intervention, outcome: 8.5 function at IT (6-month) follow-up.

Patient satisfaction

No differences between the groups were found (pooled SMD 0.02, 95% CI -0.22 to 0.26, random-effects model; I^2 = 0%) at post-treatment, short-term and intermediate-term follow-up (Figure 6).

Figure 6 **Open in figure viewer** | **Download as PowerPoint**



Forest plot of comparison: 8 EMS + another intervention versus that same intervention, outcome: 8.6 patient satisfaction at post-treatment.

Conclusion: there was low quality evidence (1 factorial designed trial, N = 336; three EMS groups, N = ˜ 40; no EMS settings or treatment schedules reported) that EMS had no significant impact on pain relief, disability and patient satisfaction when used as an adjunct to cervical mobilisation and manipulation, at post-treatment, short-term and intermediate-term follow-up.

4. EMS versus comparison

One study with a low risk of bias compared the effect of EMS to TENS for chronic myofascial pain (Hsueh 1997), and one study with a high risk of bias to treatment with iontophoresis for patients with acute WAD (Fialka 1989; see above).

Pain relief

EMS was found to be inferior to TENS for pain relief immediately following treatment. No difference was found between EMS and Iontophoresis at post-treatment and short-term follow-up.

Conclusion: there was very low quality evidence (one trial, 20 + 18 participants; one treatment only; poor clinical relevance) that EMS was inferior to TENS for pain relief of chronic neck pain. There was very low quality evidence (one trial, 2 x 15 participants) that there was no significant difference between EMS and iontophoresis for pain relief in acute WAD.

Pulsed electromagnetic field (PEMF)

1. PEMF versus placebo or sham control

Two studies with a low risk of bias examined the efficacy of non-thermal, high frequency PEMF (miniaturized high frequency (HF) generator, 27 MHz, 1.5 mW/cm^2) treatment on patients with chronic neck pain (Foley-Nolan 1990) and acute WAD (Foley-Nolan 1992). Two other trials with a low risk of bias studied the efficacy of low frequency PEMF therapy (< 100 Hz) for participants with chronic cervical osteoarthritis pain (Sutbeyaz 2006; Trock 1994). All four studies were sham-controlled by inactive devices.

Pain relief

In their first trial, the authors (Foley-Nolan 1990) found that pain intensity (VAS) was reduced post-treatment. In their second trial (Foley-Nolan 1992) no relevant effects were found. Trock 1994 reported significant pain relief after four to six weeks of treatment, but not at the one-month follow-up. Sutbeyaz 2006 reported significant pain relief, favouring the active PEMF group, after three weeks of treatment.

Function

Trock 1994 reported no differences in improvement in function.

Global perceived effects

Trock 1994 and Sutbeyaz 2006 reported no differences in effects.

Conclusion: there was very low quality evidence that non-thermal high frequency PEMF (27 MHz) reduced acute or chronic neck pain, and that low frequency PEMF (< 100 Hz) may have reduced pain from cervical spine osteoarthritis after some weeks of treatment. Even though these trials were rated as having a low risk of bias by our validity assessment team, they were imprecise, inconsistent and may have been influenced by other biases. The evidence rating was therefore reduced from moderate quality to very low for the following reasons: funding bias may have been present in Trock 1994 and Sutbeyaz 2006; the PEMF application (in a cervical collar worn 24 hours per day) in Foley-Nolan 1990 and Foley-Nolan 1992 was a very uncommon PEMF method using diathermy-like HF-pulses but with intensities far below the thermal threshold. The biological rationale for the chosen treatment was based on literature from 1940 and remains unclear.

2. PEMF versus comparison

One study with a high risk of bias (Thuile 2002) compared low frequency PEMF (< 100 Hz) treatment versus a standard therapy for WAD patients.

Pain relief

Reported results favoured PEMF therapy for neck pain relief and headache reduction in patients with WAD.

Conclusion: there was very low quality evidence (one trial, 44 + 48 participants; no placebo control; funding bias unclear) that PEMF may have reduced WAD-related neck pain and headache compared to a standard therapy.

Repetitive magnetic stimulation (rMS)

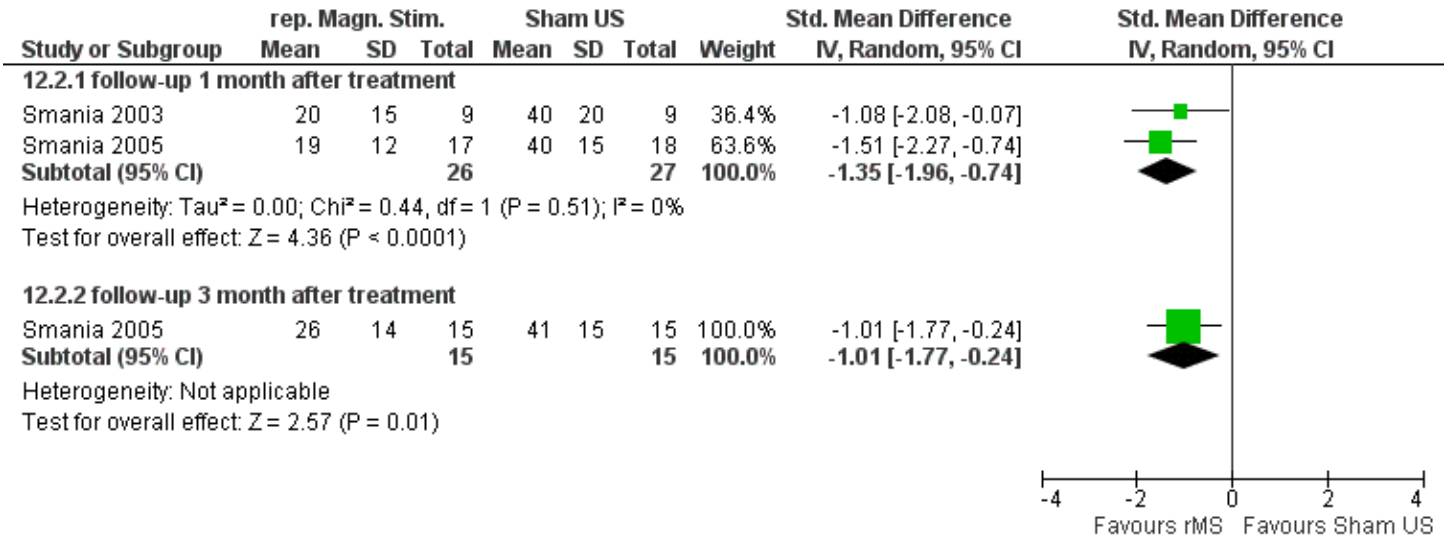
1. rMS versus placebo

Two similar studies with a low risk of bias (Smania 2003; Smania 2005) evaluated rMS therapy (400 mT, 4000 pulses per session) for patients with myofascial neck pain against placebo ultrasound.

Pain relief and function

Pain and disability (VAS, Neck Pain Disability (NPD)) reduction by rMS was more effective than placebo for the treatment of myofascial neck pain at two weeks, one month (Figure 7) (pooled SMD -1.35, 95% CI -1.96 to -0.74, random-effects model), and three months follow-up.

Figure 7 **Open in figure viewer** | **Download as PowerPoint**



Forest plot of comparison: 12 Repetitive magnetic stimulation (rMS) versus placebo ultrasound, outcome: 12.2 pain and function at ST follow-up.

Conclusion: we found very low quality evidence (two trials from the same research group, with sparse and non-generalizable data, 9 to 16 participants in either group) that rMS was effective for a short-term reduction of chronic neck pain and disability compared to placebo. However, although the NNT = 3 and treatment advantage was 46% to 56%, because of the low quality of the evidence one should treat the results with caution. Publication bias may be considered. Funding was not reported.

Static magnetic field

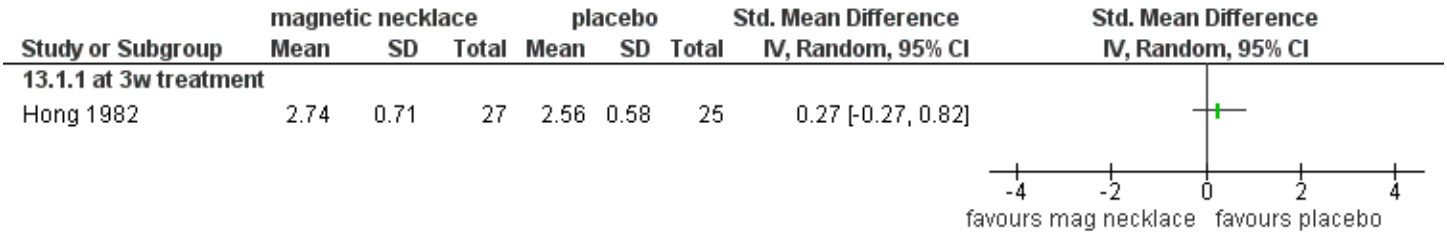
1. Static magnetic field (permanent magnets, necklace) versus sham control

One study with a low risk of bias (Hong 1982) investigated the efficacy of a magnetic necklace (120 mT) on patients with chronic neck and shoulder pain compared to a sham control group with identical but non-magnetic necklaces.

Pain relief

No differences (SMD 0.27, 95% CI -0.27 to 0.82, random-effects model) were found between the groups (Figure 8).

Figure 8 **Open in figure viewer** | **Download as PowerPoint**



Forest plot of comparison: 13 Static magnetic field (necklace) versus placebo, outcome: 13.1 pain intensity at post-treatment.

Conclusion: there was low quality evidence (one trial, 27 + 25 participants) that permanent magnets were not effective for chronic neck and shoulder pain relief.

Side effects

No adverse side effects were reported in any of the included studies evaluated above. However, studies were too small for a valid evaluation of adverse effects.

Costs

No costs were reported in any of the included studies evaluated above.

Discussion

Electrotherapy has been developed during the last two centuries. The systematic use of electric currents for therapeutic reasons began shortly after Luigi Galvani's observations (1780) that electric currents cause muscle contractions if stimulating efferent nerves. Since then, a growing variety of methods, including electromagnetic and magnetic agents, have been developed for a manifold of therapeutic reasons. Only a small selection of these methods have been investigated by the trials described above, direct or modulated Galvanic currents, iontophoresis, transcutaneous electrical nerve stimulation (TENS), electrical muscle stimulation (EMS), low or high frequency pulsed electromagnetic fields (PEMF), repetitive magnetic stimulation (rMS) and permanent magnets. A great deal of research in these fields has been published in the past 25 years (Cameron 1999), however only 20 trials examining the treatment of neck pain met our review criteria. Therefore, evidence for any of the modalities was found to be of low or very low quality, due to the

size of the trials and the heterogeneity of the populations, interventions and outcomes. This precluded meta-analysis and resulted in sparse data. The average sample size over all treatment groups was about 20 participants.

Summary of main results

For this review, there were 20 trials with 38 comparisons that met our inclusion criteria. No outcomes had high or moderate strength of evidence. The evidence for all electrotherapy interventions for neck pain is of low or very low quality, which means that we are very uncertain about the estimate of effect. Further research is very likely to have an important impact on this and our confidence in the results. Therefore, no conclusions can be drawn regarding the effectiveness of electrotherapy for neck pain based on the available small trials. Large randomized controlled trials are needed to get a valid and precise estimate of the effect of electrotherapy for neck pain.

Overall completeness and applicability of evidence

In general, convincing, high or moderate quality evidence for any of the described modalities was lacking. Thirty-eight comparisons in 20 studies examined seven different forms, and their modifications, of electrotherapy. Of the few studies that examined the same modalities, conclusions were limited by the heterogeneity of the treatment parameters or population. For example, the frequency for TENS ranged from 60 Hz to 143 Hz, with disorders from acute WAD to chronic myofascial pain. This heterogeneity made it impossible to pool the data and difficult to interpret the applicability of the results. More research needs to be done in order to confirm the positive findings, and to determine which treatment parameters are the most applicable and for which disorders.

Quality of the evidence

Performance and detection bias are the two dominant biases influencing our systematic review findings. Specifically, blinding of the patients and providers are essential considerations for future trials. Co-interventions need to be avoided to establish clearer results.

Potential biases in the review process

Language bias was avoided by including all languages during study selection, however non-English databases were not searched (that is Chinese databases).

Agreements and disagreements with other studies or reviews

The evidence presented in this review needs to be compared to the evidence described in other reviews. The limited number of reviews on the subject makes it difficult to carry out that comparison. There was conflicting evidence in the results on PEMF (Sutbeyaz 2006; Thuile 2002; Trock 1994), such that the positive

findings for PEMF were strongly doubted in other reviews (Hulme 2002; Schmidt-Rohlfing 2000). We also have these concerns and caution the reader that funding bias may be present. In particular, research support was declared as being provided by Bio-Magnetic Systems, Inc. Co-author Markoll was principle shareholder of Bio-Magnetic Sytems; Markoll and Trock were sentenced in 2001 for billing unapproved electromagnetic therapy (see FDA report:http://www.fda.gov/ora/about/enf_story/archive/2001/ch6/oci6.htm).

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References to other published versions of this review

Jump to: **included studies** | **excluded studies** | **ongoing studies** | **additional references**

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Link to article

Characteristics of studies

Characteristics of included studies [ordered by study ID]

Chiu 2005

Methods	RCT Number Analysed/Randomized: 109/145 Intension-to-treat Analysis: calculated Power Analysis: 90% power
Participants	Chronic neck pain (not specified) Duration of Complaint for Cases at baseline: Subacute (>3 months) Duration of Complaint for Control at baseline: Subacute (>3 months) G1: N = 73 G2: N = 67 G3: N = 78
Interventions	G1: TENS (TENS) a. 30 minutes of dual channel portable TENS unit (ITO model 1302). Continuous trains of 150ms square pulse at 80 Hz. 4 Electrodes (4x4cm); b) infrared irradiation, 20 min; c) education on neck care G2: Exercise Program (Ex) + IR a. deep neck flexor-using pressure sensor @20mmHg x10 min (10 sec on/15 sec off) b.Strengthening using a Multi Cervical Rehabilitation Unit (MCRU). 15 reps of flexion, extension at 20% of Peak Isometric Strength (PIS) as warm up Then Dynamic flexion and extension with variable resistance x 0-12 reps c. Infrared irradiation d. 35 minutes of exercise per session G3: a) Infrared Irradiation, 20 min; b) education on neck care Duration of Treatment: 6 weeks, 2 sessions/week Duration of Follow-up: 6 months CO-INTERVENTION: Infrared Irradiation

Outcomes	PAIN (VAS, 0 to 10) Baseline Median: G1 4.69, G2 4.61, G3 4.26 Reported Results: NS (between the three groups) SMD(Ex+IR versus TENS): -0.13 (95% CI:-0.51 to 0.26) FUNCTION (Chinese version of Northwick Park Questionnaire, 0 to 4) Baseline Median: G1 1.39, G2 1.55, G3 1.36 Reported Results: Ex + IR was favoured over TENS (P=0.02) SMD(Ex+IR versus TENS): -1.10(95% CI:-1.51 to -0.69) REASON FOR DROPOUTS: Reported SIDE EFFECT: No complications occurred COST OF CARE: NR
Notes	Different treatment times for TENS+IR and IR control group. Pathology of patients completely unknown (only selection criteria: neck pain > 3 months) MISSING DATA: A request was made to clarify data that differed slightly in two reports. Dr Chui responded to a request for clarification. "Please be informed that the subjects were the same groups (exercise and control) of patients as reported in spine but the TENS group was introduced in the Clinical Rehab article and different methods of calculation/ analysis of the neck muscle strength were used in the Clinical Rehab. article."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	reported in text
Allocation concealment (selection bias)	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - patients?	High risk	not reported
Blinding (performance bias and detection bias) All outcomes - providers?	High risk	not described

Blinding (performance bias and detection bias) All outcomes - outcome assessors?	High risk	not reported
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	reported in text
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	reported in text
Selective reporting (reporting bias)	Unclear risk	no steady protocol available
Similarity of baseline characteristics?	Low risk	reported in text
Co-interventions avoided or similar?	Unclear risk	unclear, not described
Compliance acceptable?	Unclear risk	not reported for exercise
Timing outcome assessments similar?	Low risk	reported in text

Escortell-Mayor 2011

Methods	RCT Number Analysed/Randomized: 71/90 Intension-to-treat Analysis: calculated Power Analysis: 47.5% power

Participants	subacute or chronic neck pain (grade I and II) Duration of Complaint for Cases at baseline: chronic (mean 20 weeks) Duration of Complaint for Control at baseline: chronic (mean 22 weeks) G1 TENS: N = 43
Interventions	G1: TENS (+ exercise) a. TENS electrode placement in the painful area in the metamere or in the nerve's pathway (Adel and Luykey 1996) portable digital TENS unit (Manufacturer: Enraf-Nonius; model TENSMED911). 150 microsecond pulse duration, 80Hz, adjustable amplitude, 30 minutes duration, 10 sessions on alternate days for about 1 month b. Exercise: isometric exercise, neck exercise and postural skills in the form of a handout and explained individually over two sessions to perform at home. G2: Manual Therapy (MT) + exercise a. Neuromuscular technique, post isometric stretching , spray and stretch, Jones technique (Chaitow 1991, Girardin 2004), 30 minute duration, 10 sessions on alternate days for about 1 month b. Exercise: isometric exercise, neck exercise and postural skills in the form of a handout and explained individually over two sessions to perform at home Duration of Treatment: 3 to 4 weeks, 10 sessions Duration of Follow-up: 6 months CO-INTERVENTION: medication consumption of anti-inflammatory, analgesics, and muscle relaxants; no significant difference between groups

Outcomes	PAIN Intensity (VAS, 0 to 100 mm, high score indicates worse) Baseline mean: TENS (+exercise) 56.4; MT (+exercise) 54.9 Reported results: Comparison between TENS and MT group: P = 0.9 (NS) SMD TENS versus MT : 0.11 [-0.35, 0.58] FUNCTION (NDI, 0 to 50, high score indicates worse) Baseline Mean: TENS (+exercise) 34.4; MT (+exercise) 31.63 Reported results: Comparison between TENS and MT group: P = 0.67 (NS) SMD TENS versus MT: -0.07 [-0.53, 0.40] PCS (SF-12 Physical component SF 12 summary, 0 to 50, high score indicates better) Baseline Mean: TENS (+exercise) 42.7; MT (+exercise) 43.3 Reported results: Comparison between TENS and MT group: P = 0.45 (NS) SMD TENS versus MT: 0.19 [-0.23, 0.61] REASON FOR DROPOUTS: Reported SIDE EFFECTS: no important side effects in either group COST OF CARE: NR
Notes	Location of Study: Madrid Region, Spain; the paper was judged to have serious flaws and high risks of bias

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	method of block randomisation is not clearly stated; it is not clear that complete blocks were done at each centre
Allocation concealment (selection bias)	Unclear risk	envelopes were not numbered
Blinding (performance bias and detection bias) All outcomes - patients?	High risk	not possible due to design

Blinding (performance bias and detection bias) All outcomes - providers?	High risk	not possible due to design
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	High risk	not possible due to design
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	see Figure 1
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	page 69 paragraph 2
Selective reporting (reporting bias)	Unclear risk	no protocol provided
Similarity of baseline characteristics?	Low risk	see Table 1
Co-interventions avoided or similar?	Unclear risk	not reported
Compliance acceptable?	Unclear risk	exercise compliance not reported
Timing outcome assessments similar?	Low risk	baseline one month and six months

Farina 2004

Methods	RCT Analysed/randomized: 40/40 blinding: patients evaluation examiner regarding treatment therapist regarding clinical status
Participants	Myofascial pain syndrome (upper m. trapezius) G1: N = 21 G2: N = 19
Interventions	G1: TENS (Phyacton 787, Uniphy, Netherlands) 100 Hz, 0.25 ms pulse width; placement: negative electrode on most painful trigger point; intensity: below muscular contraction (< 39mA), at patient's comfort G2: FREMS; a variation of TENS: FREquency Modulated Neural Stimulation (ETS 501-Physioflog, Lorenz Biotech, Italy); high voltage (>300V) low intensity (< 0.01 mA) and short duration impulses (0.01 msec); programmed frequency variations 1-40 Hz; placement: positive electrode at most painful trigger point Co-interventions: all patients were instructed to avoid PT for 2 months and analgesic medication for 2 weeks Treatment schedule: 10 treatment sessions, 5 days a week, for 2 consecutive weeks; duration 20 minutes each
Outcomes	NECK PAIN AND DISABILITY (NPDVAS; 0 to 10) (means only; SD not reported!) Baseline mean: G1 5.29; G2 4.81 At 1week treatment: G1 2.81; G2 2.46 Follow up 1 month: G1 3.24; G2 1.29 Follow up 3 months: G1 4.09; G2 2.73 Reported statistical analysis results: baseline versus 1 week/ 1 month/ 3 months: all P < 0,001 (except P < 0.05 for TENS 3 at months) Further outcome parameters: Algometry; Cervical ROM; Triggerpoint characteristics; similar results
Notes	Conclusion of authors: Both TENS and FREMS have positive short-term effects on MPS, but medium-term effects were achieved only with FREMS. However, no statistical significant differences between TENS and FREMS have been observed in most outcome parameters. Means and statistical results are reported, but SD values are missing (though announced).

Risk of bias

Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Unclear risk	describes a simple random scheme
Allocation concealment (selection bias)	Unclear risk	p 295 described as "patients were informed that they would be submitted to 1 of 2 possible treatments"
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - providers?	High risk	2 treatment groups involved 2 different machines
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	not described in results
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Unclear risk	not described
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Unclear risk	no ITT analysis described
Selective reporting (reporting bias)	Unclear risk	not described

Similarity of baseline characteristics?	Low risk	reported in text
Co-interventions avoided or similar?	Unclear risk	not described
Compliance acceptable?	Unclear risk	not described
Timing outcome assessments similar?	Low risk	reported in text

Fialka 1989

Methods	RCT Blinding: not patient, not observer Analysed/randomized: 60/60 patients
Participants	acute whiplash (>5 <10 days), cervicogenic headache G1: N = 15 G2: N = 15 G3: N = 15 G4: N = 15
Interventions	G1: Stereodynamic 50 Hz interferential current (Stereodynator, Siemens), treatment duration 15 minutes, 2 triple electrodes on neck and dorsal spine; intensity not reported G2: Iontophoresis: DC, duration 20 minutes, diclofenac-gel on a filter paper, placed under the electrodes on the neck, intensity 0.1 mA/cm^2 G3: Multimodal treatment : Traction, therapeutic exercise, massage (THGM) G4: Control group; no therapy Treatment schedule: start of treatment after first investigation (5-10 days after car accident); number of treatments and end of treatment not reported. Second investigation after 35 days

Outcomes	PAIN (neck; headache; patient's report) Baseline Mean: not reported Reported Results: improvement, significance not specified RR (G1 versus G4 for neck pain): 0.76 (95% CI Random: 0.18, 3.24) RR (G1 versus G4 for headache): 1.37 (95% CI Random: 0.29, 6.53) RR (G2 versus G4 for neck pain): 1.00 (95% CI Random: 0.42, 2.40) RR (G2 versus G4 for headache): 0.66 (95% CI Random: 0.28, 1.57) SIDE EFFECTS: not reported COST OF CARE: not reported
Notes	No number of treatments reported No adequate statistical evaluation No use of VAS for neck pain or headache

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	details not reported
Allocation concealment (selection bias)	High risk	not described
Blinding (performance bias and detection bias) All outcomes - patients?	High risk	not described
Blinding (performance bias and detection bias) All outcomes - providers?	High risk	not reported
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	High risk	not reported
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	reported in text
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	reported in text

Selective reporting (reporting bias)	Unclear risk	unclear
Similarity of baseline characteristics?	Low risk	reported in text
Co-interventions avoided or similar?	Unclear risk	not reported
Compliance acceptable?	Unclear risk	not reported
Timing outcome assessments similar?	Low risk	reported in text

Flynn 1987

Methods	RCT (pilot study) Blinding: not reported Analysed/randomized: 21/21 patients
Participants	whiplash associated pain (duration not reported) G1: N = 7 G2: N = 7 G3: N = 7
Interventions	G1: Ultra-Reiz 143 Hz (Endomed 404) intensity as tolerated, < 35mA; electrodes with viscose sponge at painful area; duration: 14 minutes G2: ultrasound (Multiphon unit) 3 MHZ, pulsed 1:1, intensity 0.5 W/ cm^2; duration 6 minutes G3: same treatment as in G2, but intensity 0.0 W/cm^2 (placebo) Co-interventions for all groups: posture advices and neck care including collar. Home exercises twice a day; continuing any medication as before, but not starting with new medication Treatment schedule: G1:8 times in 2 weeks G2 and G3: 8 times in 3 weeks

Outcomes	NECK PAIN (VAS 0 to 10cm) reported pre / post results (SD): G1: 7.42 (1.30) / 2.32 (1,51) (P < 0.05) G2: 5.1 (2.72) / 4.07 (2.73) (n.s.) G3: 4.43 (1.49) / 2.31 (2.31) (n.s.) reported baseline group differences: G1 versus G2: P < 0,05 G1 versus G3: P < 0,002 SIDE EFFECTS: not reported COST OF CARE: not reported
Notes	Different treatment times for G1 (2 weeks) and G2/G3 (3 weeks) The author characterized the investigation as a "pilot study" (small and uneven groups).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	method not reported
Allocation concealment (selection bias)	High risk	not described
Blinding (performance bias and detection bias) All outcomes - patients?	High risk	not reported
Blinding (performance bias and detection bias) All outcomes - providers?	High risk	not reported
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	High risk	not reported
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	High risk	not reported

Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	High risk	not reported
Selective reporting (reporting bias)	High risk	not reported, no protocol
Similarity of baseline characteristics?	High risk	significant baseline group differences, especially G1 versus G3
Co-interventions avoided or similar?	High risk	intention to avoid medication changes, but no details reported
Compliance acceptable?	High risk	not reported
Timing outcome assessments similar?	Unclear risk	different treatment duration (2 weeks and 3 weeks)

Foley-Nolan 1990

Methods	RCT Blinding: patients, observer Analysed/randomized: 20/20 patients
Participants	Chronic non-specific neck pain G1: N = 10 G2: N = 10
Interventions	G1: HF-PEMF therapy by a collar, fitted with a miniaturized short wave (HF-) generator; frequency: 27 MHz; pulse width: 0.06 ms; repetition frequency: 450/ second; mean power: 1.5 mW/cm^2 G2: placebo HF-PEMF Co-interventions G1and G2: anti-inflammatory analgesics, depending on pain intensity Treatment schedule: G1: 3 times in 3 weeks active G2: 3 weeks placebo and 3 weeks active; 8 hours daily

Outcomes	PAIN INTENSITY (VAS 10 cm): Baseline Mean: not reported Reported Results: significant at 3 weeks of treatment P < 0.05 SIDE EFFECTS: not reported COST OF CARE: not reported
Notes	This therapy is an uncommon PEMF method, using diathermy-like HF-pulses, but with intensities far below the thermal threshold. The reason for the chosen treatment is only based on a literature remark in 1940 and remains unclear.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	randomisation, not specified
Allocation concealment (selection bias)	Unclear risk	the method is unclear
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - providers?	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	reported in text
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	reported in text

Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	High risk	not reported
Selective reporting (reporting bias)	Low risk	reported in text
Similarity of baseline characteristics?	Low risk	reported in text
Co-interventions avoided or similar?	High risk	2-8 paracetamol tablets were allowed according to actual pain
Compliance acceptable?	High risk	not reported
Timing outcome assessments similar?	High risk	not reported

Foley-Nolan 1992

Methods	RCT Blinding: patients, observer Analysed/randomized: 40/40 patients
Participants	Acute whiplash injury (<3 days) G1: N = 20 G2: N = 20
Interventions	G1: HF-PEMF therapy (see: Foley-Nolan 1990) G2: placebo HF-PEMF Co-interventions G1+G2: optional anti-inflammatory analgesics; optional physiotherapy treatment after 4 weeks, if progress not satisfying Treatment schedule: 12 weeks; 8 hours daily

Outcomes	PAIN INTENSITY (VAS 10 cm): Baseline Mean: not reported Reported Results: not significant SIDE EFFECTS: not reported COST OF CARE: not reported
Notes	This therapy is an uncommon PEMF method, using diathermy-like HF pulses, but with intensities far below the thermal threshold. The reason for the chosen treatment is only based on a literature remark in 1940 and remains unclear.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	randomisation, not specified
Allocation concealment (selection bias)	Unclear risk	this is unclear and poorly described
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - providers?	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	reported in text
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	reported in text

Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Unclear risk	not reported
Selective reporting (reporting bias)	Low risk	reported in text
Similarity of baseline characteristics?	Low risk	reported in text
Co-interventions avoided or similar?	High risk	analgesics consumption (mefenamid acid) depending on pain
Compliance acceptable?	High risk	not reported
Timing outcome assessments similar?	High risk	not reported

Hendriks 1996

Methods	RCT Blinding: none Analysed/randomized: 16/16
Participants	Acute whiplash (< 3 days) G1: n = 8 G2: n = 8
Interventions	G1: group 2 treatment, plus Ultra-Reiz current 143 Hz, intensity individually graduated, 2 6x8 cm electrodes with viscose sponge placed paravertebral (C4 to T3), duration 15 minutes G2: standard physiotherapy: ice 15 minutes in clinic and 1 time per day at home; ROM exercises at home; advice on neck care, posture, use of collar Co-interventions: prescribed drugs were continued as instructed by medical staff Treatment schedule: 5 sessions within 1 week measurements: immediately after 5th session Follow-up: 6 weeks after final treatment

Outcomes	PAIN INTENSITY (VAS 100mm) Baseline Mean: not reported Reported Results: significant difference (P < 0.05) favouring Group 1 immediately post-treatment (N = 16) and at 6 weeks (N=14) follow-up (P < 0.005) SIDE EFFECT: not reported COST OF CARE: not reported
Notes	Only unrelated t-test values for A/B comparison, but no specific VAS data reported. Single group sizes not clearly specified No numbers of patients were given in tables for each group; authors failed to present information for a large number of criteria

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	reported in text
Allocation concealment (selection bias)	Unclear risk	not described
Blinding (performance bias and detection bias) All outcomes - patients?	High risk	due to difference in treatment method, not possible to blind the patient
Blinding (performance bias and detection bias) All outcomes - providers?	Unclear risk	only the treatment method was described but no report of who gave the treatment
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	High risk	pain score rated by patient
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	Tables 1-3
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	not described

Selective reporting (reporting bias)	Unclear risk	No protocol was available or referenced
Similarity of baseline characteristics?	Unclear risk	only post treatment measurements were reported
Co-interventions avoided or similar?	Unclear risk	no information given
Compliance acceptable?	Unclear risk	no information given
Timing outcome assessments similar?	Low risk	P13Lp2

Hong 1982

Methods	RCT Blinding: patients, observer Analysed/randomized: 52/52 patients (2 of 4 groups evaluated)
Participants	Chronic non-specific neck and shoulder pain G1: N = 27 G2: N = 25
Interventions	G1: necklace with magnetic samarium cobalt elements; field strength: 1200 Gauss (120 mT) flux density at surface G2: placebo necklace Treatment schedule: 3 weeks; 24 hours daily

Outcomes	PAIN INTENSITY (4-point rating scale): Baseline Mean: magnetic 2.84, non-magnetic 3.10 End of Study Mean: magnetic 2.56, non-magnetic 2.74 Absolute Benefit: magnetic 0.10, non-magnetic 0.37 Reported Results: not significant, SMD: 0.27 (95% CI Random: -0.27, 0.82) Power: 82% PATIENT PERCEIVED IMPROVEMENT: Baseline Mean: NR, Reported Results: magnetic 52% improved, non-magnetic 44% improved RR: 0.86 (95% CI Random: 0.51, 1.45) SIDE EFFECTS: not reported COST OF CARE: not reported
Notes	Two ignored groups had no pain (controls with active and placebo necklace)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	randomisation, method not described
Allocation concealment (selection bias)	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - providers?	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	reported in text
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Unclear risk	not described
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Unclear risk	not described
Selective reporting (reporting bias)	Unclear risk	not described

Similarity of baseline characteristics?	Low risk	reported in text
Co-interventions avoided or similar?	Unclear risk	not described
Compliance acceptable?	Unclear risk	not described
Timing outcome assessments similar?	Low risk	reported in text

Hou 2002

Methods	RCT Blinding: none Analysed/randomized: 71/71
Participants	Myofascial neck pain; duration of disorder not specified G1: N = 9 G2: N = 9 G3: N = 9 G4: N = 21 G5: N = 13 G6: N = 10
Interventions	G1: TENS 100 Hz/ 0.25 ms, ischemic compression, hot pack 20 minutes, Active ROM exercise G2: TENS 100 Hz/ 0.25 ms, spray and stretch, hot pack for 20 minutes, Active ROM exercises G3: interferential current (100 Hz interfering wave for 20 minutes), myofascial release technique, hot pack for 20 minutes, Active ROM exercises G4: hot pack 20 minutes, Active ROM exercise G5: ischemic compression, hot pack 20 minutes, Active ROM exercise G6: spray and stretch by Simon et al, hot pack for 20 minutes, Active ROM exercise Treatment schedule: 1 session

Outcomes	PAIN INTENSITY (VAS) reported results: all groupsG1-G6 have significantly improved concerning pre/post treatment (P < 0.05) G4 versus G3: RR: -1,20 (95% CI Random: -2.50, -0.36) = hot pack versus interference (P < 0.05) G4 versus G2: RR: -1,17 (95% CI Random: -2.02, - 0.33 = hot pack versus TENS (P < 0.05) Reported Results: G1 versus G2 not significant,G2 versus G6 not significant, G3 versus G4 significant favouring G3, G1 versus G5 not significant SMD (G1 versus G5): 0.56 (95% CI Random: -1.43, 0.31) SMD (G2 versus G6): -0.72 (95% CI Random: -1.65, 0.22) SMD (G3 versus G4): -1.20 (95% CI Random: -2.05, -0.36) SIDE EFFECTS: not reported COST OF CARE: not reported
Notes	20 minutes TENS treatment time appears to be extremely short designed, compared to usual recommendations (at least 30 minutes for TENS)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	randomisation not described
Allocation concealment (selection bias)	High risk	not concealed
Blinding (performance bias and detection bias) All outcomes - patients?	High risk	not possible
Blinding (performance bias and detection bias) All outcomes - providers?	High risk	not possible
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	High risk	VAS assessed by patients
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Unclear risk	unclear, not described in results

Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Unclear risk	not described
Selective reporting (reporting bias)	Unclear risk	no protocol
Similarity of baseline characteristics?	High risk	table 1: seven groups are different in age
Co-interventions avoided or similar?	Unclear risk	not described
Compliance acceptable?	Unclear risk	not reported
Timing outcome assessments similar?	Low risk	reported in text

Hsueh 1997

Methods	RCT Blinding: patients, observer Analysed/randomized: 60/60 patients
Participants	Chronic myofascial neck pain with trigger points at trapezius muscle G1: N = 22 G2: N = 20 G3: N = 18
Interventions	G1: Group A or TENS (60 Hz) at trapezius muscle; feel strong stimulation without muscle contraction G2: Group B or EMS (electrical muscle stimulation); 10 Hz; visible trapezius muscle stimulation G3: Group C or sham electrotherapy at trapezius muscle Treatment schedule: 1 session, 20 minutes

Outcomes	PAIN INTENSITY (VAS): Baseline Mean: not reported Reported Results: significant improvement favouring group B versus C; not significant group A versus C SMD (A versus C): -0.36 (95% CI Random: -0.99, -0.27) SMD (B versus C): -2.60 (95% CI Random: -3.48, -1.71) Power: 6% SIDE EFFECTS: not reported COST OF CARE: not reported
Notes	20 minutes TENS treatment time appears to be extremely short, compared to usual recommendations (at least 30 minutes for TENS)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	type of randomisation not described
Allocation concealment (selection bias)	Unclear risk	unclear as described
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - providers?	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	reported in text
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	reported in text
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	reported in text
Selective reporting (reporting bias)	High risk	most data given as percentage change only

Similarity of baseline characteristics?	High risk	most data given as percentage change only
Co-interventions avoided or similar?	Low risk	reported in text
Compliance acceptable?	Low risk	reported in text
Timing outcome assessments similar?	Low risk	reported in text

Hurwitz 2002

Methods	RCT (2x2x2 factorial design) Analysed/Randomized: 269/336
Participants	Subacute and chronic neck pain with or without radicular symptoms and cervicogenic headache Manipulaton groups G1/G2/G5 /G6 total N = 171 Mobilisation groups G3/ G4/ G7/ G8 total N = 165 Single groups: N = NR

Interventions	G1: Manipulation with electrical muscle stimulation (Manip/EMS): 10-minute application of EMS before manipulation; EMS parameters not reported G2: Manipulation with electrical muscle stimulation (Manip/EMS) and heat: 10-minute moist heat application and EMS simultaneously before mobilisation G3: Mobilisation with EMS (Mob/EMS): 10-minute application of this modality before mobilisation; parameters NR G4: Mobilisation with heat and electrical muscle stimulation (Manip/EMS) G5: Manipulation (Manip): at least 1 controlled, dynamic thrust applied with high velocity low amplitude force, directed at 1 or more restricted upper thoracic or cervical spine joint segments G6: Manipulation with heat (Manip/Heat): 10-minute moist heat application before manipulation G7: Mobilisation (Mob): 1 or more low velocity, variable amplitude movements directed to 1 or more restricted upper thoracic or cervical spine joint segments G8: Mobilisation with heat (Mob/Heat): 10-minute moist heat application before mobilisation Co-intervention: All participants received information on posture and body mechanics and one or more of the following: stretching, flexibility, or strengthening exercises and advice about ergonomic and workplace modifications Treatment schedule: unclear: "...at least 1 treatment..." (manip / mob) No maximum, no average number of treatments reported Measurements / follow up: 2 weeks; 6 weeks; 3 months; 6 months
Outcomes	PAIN INTENSITY (most severe pain, NRS 0 to10) Baseline Mean: Not reported for each subgroup Reported Results: no significant differences e.g.: at 6 months SMD (EMS + manip versus manip): 0.07 (95% CI -0.40 to 0.55) DISABILITY (NDI 0 to 50) Reported Results: no significant difference at 6 months SMD (EMS + manip versus manip): 0.08 (95% CI: -0.39 to 0.55) PATIENT SATISFACTION Reported Results: no significant difference at 4 weeks SMD (EMS + manip versus manip): -0.13 (95% CI: -0.60 to 0.35) SIDE EFFECTS: interviewed at 4 weeks of care, no known study-related adverse events

Notes	Factorial design. No relevant differences between EMS (G3, G4, G7, G8) v no EMS (G1, G2, G5, G6) "At least 1 treatment", but no maximum, no average number of treatments by mob/ manip or modalities reported 10 minutes modalities treatment time appears extremely short design, compared to usual recommendations (at least 30 minutes). No setting parameters for EMS were reported Missing Data: a request to clarify the specific treatment parameters was sent but no response received. However, a request for data (end of study mean and SD for each outcome) was sent and response received from Hurwitz 2002.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	reported in text
Allocation concealment (selection bias)	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - patients?	High risk	not possible; differences in treatment methods
Blinding (performance bias and detection bias) All outcomes - providers?	High risk	not possible
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	High risk	subjective rating of pain
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	reported in text

Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Unclear risk	not described
Selective reporting (reporting bias)	Unclear risk	not described
Similarity of baseline characteristics?	Low risk	reported in text
Co-interventions avoided or similar?	Unclear risk	not described
Compliance acceptable?	Low risk	reported in text
Timing outcome assessments similar?	Low risk	reported in text

Nordemar 1981

Methods	RCT Blinding: none Analysed/randomized: 30/30 patients
Participants	Acute non-specific neck pain (< 3 days; without radiation) G1: N = 10 G2: N = 10 G3: N = 10
Interventions	G1: TENS: 80 Hz; intensity just below pain threshold; neck collar, rest, exercise, analgesic G2: Manual Therapy (MT): soft tissue treatment, manual traction, neuromuscular mobilization, collar, rest, exercise, analgesic G3: Neck collar, rest, exercise, analgesic Treatment schedule: G1: 3 times per week; 15 minutes G2: 3 times per week; 30 minutes G3: intermittent collar use over 2 weeks Follow-up: after 6 weeks

Outcomes	PAIN INTENSITY (VAS 100 mm): Baseline Mean: TENS 83, MT 97, collar 90 End of Study Mean: TENS 0, MT 0, collar 0 Absolute Benefit: TENS 83, MT 97, collar 90 Reported Results: no significant difference SMD (TENS versus collar): -0.50 (-1.39, 0.39) SMD (TENS versus MT): -0.04 (-0.92, 0.83) Power: 8% SIDE EFFECTS: not reported COST OF CARE: not reported
Notes	Most patients had no need of treatment after first week in all groups

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	consecutive distribution to three groups
Allocation concealment (selection bias)	High risk	not described
Blinding (performance bias and detection bias) All outcomes - patients?	High risk	not reported
Blinding (performance bias and detection bias) All outcomes - providers?	High risk	not reported
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	High risk	not reported
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	High risk	quick recovery of most cases within one week, while therapy was planned for 3 weeks (many dropouts)
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	reported in text
Selective reporting (reporting bias)	Unclear risk	unclear

Similarity of baseline characteristics?	High risk	strong deviations because of small group size
Co-interventions avoided or similar?	High risk	self medication allowed
Compliance acceptable?	Unclear risk	not reported
Timing outcome assessments similar?	Unclear risk	not reported

Philipson 1983

Methods	RCT Blinding: patients Analysed/Randomized: 40/40 patients
Participants	Chronic non-specific neck and shoulder pain G1: N = 20 G2: N = 20
Interventions	G1: Diadynamic Current (LP) G2: Placebo group: current turned up until patient felt sensation in neck, then turned off Treatment schedule: 4 minutes each at 3 trigger points; 5 consecutive days
Outcomes	PAIN INTENSITY (VAS): Baseline Mean: not reported Reported Results: not significant difference RR: 0.69 (95% CI Random: 0.39, 1.24) Power: 13% PATIENT RATED IMPROVEMENT (5-point scale): Baseline Mean: not reported Reported Results: no significant difference; RR: 0.07 (95% CI Random: 0.33, 1.47) SIDE EFFECTS: not reported COST OF CARE: not reported
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Unclear risk	not reported
Allocation concealment (selection bias)	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - providers?	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	High risk	not reported
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Unclear risk	not reported
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Unclear risk	not reported
Selective reporting (reporting bias)	Unclear risk	not reported
Similarity of baseline characteristics?	Low risk	reported in text
Co-interventions avoided or similar?	Unclear risk	not reported
Compliance acceptable?	Unclear risk	not reported
Timing outcome assessments similar?	Low risk	reported in text

Sahin 2011

Methods	RCT Blinding: none
Participants	Forty patients with cervical myofascial pain syndrome [MPS] > 3 months Groups, randomized / analysed G1 n = 20 / 19 G2 n = 20 / 18 G3 n = 20 / 19 G4 n = 20 / 19

Interventions	G1: Conventional TENS with a frequency of 100 Hz, 40 µs duration, low amplitude G2: Acupuncture-like TENS (AL-TENS) with a frequency of 4 Hz, 250 µs duration, high amplitude G3: Burst TENS with high [100 Hz] and low [2 Hz] frequency, 40 µs, high amplitude G4: Placebo TENS: electrical stimulation until patients sensation, then turned down to zero Treatment schedule: 30 minutes, 3 times a week, until 10 sessions completed Follow up: Not reported
Outcomes	PAIN INTENSITY (VAS 0 to 10) BASELINE Mean G1 conventional TENS (n =19) 7.12 G2 AL-TENS (n = 18) 6.15 G3 Burst TENS (n = 19) 6.85 G4 Placebo TENS (n = 19) 7.56 Reported Results: no significant difference SMD (G1 versus G4) -0.07 [95% CI Random: -0.71 to 0.56] SMD (G1 versus G2) 0.20 [95% CI Random: -0.45 to 0.84] SMD (G1 versus G3) 0.39 [95% CI Random: -0.25 to 1.03] SIDE EFFECTS: not found COST OF CARE: not reported
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	not reported
Allocation concealment (selection bias)	Unclear risk	not reported

Blinding (performance bias and detection bias) All outcomes - patients?	Unclear risk	not reported
Blinding (performance bias and detection bias) All outcomes - providers?	High risk	provider would likely know what settings are used on the TENS unit
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Unclear risk	not reported
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	reported
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	High risk	not reported
Selective reporting (reporting bias)	Unclear risk	not reported
Similarity of baseline characteristics?	Unclear risk	unclear
Co-interventions avoided or similar?	Unclear risk	not reported
Compliance acceptable?	Unclear risk	not reported
Timing outcome assessments similar?	Unclear risk	not reported

Smania 2003

Methods	RCT Blinding: patients examiner regarding treatment therapist regarding clinical status Analysed/Randomized: 18/18
Participants	Myofascial neck pain (trigger points at upper trapezius; duration not specified) G1: N = 9 G2: N = 9

Interventions	G1: Repetitive Magnetic Stimulation (rMS), Magstim Super Rapid Stimulator by Magstim company, intensity up to 400 mT (4000 G), 4000 pulses, administered in 5 sec trains at 20 Hz, separated by 25 sec pauses G2: detuned ultrasound (Supersonic 1010, Italy) Co-interventions: avoid any PT for 2 months, refrain from taking any analgesic drug for 15 days, no other treatment during study Treatment schedule: 2 weeks, 10 sessions; duration: 20 minutes each Follow up: 1 week and 1 month after treatment
Outcomes	NECK PAIN AND DISABILITY (NPDVAS 0-100) Baseline Mean and other values: graphed post-treatment; SMD: -0.89 (95% CI Random:- 1.87, 0.09) follow-up 1 week after treatment; SMD: -1.39 (95% CI Random: -2.44, -0.33) follow-up 1 month after treatment: SMD -1.08 (95% CI Random: -2.08, -0.07); NNT 3; treatment advantage 56% SIDE EFFECTS: not reported COST OF CARE: not reported
Notes	Amelioration from "after treatment" to 1-month follow-up reported. Pilot study with small groups; see also Smania 2005, similar trial with 53 patients. Funding not reported.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	reported in text
Allocation concealment (selection bias)	Unclear risk	not reported
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	reported in text

Blinding (performance bias and detection bias) All outcomes - providers?	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	reported in text
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	reported in text
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	reported in text
Selective reporting (reporting bias)	Unclear risk	not reported
Similarity of baseline characteristics?	Low risk	reported in text
Co-interventions avoided or similar?	Low risk	no medication during trial
Compliance acceptable?	High risk	not reported
Timing outcome assessments similar?	Low risk	timing of final outcome is unclear

Smania 2005

Methods	RCT Blinding: patients examiner regarding treatment therapist regarding clinical status Analysed/Randomized: 53/53

Participants	Myofascial neck pain syndrome (trigger points at upper trapezius; duration not specified) G1: N = 17 G2: N = 18 G3: N = 18 at 3 month follow-up: G1: N = 15 G2: N = 16 G3: N = 15 32 patients excluded (from 85) before randomization (53)
Interventions	G1: Repetitive Magnetic Stimulation (rMS), Magstim Super Rapid Stimulator by Magstim company, intensity up to 400 mT (4000 G), 4000 pulses, administered in 5 sec trains at 20 Hz, separated by 25 sec pauses; 20 minutes duration G2: TENS (Phyacton 787; Uniphy, Netherlands) 100 Hz; 0,25 ms pulse width; asymmetrical rectangular biphasic wave form; intensity at comfort below muscular contraction; placement: negative electrode over most painful trigger point G3: detuned ultrasound (Supersonic 1010, Italy) Co-interventions: no PT for 2 months, no analgesic drug for 15 days, no other treatment during study Treatment schedule: 2 weeks, 10 sessions; duration: 20 minutes each Follow up: 1 week, 1 month and 3 months after treatment
Outcomes	NECK PAIN AND DISABILITY (NPDVAS 0-100) Baseline Mean and other values: graphed rMS versus Placebo US: G1 versus G3: post-treatment; SMD: -0.77 (95% CI Random:- 1.46, -0.08) G1 versus G3: follow-up 1 month after treatment; SMD-1.51 (95% CI Random: -2.27, -0.74); NNT 3; treatment advantage: 45.6% G1 versus G3: follow-up 3 month after treatment: SMD -1.01 (95% CI Random: -1.77, -0.24) TENS versus Placebo US: G2 versus G3: post-treatment; SMD: -0.89 (95%CI Random: -1.76, -0.28) G2 versus G3: follow-up 1 month after treatment; SMD -0.65 (95% CI Random: -1.32, -0.02) G2 versus G3: follow-up 3 month after treatment: SMD -0.52 (95% CI Random: -1.24, -0.20) SIDE EFFECTS: not reported COST OF CARE: not reported
Notes	See also Smania 2003, similar trial with 18 patients in total

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	reported in text
Allocation concealment (selection bias)	Unclear risk	not reported
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - providers?	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	reported in text
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Unclear risk	not described, but reported in fig. 1
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Unclear risk	not described
Selective reporting (reporting bias)	Unclear risk	not described
Similarity of baseline characteristics?	High risk	table 1 age: much different in the placebo group

Co-interventions avoided or similar?	Unclear risk	no medication during trial
Compliance acceptable?	Unclear risk	not described
Timing outcome assessments similar?	Low risk	reported in text

Sutbeyaz 2006

Methods	RCT Blinding: patients, observer Analysed/randomized: 32/34 (27 patients excluded before randomizations)
Participants	Cervical osteoarthritis G1: N = 17 G2: N = 15
Interventions	G1: PEMF System: Wave Ranger Professional (MRS 2000+ Home, FL-9492 Eschen); intensity 0,04 mT; frequency range 0.1- 64Hz, applied frequency not reported; application by whole body mat 1.8x0.6 m size G2: same conditions as in G1, PEMF inactivated (sham control) Co-interventions: NSAIDs if necessary, need recorded at end of study Treatment schedule: 3 weeks, 2 times a day; duration 30 minutes

Outcomes	PAIN INTENSITY (VAS; 0 to 10 points) after 3w treatment; SMD: -3.17(95% CI Random:- 4.25 to -2.09) NECK PAIN AND DISABILITY SCORE (NPDS; 0 to 100 points) after 3w treatment; SMD: -3.56 (95% CI Random:- 4.72 to -2.40) Reported statistical analysis: G1 pre/post: P<0.001 for all items G2 pre/post: not significant for all items Baseline values differences: not significant for all items GLOBAL PERCEIVED EFFECT (0 to 3, more is better) after 3w treatment; SMD: -3.17(95% CI Random:-4.25 to -2.09) SIDE EFFECTS: not reported COST OF CARE: not reported
Notes	The credibility of the results, strongly favouring PEMF and contrasting with no sham control effects, seems very low. Support e.g. by MRS 2000 company is neither reported, nor excluded, so funding bias has to be taken in account.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	reported in text
Allocation concealment (selection bias)	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - providers?	High risk	primary outcome VAS assessed by patients

Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	reported in text
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	reported in text
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	reported in text
Selective reporting (reporting bias)	Unclear risk	not reported
Similarity of baseline characteristics?	Low risk	reported in text
Co-interventions avoided or similar?	Unclear risk	not reported
Compliance acceptable?	Low risk	reported in text
Timing outcome assessments similar?	Low risk	reported in text

Thuile 2002

Methods	RCT Blinding: none Analysed/Randomized: 92/92
Participants	Whiplash I and II (WAD) pain in neck and/or "in the back of the head" (duration not specified) G1: N = 44 G2: N = 48

Interventions	G1: PEMF System, MRS 2000 plus MED (Vitalife Inc, Austria); intensity 0,01 to 0,03 mT, basic frequency 64Hz; duration: 16 minutes local magnetic cushion application, followed by 8 minutes whole body mat treatment ; medication: diclofenac, tizanidine G2: Standard Therapy, diclofenac, tizanidine (no sham control) Treatment schedule: 2 weeks, 2 times per day (G1)
Outcomes	PAIN INTENSITY (VAS, 0-10) Baseline Mean: G1 6.3, G2 5.3 End of Study Mean: G1 1.9, G2 4.6 Absolute Benefit: G1 4.4, G2 0.7 Reported Results: significant differences, P<0.03 each SMD (neck pain): -2.86 (95% CI Random: -2.79, -1.74) SMD (headache): -2.27 (95% CI Random: -2.81, -1.75) SIDE EFFECTS: not reported COST OF CARE: not reported
Notes	Control group with standard medication only, no placebo magnetic field therapy; The credibility of the results appears to be very low. Support, e.g. by Vitalife Inc, Austria, is neither reported, nor excluded, so funding bias is possible.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	patients were assigned on a 1:1 ratio
Allocation concealment (selection bias)	Unclear risk	not described
Blinding (performance bias and detection bias) All outcomes - patients?	Unclear risk	not described

Blinding (performance bias and detection bias) All outcomes - providers?	High risk	blinding of observer not reported
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	High risk	pain score rated by patient
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Unclear risk	not described in results, but in methods on page 64
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Unclear risk	not described
Selective reporting (reporting bias)	Unclear risk	not described
Similarity of baseline characteristics?	Low risk	reported in text
Co-interventions avoided or similar?	Unclear risk	not described
Compliance acceptable?	Unclear risk	not described
Timing outcome assessments similar?	Low risk	reported in text

Trock 1994

Methods	RCT Blinding: patients, observer Analysed/randomized: 70/81 Intention-to-treat: not reported
Participants	Chronic non-specific neck pain with radiologic findings of degenerative changes G1: N = 42 G2: N = 39
Interventions	G1: PEMF therapy (5/10/12 Hz, rectangular; 10 minutes for each frequency) G2: sham PEMF Co-interventions: medication, physiotherapy Treatment schedule: 18 sessions lasting 30 minutes each, over 4 to 6 weeks Follow-up: 1 month after treatment
Outcomes	PAIN INTENSITY (VAS 100 mm): Baseline Median: PEMF 72.02, placebo 62.30 End of Study Median: PEMF 46.16, placebo 47.64 Absolute Benefit: PEMF 25.88, placebo 14.66 at ST follow-up; SMD:-0.37 [95% CI Random:-0.85 to 0.10] Reported Results: short term benefits, significant , P < 0.04 at end of treatment; not significant, P = 0.1 at 1 month follow-up Power: 41% FUNCTION (Acivity of Daily Living; 0 to 24): Baseline Mean: PEMF 11.94, placebo 11.5 End of Study: PEMF 8.16, placebo 9.36 Absolute Benefit: PEMF 3.78, placebo 2.14 at ST follow-up; SMD: -0.25 [95% CI Random:-0.72 to 0.23] Reported Results: not significant GLOBAL RATING OF IMPROVEMENT (VAS 0 to 10 cm, more is better): at ST follow-up; SMD 0.03 (95% CI Random: 0.03 (-0.44 to 0.50) Reported Results: not significant SIDE EFFECTS: not reported COST OF CARE: not reported
Notes	Funding bias may be present. Research support declared as Bio-Magnetic Systems, Inc. (Co-author Markoll was principle shareholder of Bio-Magnetic Sytems; Markoll and Trock were sentenced in 2001 for billing unapproved electro-magnetic therapy (see FDA report: http://www.fda.gov/ora/about/enf_story/archive/2001/ch6/oci6.htm).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	reported in text
Allocation concealment (selection bias)	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - patients?	Low risk	reported in text
Blinding (performance bias and detection bias) All outcomes - providers?	Unclear risk	not reported
Blinding (performance bias and detection bias) All outcomes - outcome assessors?	Low risk	reported in text
Incomplete outcome data (attrition bias) All outcomes - drop-outs?	Low risk	reported in text
Incomplete outcome data (attrition bias) All outcomes - ITT analysis?	Low risk	reported in text

Selective reporting (reporting bias)	Unclear risk	not reported
Similarity of baseline characteristics?	High risk	table 1 showed differences in age table 2 showed differences in pain
Co-interventions avoided or similar?	Unclear risk	instruction: not to change medication during trial
Compliance acceptable?	Unclear risk	unclear at least for medication (not controlled)
Timing outcome assessments similar?	Low risk	reported in text

N = number of participants
DC = direct current
PT = physiotherapy

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Ammer 1990	Intervention: multimodal treatment; the unique contribution of electrotherapy could not be determined
Chee 1986	Design: quasi-RCT (drew cards and divided in two groups); extremely small sample size (7 versus 9 patients) Outcome: palpatory evaluation of the presence of trigger point was no a pain or surrogate pain intensity measure
Chen 2007	Population: Headache only, unable to split cervicogenic headache data
Coletta 1988	Population: Unable to split data
Dusunceli 2009	Comparison: Both comparison studies received the same TENS treatment
Fernadez-de-las Penas2004	Intervention: Multimodal treatment for control group; no description of specific parameters for electrotherapy; unable to split data; no further data from authors available on request

Study	Reason for exclusion
Forestier 2007a	Intervention: Thermal agent used (pulsed short wave, 200W)
Forestier 2007b	Intervention: Thermal agent used (pulsed short wave, 200W)
Gabis 2003	Population: 20 patients, only three of them with cervicogenic headache
Gabis 2009	Intervention: trancranial electrical stimulation is not classical TENS Population: chronic pain only 23 had cervical pain Outcome: insufficient data on neck
Garrido-Elustondo 2010	Outcome: Key parameter is only satisfaction of patients with all kinds of physiotherapy; TENS is only mentioned
Gemmell 2011	No neck pain; just stimulated trigger points
Gonzales-Iglesias 2009	Intervention: Both comparison groups received TENS
Hansson 1983	Population: Not neck pain (oro-facial pain)
Jahanshahi 1991	Population: Not neck pain
Klaber-Moffett 2005	Intervention: Multimodal treatment; unable to split data; less than 10% of patients received 6 different kinds of electrotherapy
Lee 1997	Intervention: Small group size (4groups with a total of 26 patients); multimodal treatment (combination of medium frequency AC+DC electrotherapy plus ultrasound)
Persson 2001	Intervention: Multimodal treatment; the unique contribution of electrotherapy could not be determined
Porzio 2000	Population: Fewer than 80% of included patients had neck pain
Provinciali 1996	Intervention: Multimodal treatment; the unique contribution of electrotherapy could not be determined
Rigato 2002	Population: Fewer than 80% of included patients had neck pain
Vas 2006	Intervention: Placebo TENS, no active intervention of electrotherapy
Vikne 2007	Intervention: Electrotherapy mentioned, but no modality type or parameters mentioned

Study	Reason for exclusion
Vitiello 2007	Design: Data were severely flawed in many points (recalculated and evaluated by a statistician). The communication with authors did not improve the credibility, neither of the data, nor of the results
Wang 2007	Population: 4 x 30 patients with pain of neck, shoulder, loin and legs, treated with four different kinds of electro-acupuncture (excluded in this review). Unable to split data
Wilson 1974	Population: Not neck pain (soft tissue injury as a result of inversion injury of the ankle)
Yip 2007	Design: Quasi-RCT

Characteristics of ongoing studies [ordered by study ID]

Guayasamín 2013

Trial name or title	Study of clinical documentation, controlled, double-blind, randomized, multicenter, designed to evaluate the effectiveness and tolerance of fixed combination of thiocolchicoside plus diclofenac potassium in reduction of acute painful muscle contracture
Methods	Dr. Ivan Guayasamín, Medical Surgeon
Participants	Acute painful striated muscle contracture,(cervical pain, backache, low back pain without sciatica, etc.); age 18 to 58; male/female
Interventions	Group I (experimental): 1 single tablet that contains in combination thiocolchicoside 4mg plus potassium diclofenac 50 mg every 12 hours by mouth to complete 10 doses, 5 days of treatment (TIO+DICLOK). Group II (Control): placebo, 1 tablet inactive every 12 hours orally to complete 10 doses, 5 days of treatment. Group I and Group II: Acetaminophen 500 mg as rescue medication PRN; Sample size n=90

Outcomes	Primary outcome(s): 1. Evaluation of efficacy 1.1 Muscular contracture degree by a visual inspection (Contracture visible muscle mass with fixed-antalgic attitude, Contracture visible muscle mass without fixed-antalgic attitude, No visual signs of muscle contracture). Measuring time: at baseline and after finished the treatment (Day 5). 1.2 Muscular contracture degree by palpation (Contracture severe with evoked pain during palpation, Contracture moderate with evoked pain during palpation, Contracture mild without evoked pain during palpation, Absence contracture). Measuring time: at baseline and after finished the treatment (Day 5). 1.3 Degree of overall pain intensity (Visual Analogue Scale (VAS) of 10 cm, ranging from no pain to worst pain imaginable very severe). Measuring time: at baseline and after finished the treatment (Day 5). 2. Evaluation of tolerability 2.1 Possible Adverse Reactions (AR). Measuring time: after finished the treatment (Day 5): - Occurrence of some AR in the subject (yes / no) - Nature of the AR (adverse event name) - Intensity of AR (Mild, moderate, severe) - Duration of AR (difference between the start date and the completion of the event) - Causation (causal categories described by the Uppsala Monitoring Centre (WHO): Definite, probable, possible, unlikely, conditional, not evaluable) - Treatment (medication withdrawal, other) - Severity of AR (Severe / serious; Not severe / not serious) Key secondary outcomes: 1. Efficacy 1.1 Efficacy of treatment by the patient (Very effective, Effective, Moderately Effective, Not effective (Ineffective). Measuring time: at the end of the treatment (Day 5) 1.2 Rescue medication (yes / no). Measuring time: at the end of the treatment (Day 5) 1.3 Total Tablets of rescue medication (Number of tablets). Measuring time: at the end of the treatment (Day 5) 1.4 Daily Tablets of rescue medication (Number of tablets). Measuring time: daily during the treatment 2. Tolerability 2.1 Tolerability of treatment by the patient (Very good, Good, Fair, Poor). Measuring time: at the end of the treatment (Day 5) 2.2 Degree of alertness - sleepiness (Visual Analogue Scale (VAS) of 10 cm, ranging from awake (alert) to severe sleepiness (sleeping)). Measuring time: at baseline and after finished the treatment (Day 5) 2.3 Psychomotor activity level (Tapping test (hitting the keyboard of a personal computer as soon as possible) for 30 seconds, record the number of hits). Measuring time: at baseline and after finished the treatment (Day 5) 2.4 Psychomotor activity level (Pauli Test for 3 minutes, recorded the number of successes achieved). Measuring time: at baseline and after finished the treatment (Day 5) 3. Efficacy and Tolerability 3.1 Overall rating of treatment by the investigator (Clinical Global Impression scale). Measuring time: at the end of the treatment (Day 5) 3.2 Overall treatment satisfaction by the investigator (Very Satisfied, Satisfied, Moderately satisfied, not satisfied (dissatisfied)). Measuring time: at the end of the treatment (Day 5) 3.3 Overall treatment satisfaction by the patient (Very Satisfied, Satisfied, Moderately satisfied, not satisfied (dissatisfied)). Measuring time: at the end of the treatment (Day 5)
Starting date	Recruitment status: Complete Date of first enrollment: 2012/04/15
Contact information	First Name: Ana Middle Name: María Last Name: Fallas Quezada Affiliation: Gutis Ltda. Postal Address: Zona industrial de Pavas, 300 metros al oeste de las oficinas centrales de Pizza Hut City: San Jose País: Costa Rica Zip Code: Apdo. 5391-1000 Telephone: +(506) 2549 8300 Dirección de correo electrónico: a.fallas@gutis.com
Notes	Ecuador

Taniguchi 2010

Trial name or title	Effect of neck-type magnetotherapeutic device (magneloop) for neck and shoulder pain
Methods	
Participants	

Interventions	
Outcomes	
Starting date	
Contact information	
Notes	Abstract of a congress presentation Unpublished data only [14th Congress of Asia Pacific League of Associations for Rheumatology, APLAR 2010 Hong Kong Hong Kong. Conference Start: 20100711 Conference End: 20100715. Conference Publication: 230.; Taniguchi N, Kanai S. In: International Journal of Rheumatic Diseases. 2010

Triano 2009

Trial name or title	InterX 5000 - A new treatment technique for people with chronic neck and shoulder pain
Methods	a nerve stimulation device called the InterX 5000
Participants	chronic neck and shoulder pain, > 3 months
Interventions	InterX 5000 neurostimulator; 3 consecutive sessions, 3 times per week, 6 weeks, 20 minute sessions
Outcomes	Electromyography scan or an EMG, the Neck Walk Index (NWl), the Upper Limb Coordination During an Overhead Reach (ULCS) test, and the Task Limitation (Tl)/Functional lmpairment Test-Head and Neck, Shoulder, Arm (FlT-HaNSA)
Starting date	2007 to June 2011
Contact information	Dr. John J. Triano, Canadian Memorial Chiropractic College Dr Linda Woodhouse at the School of Rehabilitation Science at McMaster University, 905-525-9140 Ext.2259
Notes	Industry Funder: Neuro Resource Group INC Woodhouse L & Triano J. Proposal to evaluate the efficacy of the InterX5000 in the treatment of chronic neck and shoulder pain. Neuro Group Inc, $100,000, 2007-06/2009-05.

Weintraub 2007

Trial name or title	Study on Magnetic Field Therapy to Improve Quality of Sleep and Reduction of Chronic Spine Pain (SLEEP/MAG)

Methods	Allocation: Randomized Endpoint Classification: Efficacy Study Intervention Model: Parallel Assignment Masking: Double-Blind Primary Purpose: Treatment
Participants	18 Years to 85 Years; male/female Inclusion Criteria: • Female or male subjects age 18-80. • Capable of understanding and complying with study protocols. • Chronic cervical, thoracic or lumbar pain for at least six months. • Sleep difficulties and/or insomnia Exclusion Criteria: • Unable to understand informed consent (mental retardation, psychosis, communicative impairment). • Cardiac pacemaker or other mechanical internal devices. • Tumor in the spine/history of malignancy. • Pregnancy. • Prior spine surgery
Interventions	Treated subjects will receive a permanent/static magnetic sleeping pad with a nominal strength of less than 1000 Gauss. Control subjects will receive physically identical sleeping pad with a nominal surface field strength of 0 Gauss (placebo). The magnets will be contained in a standard mattress pad and subjects will sleep on the pad.
Outcomes	Primary Outcome Measures: VAS Pain scores/Pittsburgh Sleep scores/Insomnia sleep scores/SF 15 pain descriptor scores/PGIC/ Secondary Outcome Measures: Autonomic Nerve Functions
Starting date	September 26, 2007
Contact information	Weintraub, Michael I., MD, FACP, FAAN; miwneuro@pol.net
Notes	The recruitment status of this study is unknown because the information has not been verified recently.

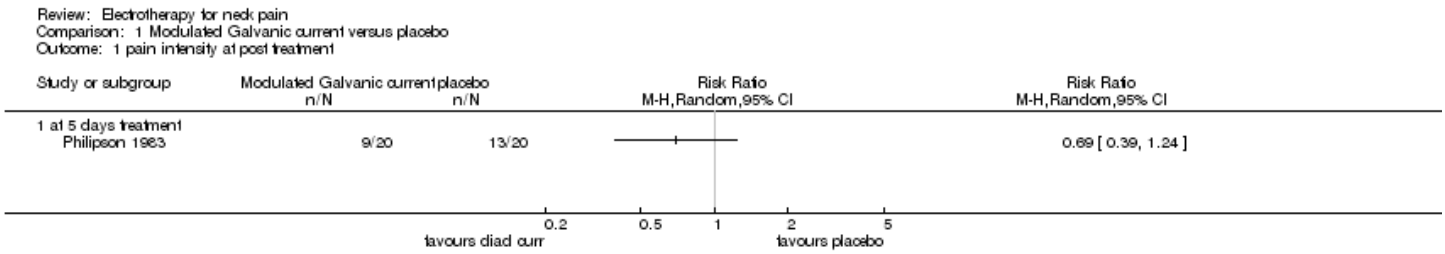
Data and analyses

Comparison 1. Modulated Galvanic current versus placebo **Open in table viewer**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 pain intensity at post treatment Show forest plot	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 1.1

Open in figure viewer | Download as PowerPoint



Comparison 1 Modulated Galvanic current versus placebo, Outcome 1 pain intensity at post treatment.

1.1 at 5 days treatment	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 patient rated improvement at post treatment Show forest plot	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 1.2

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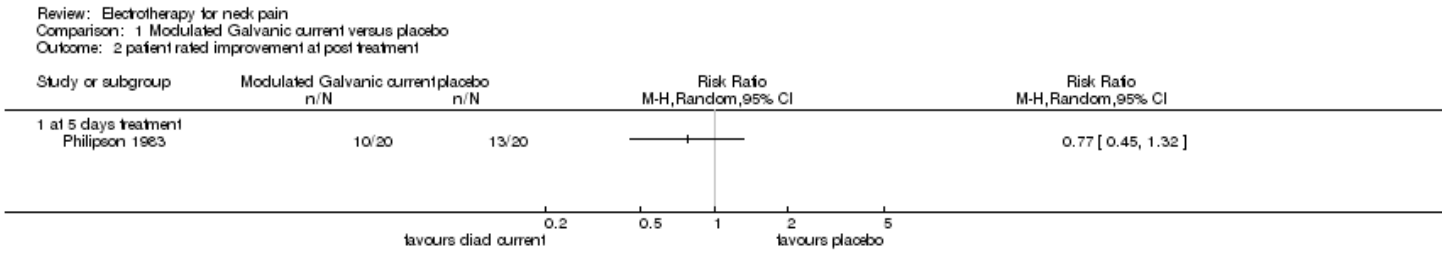


Comparison 1 Modulated Galvanic current versus placebo, Outcome 2 patient rated improvement at post treatment.

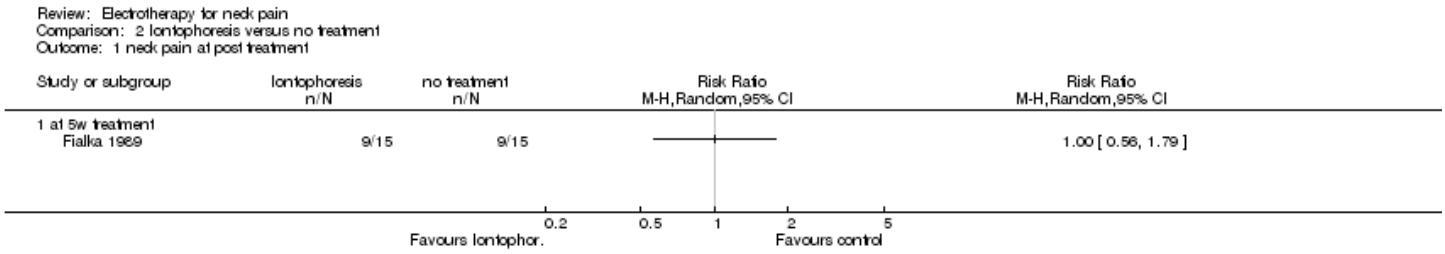
2.1 at 5 days treatment	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 2. Iontophoresis versus no treatment **Open in table viewer**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 neck pain at post treatment Show forest plot	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 2.1

Open in figure viewer | **Download as PowerPoint**

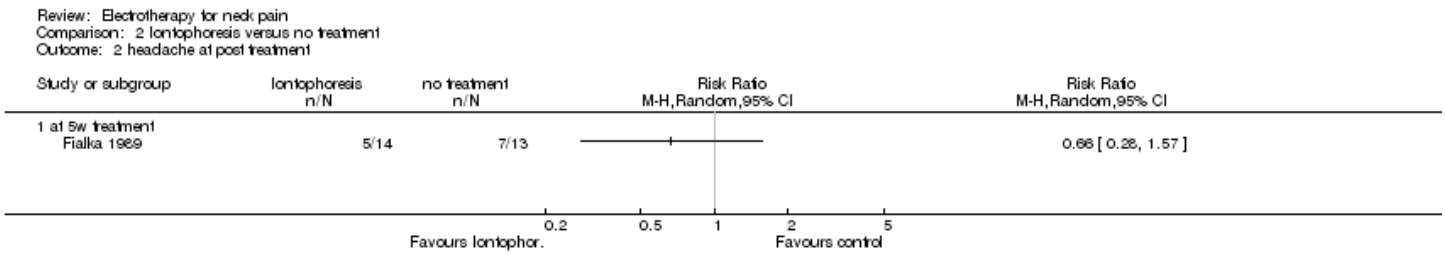


Comparison 2 Iontophoresis versus no treatment, Outcome 1 neck pain at post treatment.

1.1 at 5w treatment	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 headache at post treatment Show forest plot	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 2.2

Open in figure viewer | **Download as PowerPoint**



Comparison 2 Iontophoresis versus no treatment, Outcome 2 headache at post treatment.

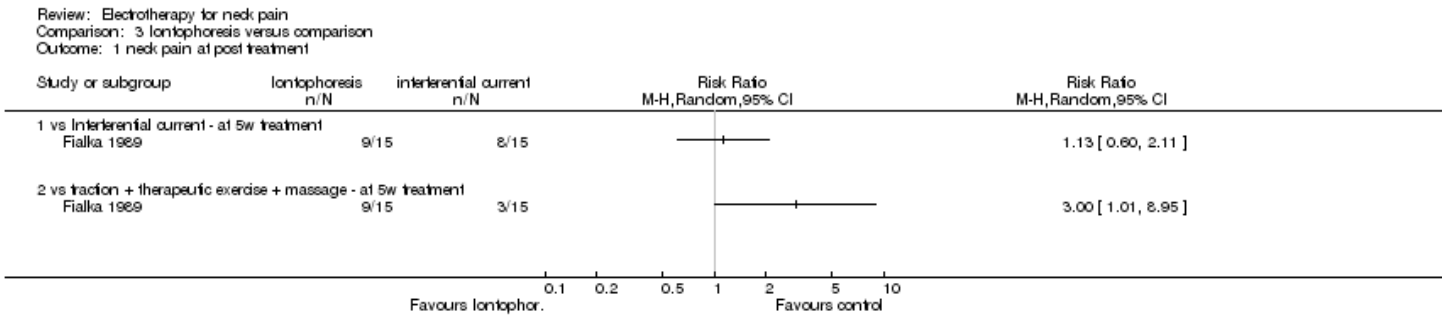
2.1 at 5w treatment	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 3. Iontophoresis versus comparison **Open in table viewer**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 neck pain at post treatment Show forest plot	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 3.1

Open in figure viewer | Download as PowerPoint



Comparison 3 Iontophoresis versus comparison, Outcome 1 neck pain at post treatment.

1.1 vs Interferential current - at 5w treatment	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 vs traction + therapeutic exercise + massage - at 5w treatment	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 4. TENS versus placebo or sham

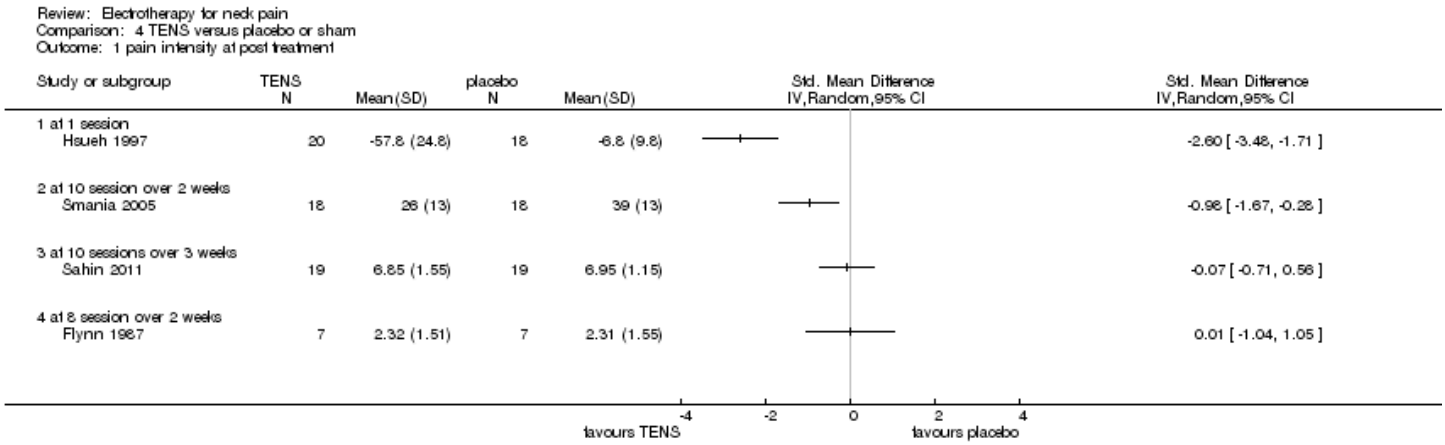
Open in table viewer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 pain intensity at post treatment Show forest plot	4		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 4.1

Open in figure viewer | Download as PowerPoint

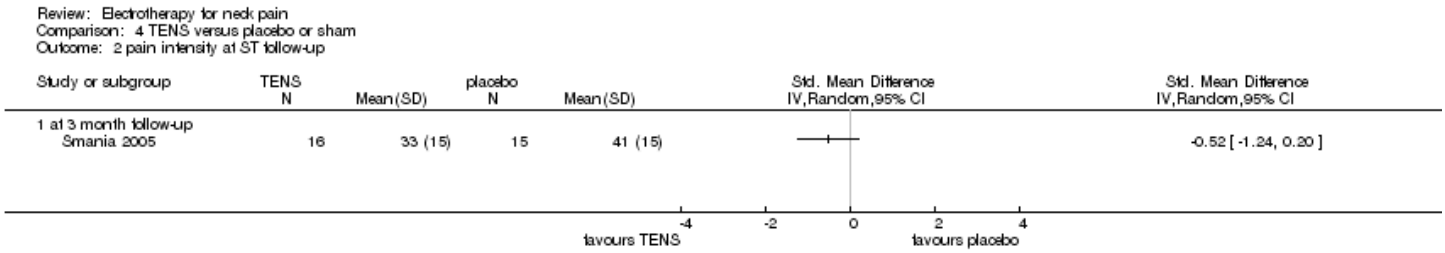


Comparison 4 TENS versus placebo or sham, Outcome 1 pain intensity at post treatment.

1.1 at 1 session	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 at 10 session over 2 weeks	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 at 10 sessions over 3 weeks	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 at 8 session over 2 weeks	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 pain intensity at ST follow-up Show forest plot	1	Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

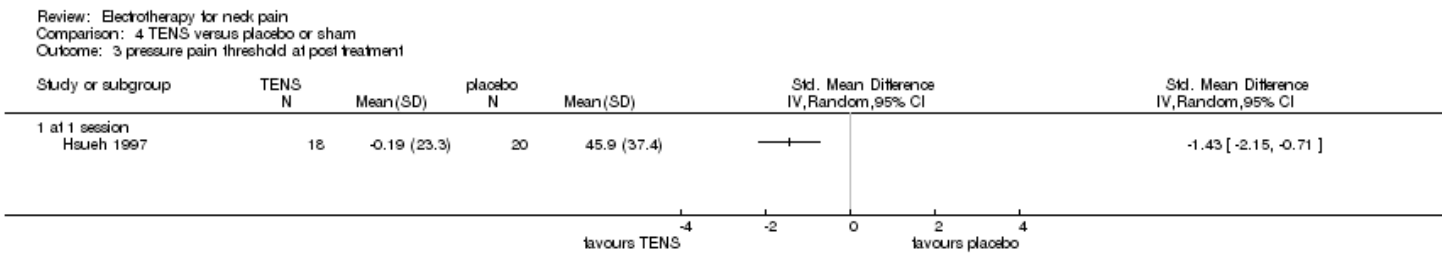
Analysis 4.2 Open in figure viewer | Download as PowerPoint



Comparison 4 TENS versus placebo or sham, Outcome 2 pain intensity at ST follow-up.

2.1 at 3 month follow-up	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 pressure pain threshold at post treatment Show forest plot	1	Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 4.3 Open in figure viewer | Download as PowerPoint



Comparison 4 TENS versus placebo or sham, Outcome 3 pressure pain threshold at post treatment.

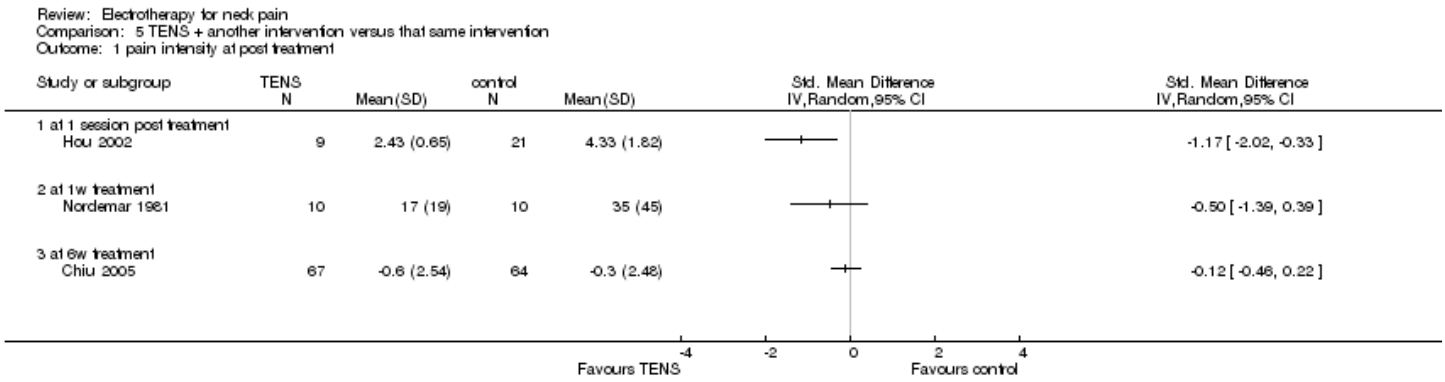
3.1 at 1 session	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 5. TENS + another intervention versus that same intervention Open in table viewer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 pain intensity at post treatment Show forest plot	3		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 5.1

Open in figure viewer | Download as PowerPoint



Comparison 5 TENS + another intervention versus that same intervention, Outcome 1 pain intensity at post treatment.

1.1 at 1 session post treatment	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 at 1w treatment	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 at 6w treatment	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 pain intensity at IT (6 month) follow-up Show forest plot	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 5.2

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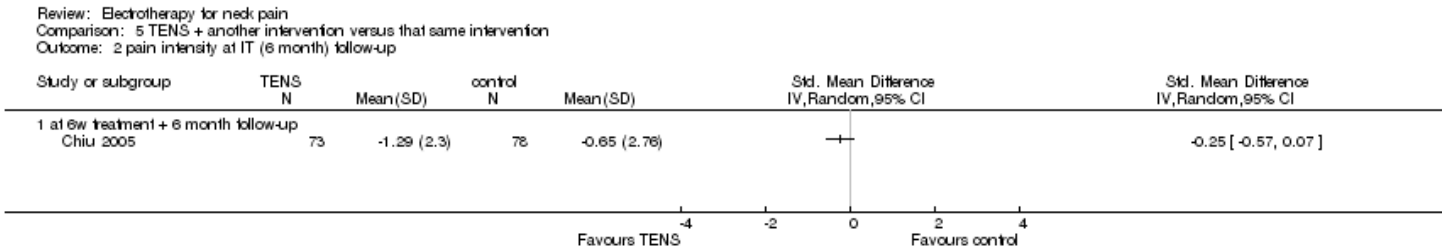

Comparison 5 TENS + another intervention versus that same intervention, Outcome 2 pain intensity at IT (6 month) follow-up.

2.1 at 6w treatment + 6 month follow-up	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 6. TENS versus comparison

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 pain intensity at post treatment Show forest plot	5		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 6.1

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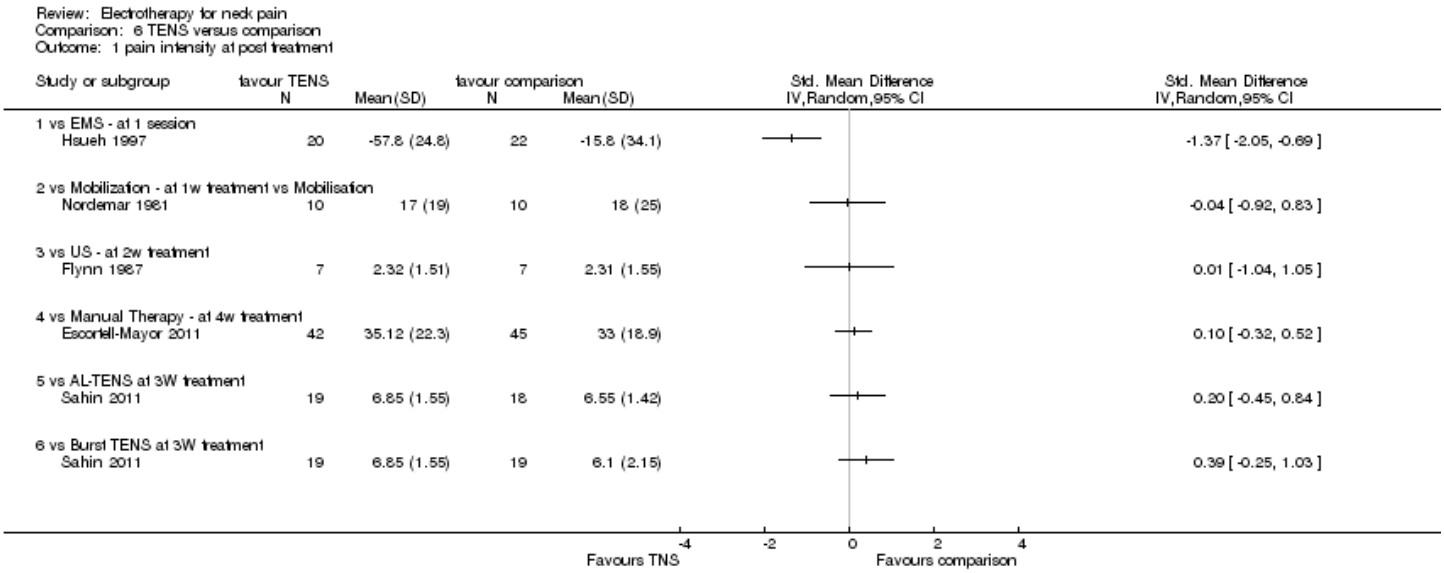

Comparison 6 TENS versus comparison, Outcome 1 pain intensity at post treatment.

1.1 vs EMS - at 1 session	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 vs Mobilization - at 1w treatment vs Mobilisation	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 vs US - at 2w treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 vs Manual Therapy - at 4w treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 vs AL-TENS at 3W treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.6 vs Burst TENS at 3W treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 pain at IT (5 month) follow-up Show forest plot	1	Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 6.2

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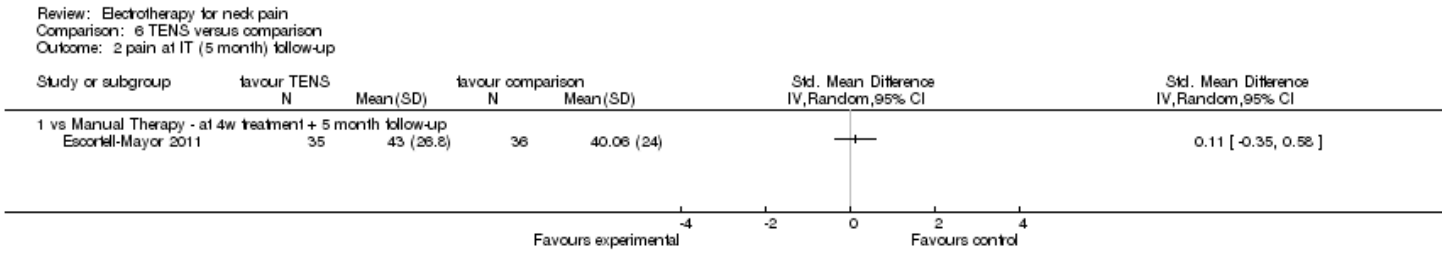

Comparison 6 TENS versus comparison, Outcome 2 pain at IT (5 month) follow-up.

2.1 vs Manual Therapy - at 4w treatment + 5 month follow-up	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 function at post treatment Show forest plot	1	Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 6.3

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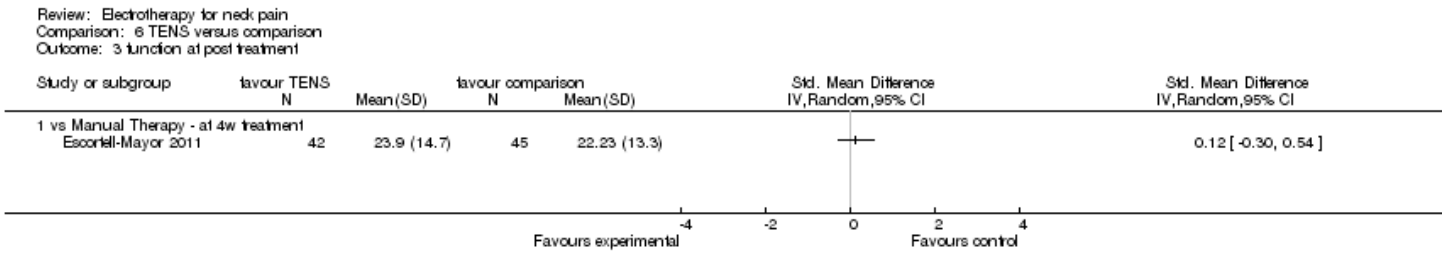

Comparison 6 TENS versus comparison, Outcome 3 function at post treatment.

3.1 vs Manual Therapy - at 4w treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 function at IT (5 month) follow-up Show forest plot	1	Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 6.4

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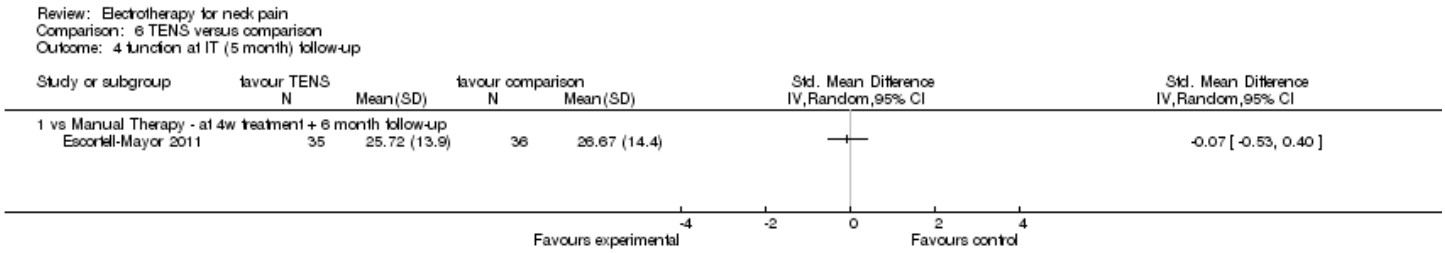

Comparison 6 TENS versus comparison, Outcome 4 function at IT (5 month) follow-up.

4.1 vs Manual Therapy - at 4w treatment + 6 month follow-up	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 QoL at post treatment Show forest plot	1	Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 6.5

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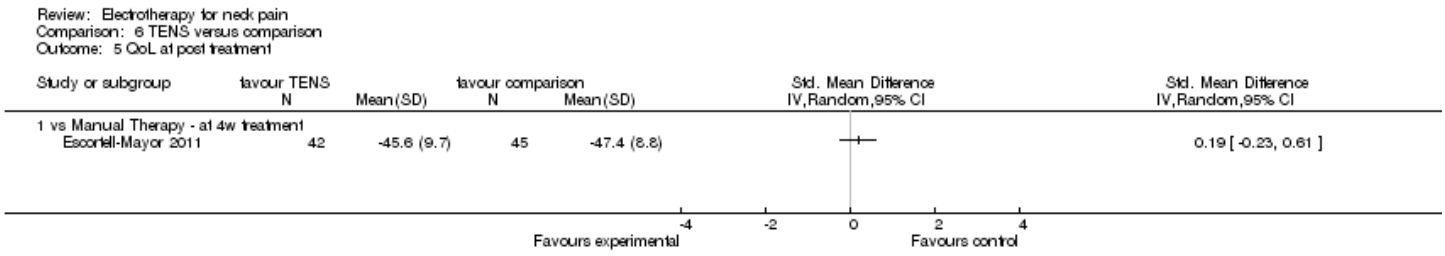
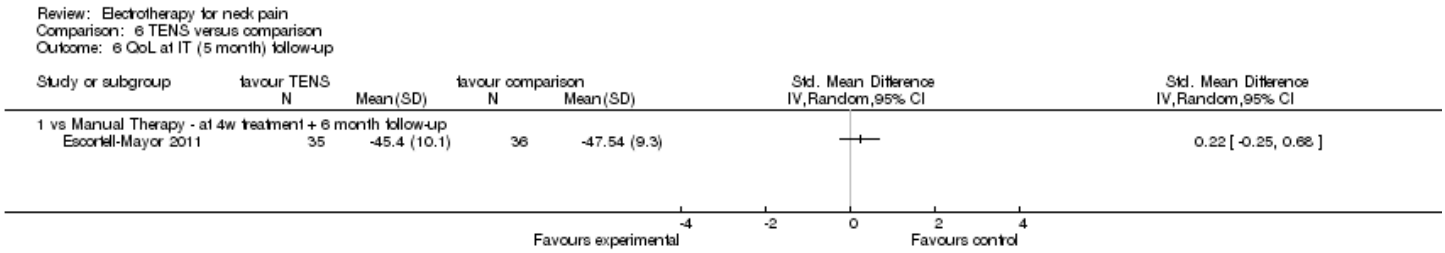


Comparison 6 TENS versus comparison, Outcome 5 QoL at post treatment.

5.1 vs Manual Therapy - at 4w treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6 QoL at IT (5 month) follow-up Show forest plot	1	Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 6.6 Open in figure viewer | Download as PowerPoint



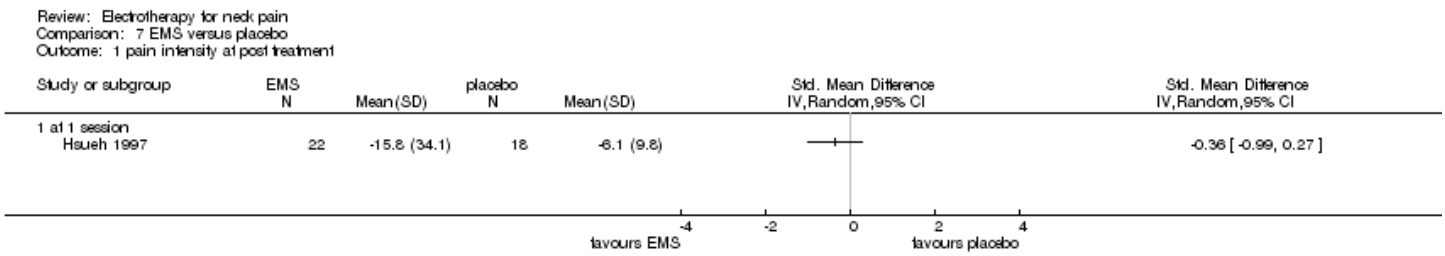
Comparison 6 TENS versus comparison, Outcome 6 QoL at IT (5 month) follow-up.

6.1 vs Manual Therapy - at 4w treatment + 6 month follow-up	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 7. EMS versus placebo Open in table viewer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 pain intensity at post treatment Show forest plot	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 7.1 Open in figure viewer | Download as PowerPoint



Comparison 7 EMS versus placebo, Outcome 1 pain intensity at post treatment.

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 at 1 session	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 pressure pain threshold at post treatment Show forest plot	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 7.2

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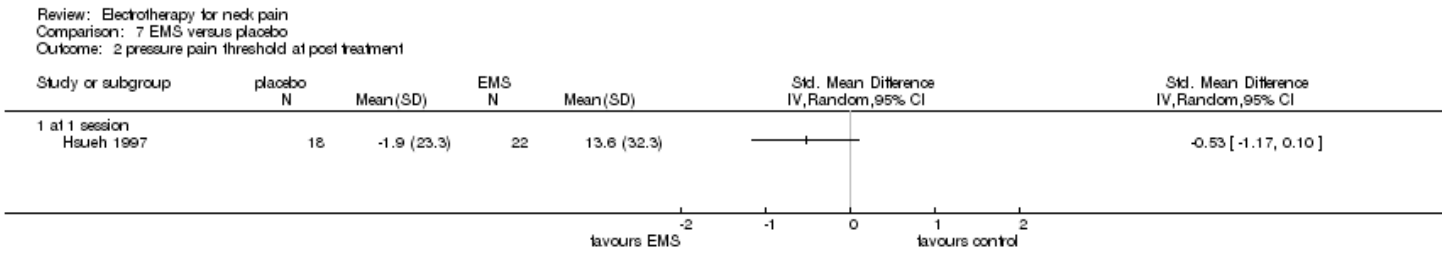


Comparison 7 EMS versus placebo, Outcome 2 pressure pain threshold at post treatment.

2.1 at 1 session	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

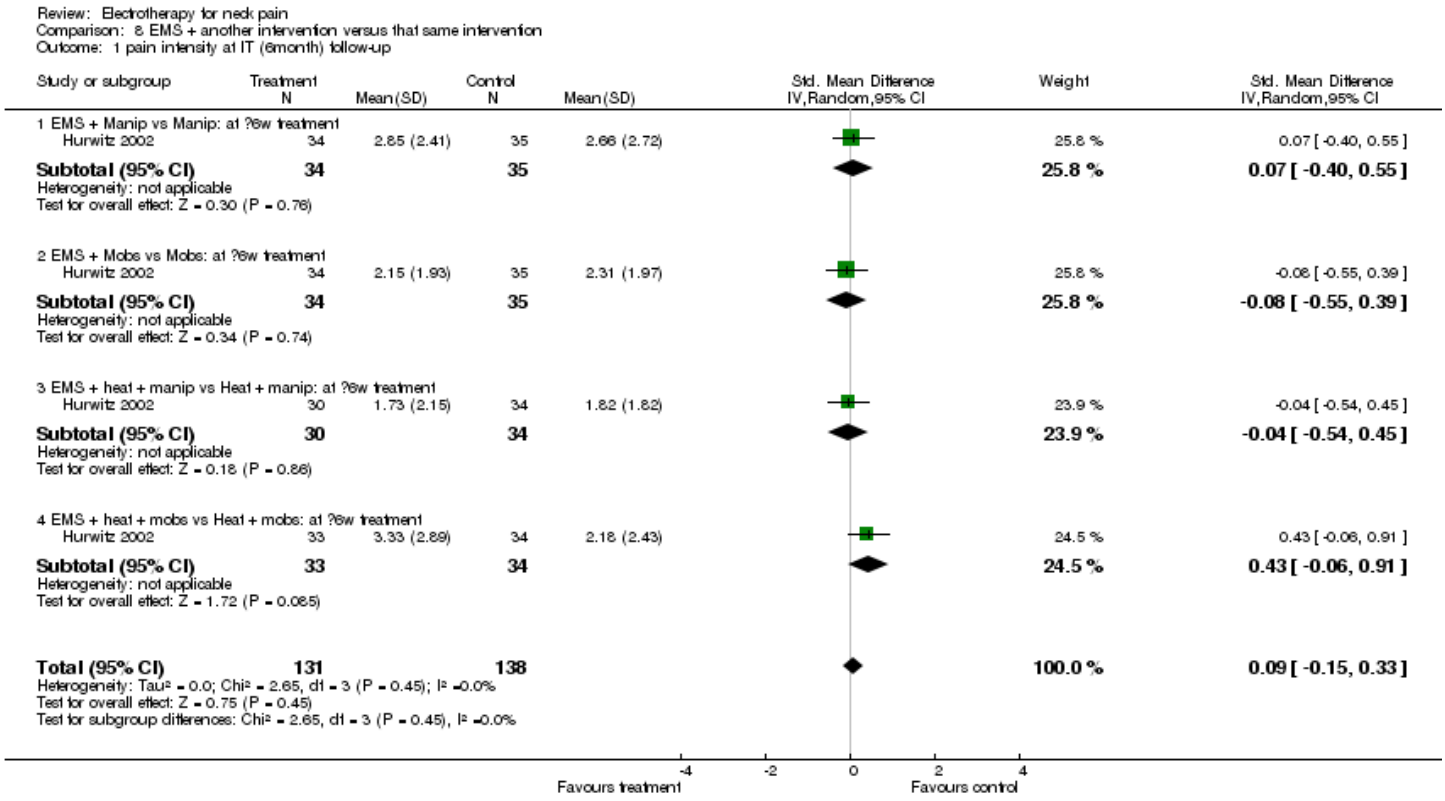
Comparison 8. EMS + another intervention versus that same intervention — Open in table viewer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 pain intensity at IT (6month) follow-up Show forest plot	1	269	Std. Mean Difference (IV, Random, 95% CI)	0.09 [-0.15, 0.33]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 8.1

Open in figure viewer | Download as PowerPoint



Comparison 8 EMS + another intervention versus that same intervention, Outcome 1 pain intensity at IT (6month) follow-up.

1.1 EMS + Manip vs Manip: at ?6w treatment	1	69	Std. Mean Difference (IV, Random, 95% CI)	0.07 [-0.40, 0.55]
1.2 EMS + Mobs vs Mobs: at ?6w treatment	1	69	Std. Mean Difference (IV, Random, 95% CI)	-0.08 [-0.55, 0.39]
1.3 EMS + heat + manip vs Heat + manip: at ?6w treatment	1	64	Std. Mean Difference (IV, Random, 95% CI)	-0.04 [-0.54, 0.45]
1.4 EMS + heat + mobs vs Heat + mobs: at ?6w treatment	1	67	Std. Mean Difference (IV, Random, 95% CI)	0.43 [-0.06, 0.91]
2 function at IT (6 months) follow-up Show forest plot	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 8.2

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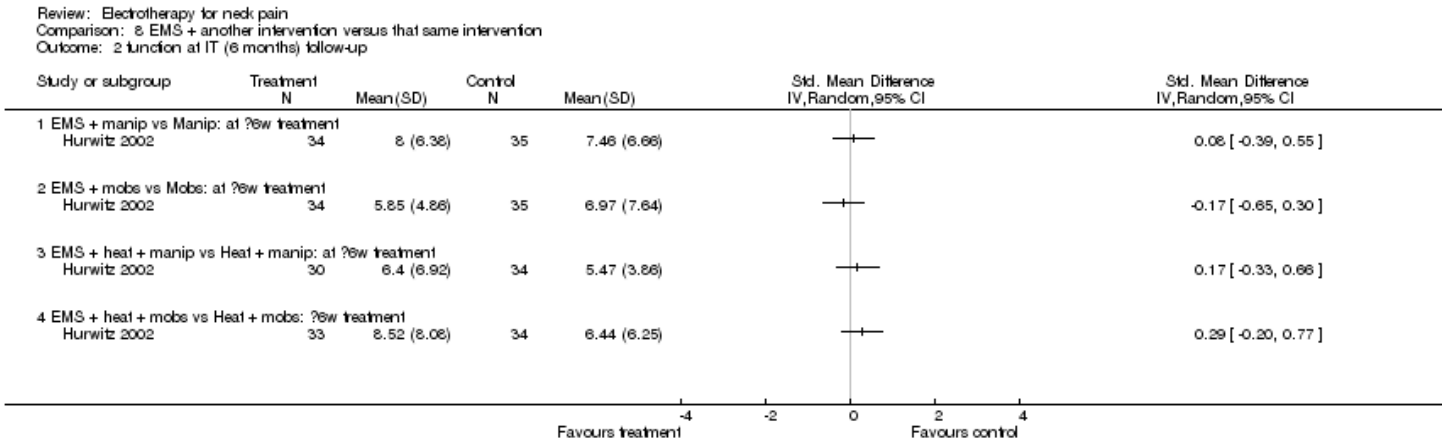

Comparison 8 EMS + another intervention versus that same intervention, Outcome 2 function at IT (6 months) follow-up.

2.1 EMS + manip vs Manip: at ?6w treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 EMS + mobs vs Mobs: at ?6w treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 EMS + heat + manip vs Heat + manip: at ?6w treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.4 EMS + heat + mobs vs Heat + mobs: ?6w treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 patient satisfaction at post treatment Show forest plot	1	Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 8.3

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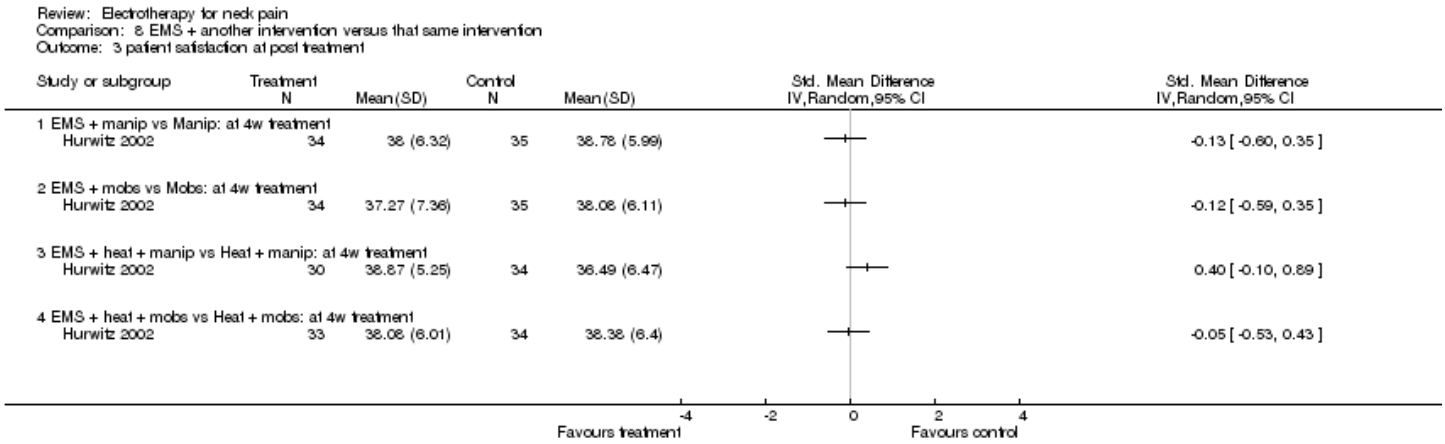


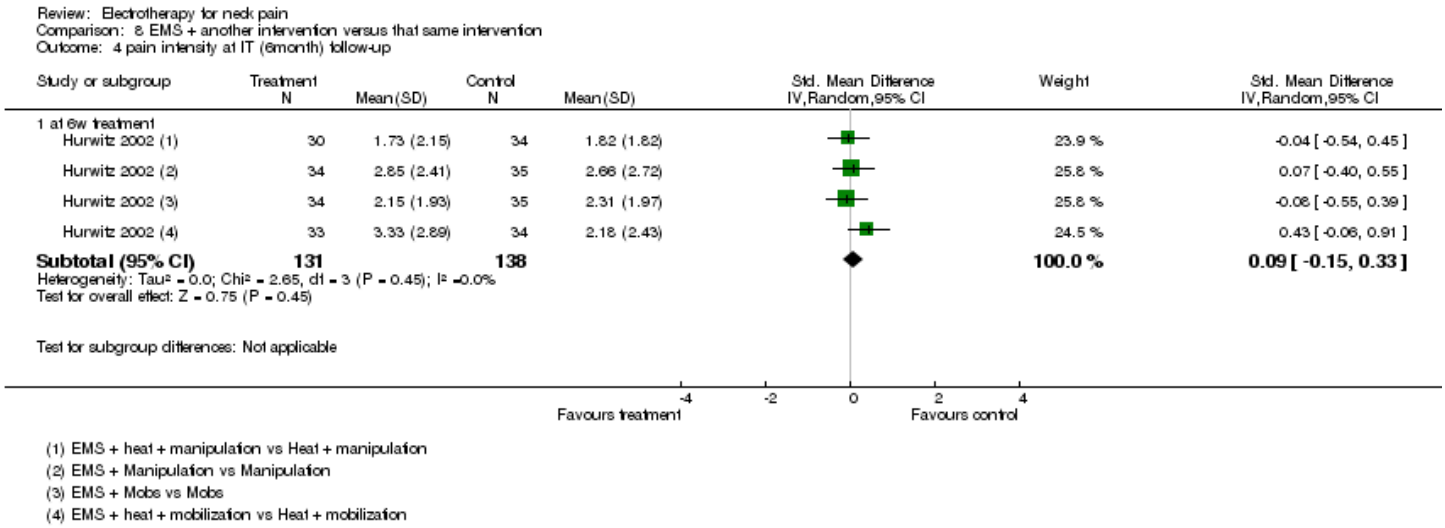
Comparison 8 EMS + another intervention versus that same intervention, Outcome 3 patient satisfaction at post treatment.

3.1 EMS + manip vs Manip: at 4w treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.2 EMS + mobs vs Mobs: at 4w treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.3 EMS + heat + manip vs Heat + manip: at 4w treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.4 EMS + heat + mobs vs Heat + mobs: at 4w treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 pain intensity at IT (6month) follow-up Show forest plot	1	Std. Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 8.4

Open in figure viewer | Download as PowerPoint



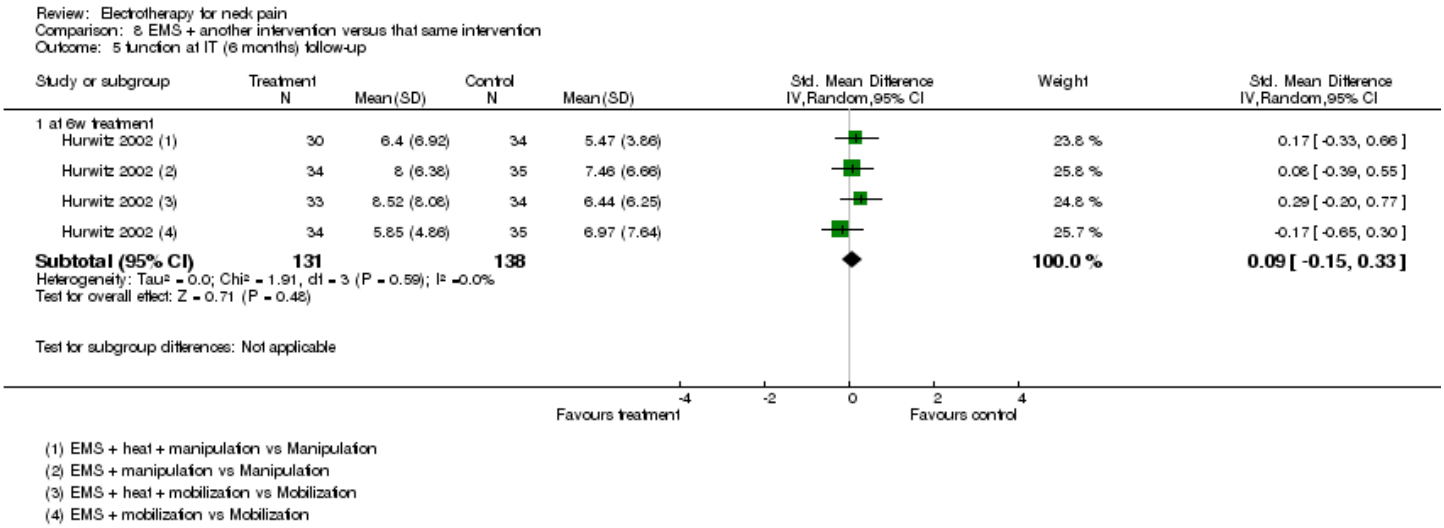
Comparison 8 EMS + another intervention versus that same intervention, Outcome 4 pain intensity at IT (6month) follow-up.

4.1 at 6w treatment	1	269	Std. Mean Difference (IV, Random, 95% CI)	0.09 [-0.15, 0.33]
5 function at IT (6 months) follow-up Show forest plot	1		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 8.5

Open in figure viewer | Download as PowerPoint



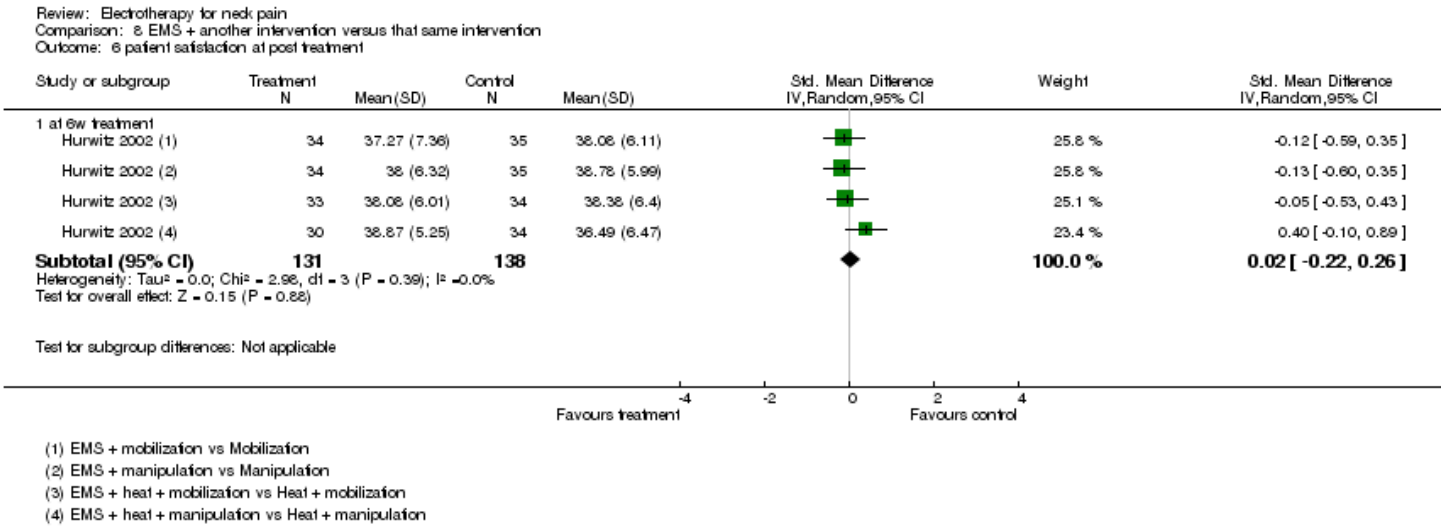
Comparison 8 EMS + another intervention versus that same intervention, Outcome 5 function at IT (6 months) follow-up.

5.1 at 6w treatment	1	269	Std. Mean Difference (IV, Random, 95% CI)	0.09 [-0.15, 0.33]
6 patient satisfaction at post treatment Show forest plot	1		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 8.6

Open in figure viewer | Download as PowerPoint



Comparison 8 EMS + another intervention versus that same intervention, Outcome 6 patient satisfaction at post treatment.

6.1 at 6w treatment	1	269	Std. Mean Difference (IV, Random, 95% CI)	0.02 [-0.22, 0.26]

Comparison 9. EMS (inferential current) versus no treatment

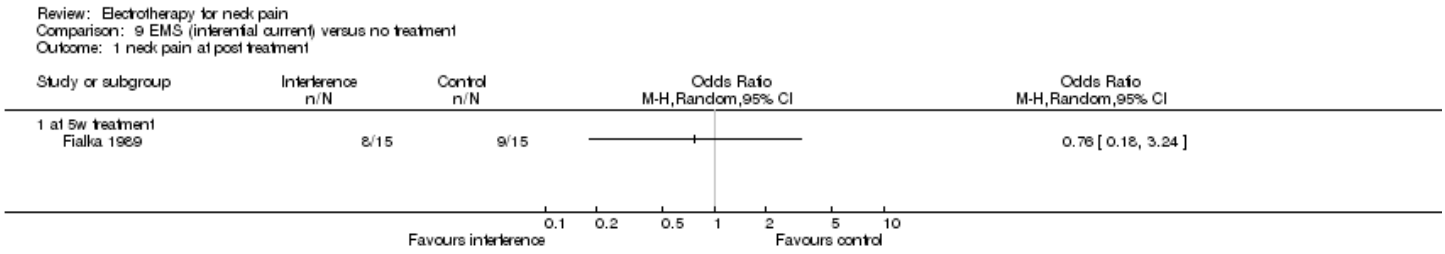
Open in table viewer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 neck pain at post treatment Show forest plot	1		Odds Ratio (M-H, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 9.1

Open in figure viewer | Download as PowerPoint



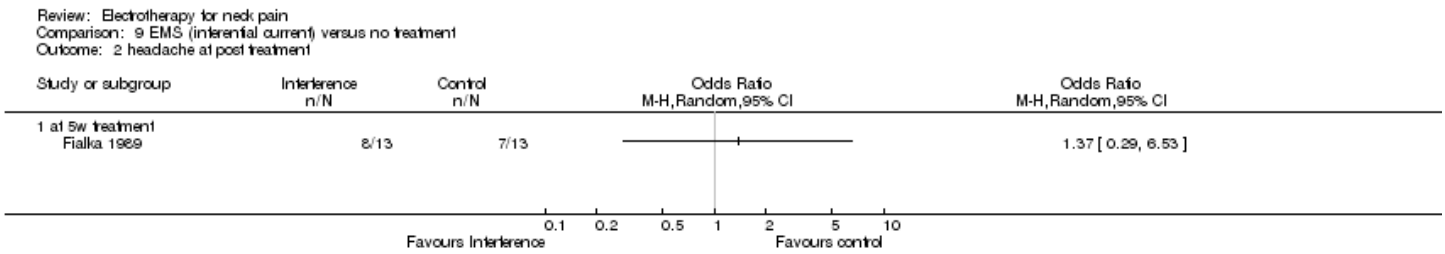
Comparison 9 EMS (inferential current) versus no treatment, Outcome 1 neck pain at post treatment.

1.1 at 5w treatment	1	Odds Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 headache at post treatment	1	Odds Ratio (M-H, Random, 95% CI)	Totals not selected

Show forest plot

Analysis 9.2

Open in figure viewer | Download as PowerPoint



Comparison 9 EMS (inferential current) versus no treatment, Outcome 2 headache at post treatment.

2.1 at 5w treatment	1	Odds Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 10. PEMF (low frequency) versus sham

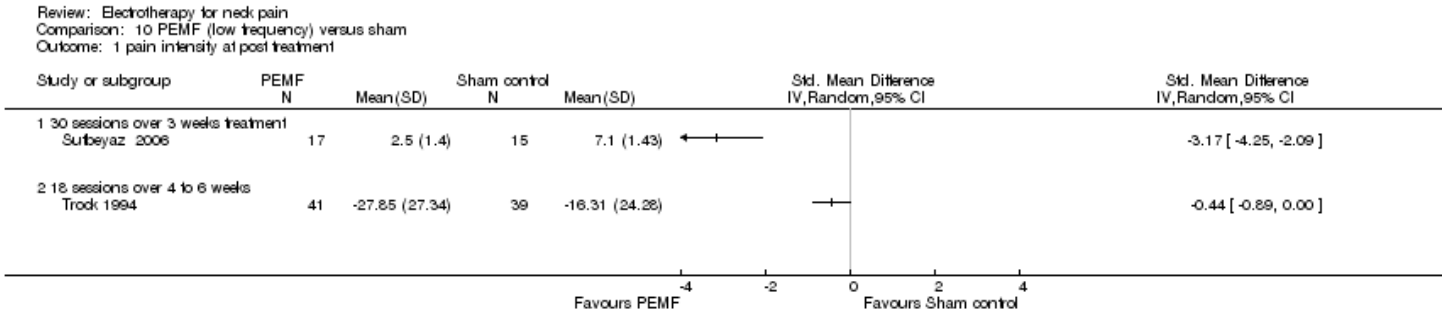
Open in table viewer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 pain intensity at post treatment Show forest plot	2		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 10.1

Open in figure viewer | Download as PowerPoint

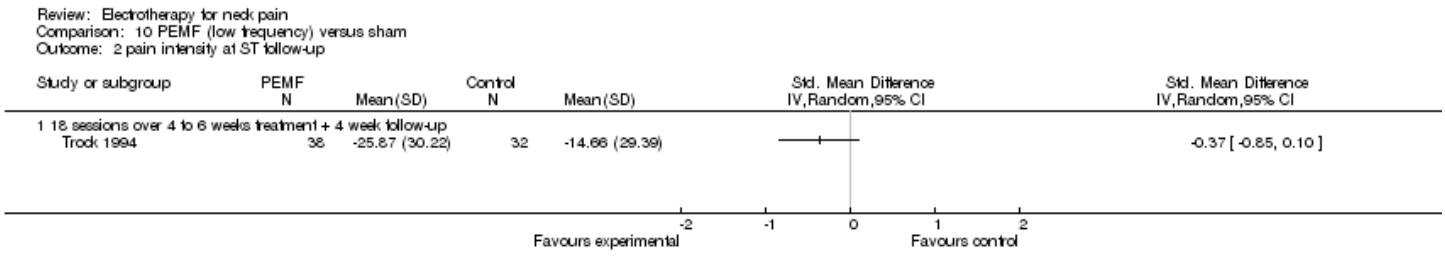


Comparison 10 PEMF (low frequency) versus sham, Outcome 1 pain intensity at post treatment.

1.1 30 sessions over 3 weeks treatment	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 18 sessions over 4 to 6 weeks	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 pain intensity at ST follow-up Show forest plot	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 10.2

Open in figure viewer | Download as PowerPoint

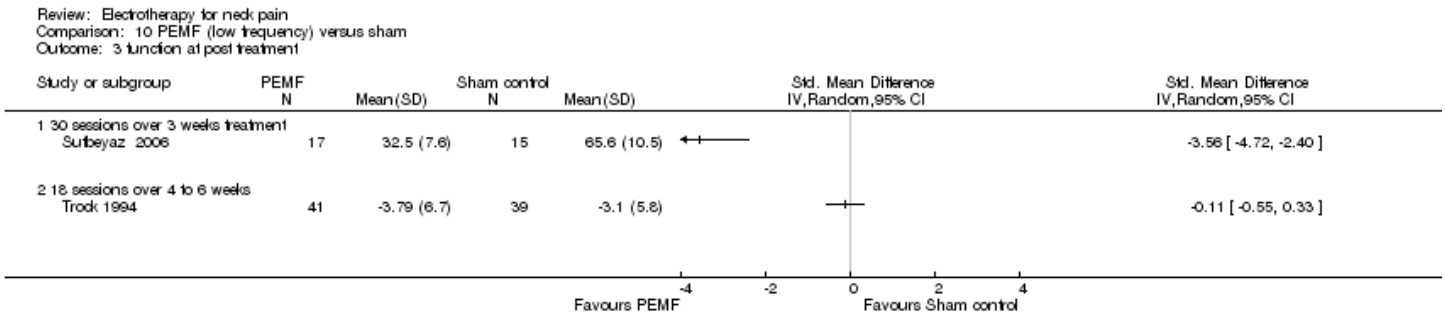


Comparison 10 PEMF (low frequency) versus sham, Outcome 2 pain intensity at ST follow-up.

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 18 sessions over 4 to 6 weeks treatment + 4 week follow-up	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 function at post treatment Show forest plot	2		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 10.3

Open in figure viewer | Download as PowerPoint



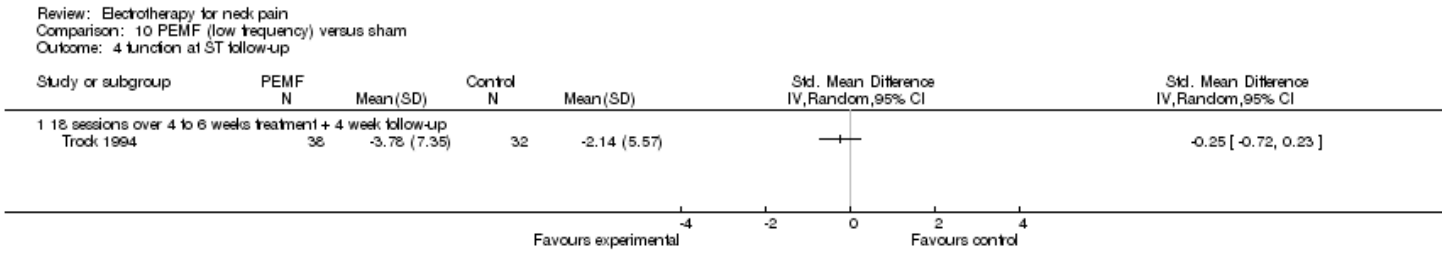
Comparison 10 PEMF (low frequency) versus sham, Outcome 3 function at post treatment.

3.1 30 sessions over 3 weeks treatment	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.2 18 sessions over 4 to 6 weeks	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 function at ST follow-up Show forest plot	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 10.4

Open in figure viewer | Download as PowerPoint

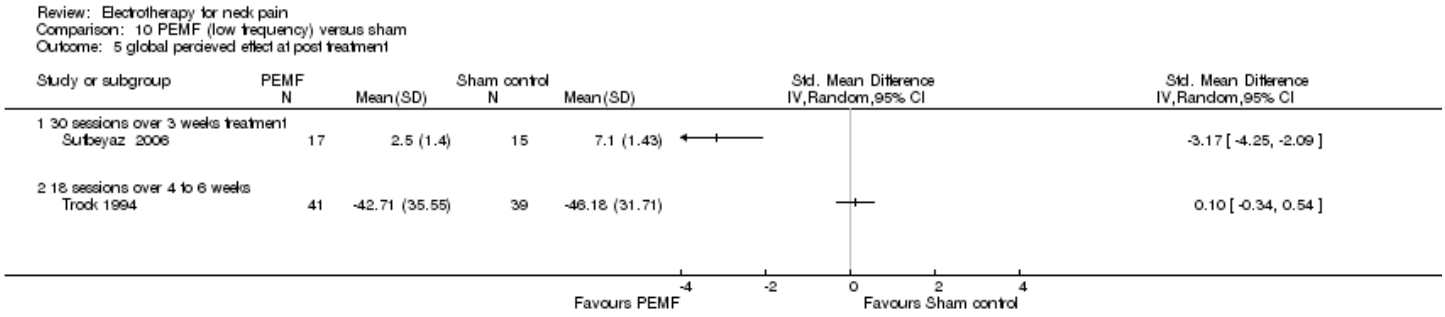


Comparison 10 PEMF (low frequency) versus sham, Outcome 4 function at ST follow-up.

4.1 18 sessions over 4 to 6 weeks treatment + 4 week follow-up	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 global percieved effect at post treatment Show forest plot	2	Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 10.5

Open in figure viewer | Download as PowerPoint

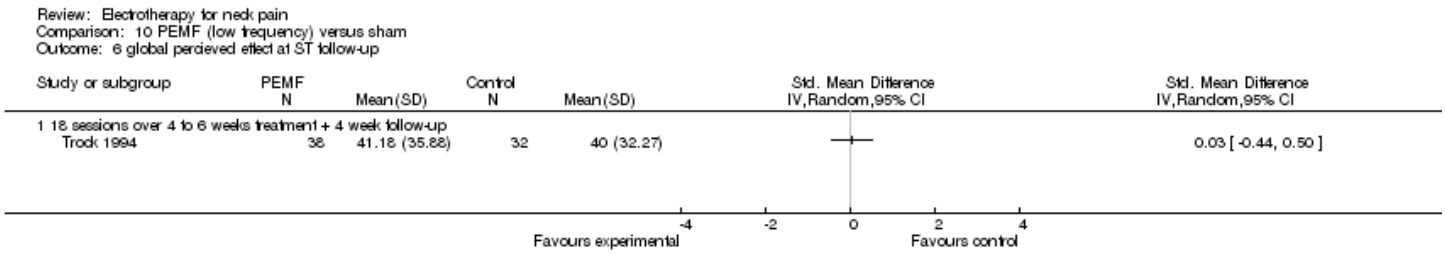


Comparison 10 PEMF (low frequency) versus sham, Outcome 5 global percieved effect at post treatment.

5.1 30 sessions over 3 weeks treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5.2 18 sessions over 4 to 6 weeks	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6 global percieved effect at ST follow-up Show forest plot	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 10.6 Open in figure viewer | Download as PowerPoint



Comparison 10 PEMF (low frequency) versus sham, Outcome 6 global percieved effect at ST follow-up.

6.1 18 sessions over 4 to 6 weeks treatment + 4 week follow-up	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

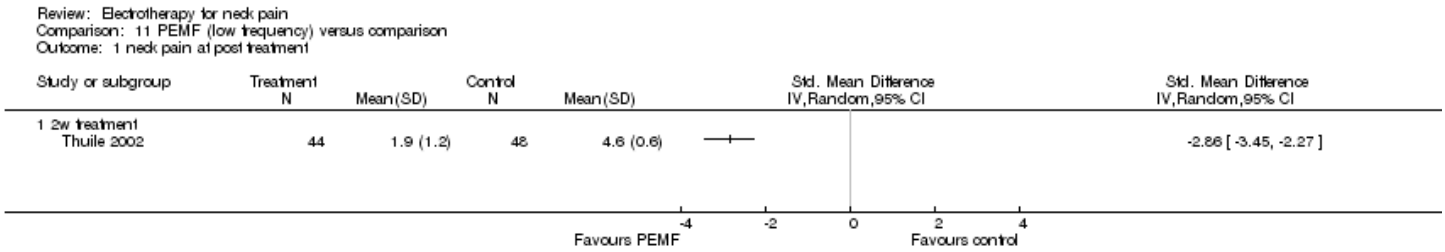
Comparison 11. PEMF (low frequency) versus comparison Open in table viewer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 neck pain at post treatment Show forest plot	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 11.1

Open in figure viewer | Download as PowerPoint



Comparison 11 PEMF (low frequency) versus comparison, Outcome 1 neck pain at post treatment.

1.1 2w treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Comparison 12. Repetitive magnetic stimulation (rMS) versus placebo ultrasound

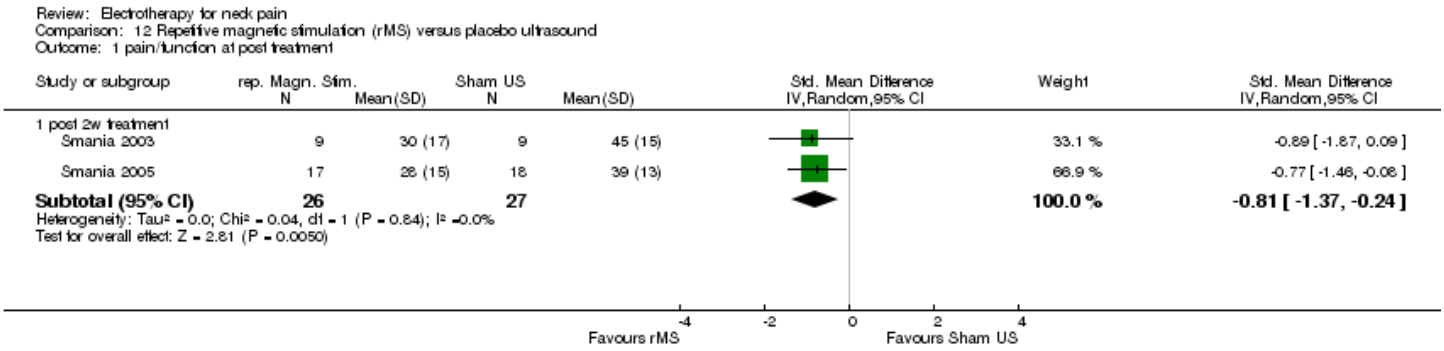
Open in table viewer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 pain/function at post treatment Show forest plot	2		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 12.1

Open in figure viewer | Download as PowerPoint



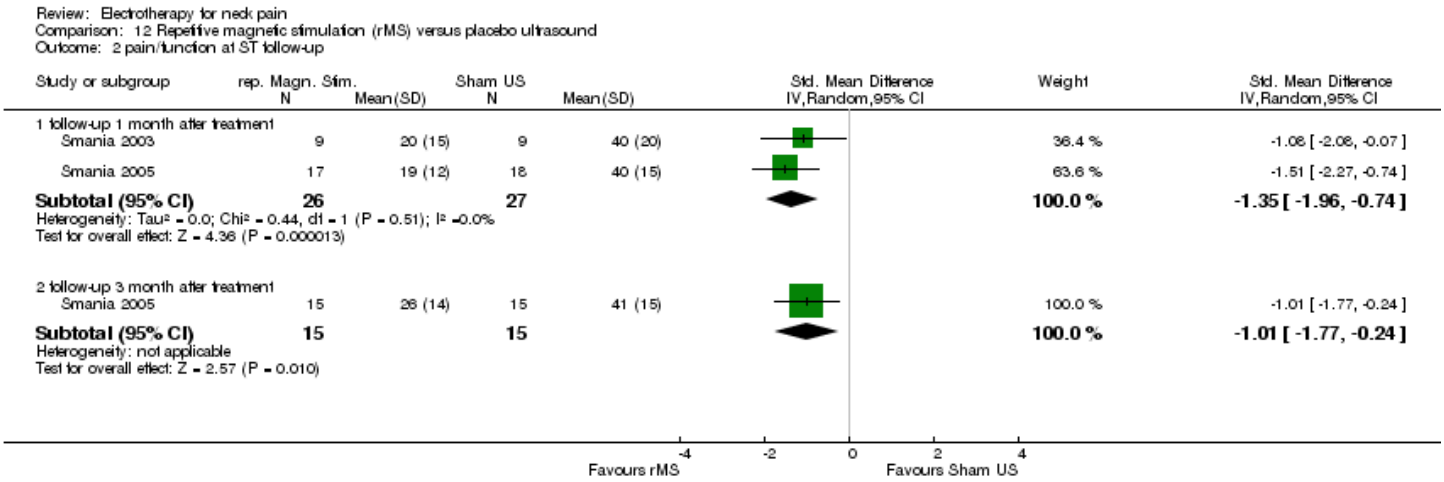
Comparison 12 Repetitive magnetic stimulation (rMS) versus placebo ultrasound, Outcome 1 pain/function at post treatment.

1.1 post 2w treatment	2	53	Std. Mean Difference (IV, Random, 95% CI)	-0.81 [-1.37, -0.24]
2 pain/function at ST follow-up Show forest plot	2		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 12.2

Open in figure viewer | Download as PowerPoint



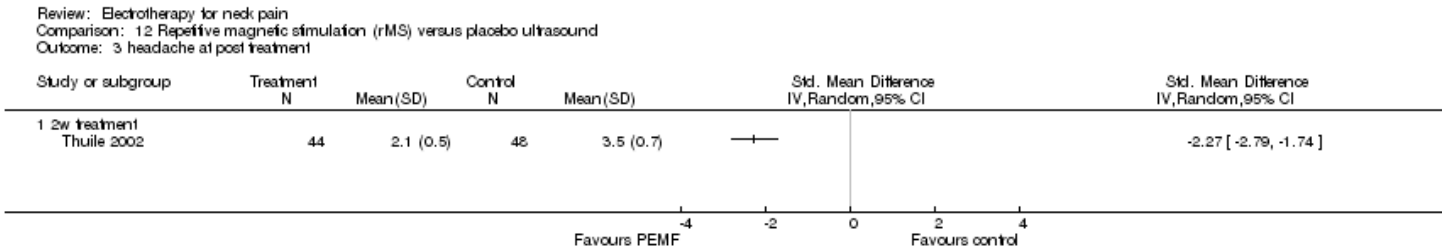
Comparison 12 Repetitive magnetic stimulation (rMS) versus placebo ultrasound, Outcome 2 pain/function at ST follow-up.

2.1 follow-up 1 month after treatment	2	53	Std. Mean Difference (IV, Random, 95% CI)	-1.35 [-1.96, -0.74]
2.2 follow-up 3 month after treatment	1	30	Std. Mean Difference (IV, Random, 95% CI)	-1.01 [-1.77, -0.24]
3 headache at post treatment Show forest plot	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 12.3

Open in figure viewer | Download as PowerPoint



Comparison 12 Repetitive magnetic stimulation (rMS) versus placebo ultrasound, Outcome 3 headache at post treatment.

3.1 2w treatment	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

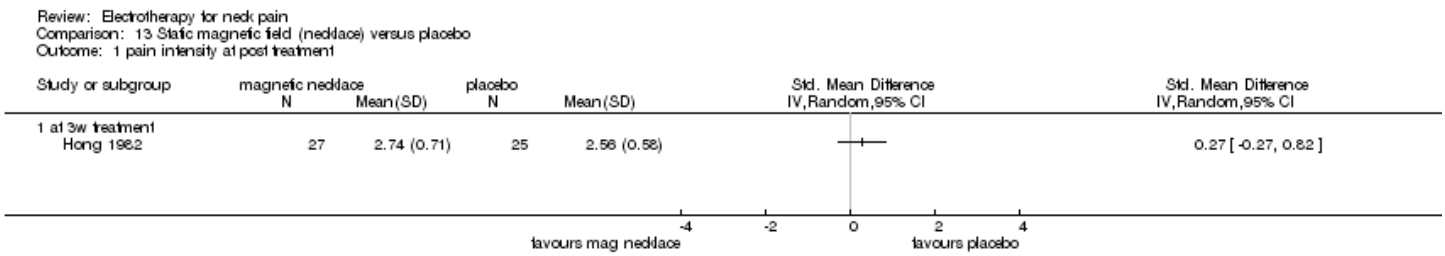
Comparison 13. Static magnetic field (necklace) versus placebo

Open in table viewer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 pain intensity at post treatment Show forest plot	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 13.1

Open in figure viewer | Download as PowerPoint

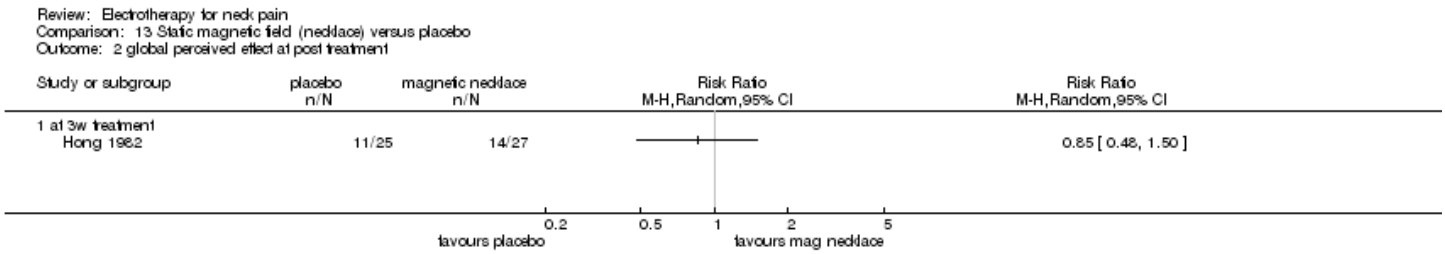


Comparison 13 Static magnetic field (necklace) versus placebo, Outcome 1 pain intensity at post treatment.

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 at 3w treatment	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 global perceived effect at post treatment Show forest plot	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 13.2

Open in figure viewer | Download as PowerPoint



Comparison 13 Static magnetic field (necklace) versus placebo, Outcome 2 global perceived effect at post treatment.

2.1 at 3w treatment	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Information

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Cochrane Database of Systematic Reviews

Version published:

26 August 2013 see what's new

Type:

Intervention

Stage:

Review

Cochrane Editorial Group:

Cochrane Back and Neck Group

Article metrics

Altmetric:

Tweeted by **12**
Referenced in **2** Wikipedia pages
271 readers on Mendeley

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Collapse

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- Hamilton Hospital Association, Ontario, Canada.

Declarations of interest

No conflicts of interest known

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We thank our volunteer translators and the Cochrane Back Review Group editors.

What's new

Last assessed as up-to-date: 17 January 2013.

Date	Event	Description
4 July 2013	New citation required but conclusions have not changed	Updated literature search from 2009 to August 2012, 2 new publications were included, 7 publications were excluded.
4 July 2013	New search has been performed	20 studies (21 publications) included in qualitative synthesis: galvanic current versus placebo (n = 1); iontophoresis versus no treatment (n = 1), versus comparison (n = 1); TENS versus placebo (n = 3), + another treatment versus that same treatment (n = 3), versus comparison (n = 3), versus other dosage (n = 1); EMS versus placebo (n = 1), versus no treatment (n = 1), + another intervention versus that same intervention (n = 1), versus comparison (n = 1); Static magnetic field versus placebo (n = 1); PEMF versus placebo (n = 1), versus comparison (n = 1);

History

Protocol first published: Issue 2, 2003

Review first published: Issue 2, 2005

Date	Event	Description
4 August 2009	New citation required but conclusions have not changed	Inclusion criteria modified and contracted to clearly isolate the unique effect of electrotherapy, resulting in four publications excluded from the 2005 version of the review. An additional kind of electrotherapy was also identified (repetitive magnetic stimulation, rMS). However, there were no essential changes in conclusions - the evidence neither supports nor refutes the efficacy of electrotherapy for the management of neck pain. Further research is very likely to change both the estimate of effect and our confidence in the results.

Date	Event	Description
15 June 2008	Amended	Converted to new review format.
14 June 2008	New citation required and conclusions have changed	Substantive amendment

Version history

Title	Stage	Authors	Version	Publication Date
Electrotherapy for neck pain	Review	Peter Kroeling, Anita Gross, Nadine Graham, Stephen J Burnie, Grace Szeto, Charles H Goldsmith, Ted Haines, Mario Forget	https://doi.org/10.1002/14651858.CD004251.pub5	26 August 2013
Electrotherapy for neck pain	Review	Peter Kroeling, Anita Gross, Charles H Goldsmith, Stephen J Burnie, Ted Haines, Nadine Graham, Aron Brant	https://doi.org/10.1002/14651858.CD004251.pub4	7 October 2009
Electrotherapy for neck disorders	Review	Peter Kroeling, Anita Gross, Charles H Goldsmith, Pamela E Houghton, Cervical Overview Group	https://doi.org/10.1002/14651858.CD004251.pub3	8 July 2009
Electrotherapy for neck disorders	Protocol	Peter Kroeling, Anita Gross, Charles H Goldsmith, Pamela E Houghton, G roup Cervical Overview	https://doi.org/10.1002/14651858.CD004251.pub2	21 July 2003
Electrotherapy for neck disorders	Protocol	Kroeling P, Gross AR, Goldsmith C, Houghton PE, Cervical Overview Group	https://doi.org/10.1002/14651858.CD004251	22 April 2003

Differences between protocol and review

Assessment of risk of bias, GRADE method application, inclusion criteria

What's new

Last assessed as up-to-date: 17 January 2013.

Date	Event	Description
4 July 2013	New citation required but conclusions have not changed	Updated literature search from 2009 to August 2012, 2 new publications were included, 7 publications were excluded.
4 July 2013	New search has been performed	20 studies (21 publications) included in qualitative synthesis: galvanic current versus placebo (n = 1); iontophoresis versus no treatment (n = 1), versus comparison (n = 1); TENS versus placebo (n = 3), + another treatment versus that same treatment (n = 3), versus comparison (n = 3), versus other dosage (n = 1); EMS versus placebo (n = 1), versus no treatment (n = 1), + another intervention versus that same intervention (n = 1), versus comparison (n = 1); Static magnetic field versus placebo (n = 1); PEMF versus placebo (n = 1), versus comparison (n = 1);

Appendices

Appendix 1. MEDLINE search strategy

Physical Medicine-COG_NeckPain_

July 11 2010

1. Neck Pain/

2. exp Brachial Plexus Neuropathies/

3. exp neck injuries/ or exp whiplash injuries/

4. cervical pain.mp.

5. neckache.mp.

6. whiplash.mp.

7. cervicodynia.mp.

8. cervicalgia.mp.

9. brachialgia.mp.

10. brachial neuritis.mp.

11. brachial neuralgia.mp.

12. neck pain.mp.

13. neck injur*.mp.

14. brachial plexus neuropath*.mp.

15. brachial plexus neuritis.mp.

16. thoracic outlet syndrome/ or cervical rib syndrome/

17. Torticollis/

18. exp brachial plexus neuropathies/ or exp brachial plexus neuritis/

19. cervico brachial neuralgia.ti,ab.

20. cervicobrachial neuralgia.ti,ab.

21. (monoradicul* or monoradicl*).tw.

22. or/1-21

23. exp headache/ and cervic*.tw.

24. exp genital diseases, female/

25. genital disease*.mp.

26. or/24-25

27. 23 not 26

28. 22 or 27

29. neck/

30. neck muscles/

31. exp cervical plexus/

32. exp cervical vertebrae/

33. atlanto-axial joint/

34. atlanto-occipital joint/

35. Cervical Atlas/

36. spinal nerve roots/

37. exp brachial plexus/

38. (odontoid* or cervical or occip* or atlant*).tw.

39. axis/ or odontoid process/

40. Thoracic Vertebrae/

41. cervical vertebrae.mp.

42. cervical plexus.mp.

43. cervical spine.mp.

44. (neck adj3 muscles).mp.

45. (brachial adj3 plexus).mp.

46. (thoracic adj3 vertebrae).mp.

47. neck.mp.

48. (thoracic adj3 spine).mp.

49. (thoracic adj3 outlet).mp.

50. trapezius.mp.

51. cervical.mp.

52. cervico*.mp.

53. 51 or 52

54. exp genital diseases, female/

55. genital disease*.mp.

56. exp *Uterus/

57. 54 or 55 or 56

58. 53 not 57

59. 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 58

60. exp pain/

61. exp injuries/

62. pain.mp.

63. ache.mp.

64. sore.mp.

65. stiff.mp.

66. discomfort.mp.

67. injur*.mp.

68. neuropath*.mp.

69. or/60-68

70. 59 and 69

71. Radiculopathy/

72. exp temporomandibular joint disorders/ or exp temporomandibular joint dysfunction syndrome/

73. myofascial pain syndromes/

74. exp "Sprains and Strains"/

75. exp Spinal Osteophytosis/

76. exp Neuritis/

77. Polyradiculopathy/

78. exp Arthritis/

79. Fibromyalgia/

80. spondylitis/ or discitis/

81. spondylosis/ or spondylolysis/ or spondylolisthesis/

82. radiculopathy.mp.

83. radiculitis.mp.

84. temporomandibular.mp.

85. myofascial pain syndrome*.mp.

86. thoracic outlet syndrome*.mp.

87. spinal osteophytosis.mp.

88. neuritis.mp.

89. spondylosis.mp.

90. spondylitis.mp.

91. spondylolisthesis.mp.

92. or/71-91

93. 59 and 92

94. exp neck/

95. exp cervical vertebrae/

96. Thoracic Vertebrae/

97. neck.mp.

98. (thoracic adj3 vertebrae).mp.

99. cervical.mp.

100. cervico*.mp.

101. 99 or 100

102. exp genital diseases, female/

103. genital disease*.mp.

104. exp *Uterus/

105. or/102-104

106. 101 not 105

107. (thoracic adj3 spine).mp.

108. cervical spine.mp.

109. 94 or 95 or 96 or 97 or 98 or 106 or 107 or 108

110. Intervertebral Disk/

111. (disc or discs).mp.

112. (disk or disks).mp.

113. 110 or 111 or 112

114. 109 and 113

115. herniat*.mp.

116. slipped.mp.

117. prolapse*.mp.

118. displace*.mp.

119. degenerat*.mp.

120. (bulge or bulged or bulging).mp.

121. 115 or 116 or 117 or 118 or 119 or 120

122. 114 and 121

123. intervertebral disk degeneration/ or intervertebral disk displacement/

124. intervertebral disk displacement.mp.

125. intervertebral disc displacement.mp.

126. intervertebral disk degeneration.mp.

127. intervertebral disc degeneration.mp.

128. 123 or 124 or 125 or 126 or 127

129. 109 and 128

130. 28 or 70 or 93 or 122 or 129

131. animals/ not (animals/ and humans/)

132. 130 not 131

133. exp *neoplasms/

134. exp *wounds, penetrating/

135. 133 or 134

136. 132 not 135

137. Neck Pain/rh [Rehabilitation]

138. exp Brachial Plexus Neuropathies/rh

139. exp neck injuries/rh or exp whiplash injuries/rh

140. thoracic outlet syndrome/rh or cervical rib syndrome/rh

141. Torticollis/rh

142. exp brachial plexus neuropathies/rh or exp brachial plexus neuritis/rh

143. 137 or 138 or 139 or 140 or 141 or 142

144. Radiculopathy/rh

145. exp temporomandibular joint disorders/rh or exp temporomandibular joint dysfunction syndrome/rh

146. myofascial pain syndromes/rh

147. exp "Sprains and Strains"/rh

148. exp Spinal Osteophytosis/rh

149. exp Neuritis/rh

150. Polyradiculopathy/rh

151. exp Arthritis/rh

152. Fibromyalgia/rh

153. spondylitis/rh or discitis/rh

154. spondylosis/rh or spondylolysis/rh or spondylolisthesis/rh

155. or/144-154

156. 59 and 155

157. exp Combined Modality Therapy/

158. Exercise/

159. Physical Exertion/

160. exp Exercise Therapy/

161. exp Rehabilitation/

162. exp Physical Therapy Modalities/

163. Hydrotherapy/

164. postur* correction.mp.

165. Feldenkrais.mp.

166. (alexander adj (technique or method)).tw.

167. Relaxation Therapy/

168. Biofeedback, Psychology/

169. or/157-168

170. 136 and 169

171. 143 or 156 or 170

172. animals/ not (animals/ and humans/)

173. 171 not 172

174. exp randomized controlled trials as topic/

175. randomized controlled trial.pt.

176. controlled clinical trial.pt.

177. (random* or sham or placebo*).tw.

178. placebos/

179. random allocation/

180. single blind method/

181. double blind method/

182. ((singl* or doubl* or trebl* or tripl*) adj25 (blind* or dumm* or mask*)).ti,ab.

183. (rct or rcts).tw.

184. (control* adj2 (study or studies or trial*)).tw.

185. or/174- 184

186. 173 and 185

187. limit 186 to yr="2006 -Current"

188. limit 186 to yr="1902 - 2005"

189. guidelines as topic/

200. practice guidelines as topic/

201. guideline.pt.

202. practice guideline.pt.

203. (guideline? or guidance or recommendations).ti.

204. consensus.ti.

205. or/189-204

206. 173 and 205

207. 136 and 205

208. 206 or 207

209. limit 208 to yr="2006 -Current"

210. limit 208 to yr="1902 - 2005"

211. meta-analysis/

212. exp meta-analysis as topic/

213. (meta analy* or metaanaly* or met analy* or metanaly*).tw.

214. review literature as topic/

215. (collaborative research or collaborative review* or collaborative overview*).tw.

216. (integrative research or integrative review* or intergrative overview*).tw.

217. (quantitative adj3 (research or review* or overview*)).tw.

218. (research integration or research overview*).tw.

219. (systematic* adj3 (review* or overview*)).tw.

220. (methodologic* adj3 (review* or overview*)).tw.

221. exp technology assessment biomedical/

222. (hta or thas or technology assessment*).tw.

223. ((hand adj2 search*) or (manual* adj search*)).tw.

224. ((electronic adj database*) or (bibliographic* adj database*)).tw.

225. ((data adj2 abstract*) or (data adj2 extract*)).tw.

226. (analys* adj3 (pool or pooled or pooling)).tw.

227. mantel haenszel.tw.

228. (cohrane or pubmed or pub med or medline or embase or psycinfo or psyclit or psychinfo or psychlit or cinahl or science citation indes).ab.

229. or/211-228

230. 173 and 229

231. limit 230 to yr="2006 -Current"

Appendix 2. Criteria for assessing risk of bias for internal validity (Higgins 2011)

Random sequence generation (selection bias)

Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence

There is a low risk of selection bias if the investigators describe a random component in the sequence generation process such as: referring to a random number table, using a computer random number generator, coin tossing, shuffling cards or envelopes, throwing dice, drawing of lots, minimisation (minimisation may be implemented without a random element, and this is considered to be equivalent to being random).

There is a high risk of selection bia*s* if the investigators describe a non-random component in the sequence generation process, such as: sequence generated by odd or even date of birth, date (or day) of admission, hospital or clinic record number; or allocation by judgement of the clinician, preference of the participant, results of a laboratory test or a series of tests, or availability of the intervention.

Allocation concealment (selection bias)

Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment

There is a low risk of selection bias if the participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based and pharmacy-controlled randomisation); sequentially numbered drug containers of identical appearance; or sequentially numbered, opaque, sealed envelopes.

There is a high risk of bias if participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; or other explicitly unconcealed procedures.

Blinding of participants

Performance bias due to knowledge of the allocated interventions by participants during the study

There is a low risk of performance bias if blinding of participants was ensured and it was unlikely that the blinding could have been broken; or if there was no blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding.

Blinding of personnel/ care providers (performance bias)

Performance bias due to knowledge of the allocated interventions by personnel or care providers during the study

There is a low risk of performance bias if blinding of personnel was ensured and it was unlikely that the blinding could have been broken; or if there was no blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding.

Blinding of outcome assessor (detection bias)

Detection bias due to knowledge of the allocated interventions by outcome assessors

There is low risk of detection bias if the blinding of the outcome assessment was ensured and it was unlikely that the blinding could have been broken; or if there was no blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding, or:

- for patient-reported outcomes in which the patient was the outcome assessor (e.g. pain, disability): there is a low risk of bias for outcome assessors if there is a low risk of bias for participant blinding (Boutron 2005);
- for outcome criteria that are clinical or therapeutic events that will be determined by the interaction between patients and care providers (e.g. co-interventions, length of hospitalisation, treatment failure), in which the care provider is the outcome assessor: there is a low risk of bias for outcome assessors if there is a low risk of bias for care providers (Boutron 2005);
- for outcome criteria that are assessed from data from medical forms: there is a low risk of bias if the treatment or adverse effects of the treatment could not be noticed in the extracted data (Boutron 2005).

Incomplete outcome data (attrition bias)

Attrition bias due to amount, nature or handling of incomplete outcome data

There is a low risk of attrition bias if there were no missing outcome data; reasons for missing outcome data were unlikely to be related to the true outcome (for survival data, censoring unlikely to be introducing bias); missing outcome data were balanced in numbers, with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with the observed event risk was not enough to have a clinically relevant impact on the intervention effect estimate; for continuous

outcome data, the plausible effect size (difference in means or standardised difference in means) among missing outcomes was not enough to have a clinically relevant impact on observed effect size, or missing data were imputed using appropriate methods (if drop-outs are very large, imputation using even "acceptable" methods may still suggest a high risk of bias) (van Tulder 2003). The percentage of withdrawals and drop-outs should not exceed 20% for short-term follow-up and 30% for long-term follow-up and should not lead to substantial bias (these percentages are commonly used but arbitrary, not supported by literature) (van Tulder 2003).

Selective Reporting (reporting bias)

Reporting bias due to selective outcome reporting

There is low risk of reporting bias if the study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way, or if the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon).

There is a high risk of reporting bias if not all of the study's pre-specified primary outcomes have been reported; one or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified; one or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; the study report fails to include results for a key outcome that would be expected to have been reported for such a study.

Group similarity at baseline (selection bias)

Bias due to dissimilarity at baseline for the most important prognostic indicators.

There is low risk of bia*s* if groups are similar at baseline for demographic factors, value of main outcome measure(s), and important prognostic factors (examples in the field of back and neck pain are duration and severity of complaints, vocational status, percentage of patients with neurological symptoms) (van Tulder 2003).

Co-interventions (performance bias)

Bias because co-interventions were different across groups

There is low risk of bias if there were no co-interventions or they were similar between the index and control groups (van Tulder 2003).

Compliance (performance bias)

Bias due to inappropriate compliance with interventions across groups

There is low risk of bias if compliance with the interventions was acceptable, based on the reported intensity/dosage, duration, number and frequency for both the index and control intervention(s). For single-session interventions (e.g. surgery), this item is irrelevant (van Tulder 2003).

Intention-to-treat-analysis

There is low risk of bias if all randomized patients were reported/analysed in the group to which they were allocated by randomisation.

Timing of outcome assessments (detection bias)

Bias because important outcomes were not measured at the same time across groups

There is low risk of bias if all important outcome assessments for all intervention groups were measured at the same time (van Tulder 2003).

Other bias

Bias due to problems not covered elsewhere in the table

There is a low risk of bias if the study appears to be free of other sources of bias not addressed elsewhere (e.g. study funding).

Appendix 3. Grading the quality of evidence - definition of domains

Factors that might reduce the quality of the evidence

Study Design refers to type of study (i.e. randomized, observational study)

Limitations within Study Design (Quality) refers to the 12 risk of bias criteria noted in Appendix 2.

Consistency (heterogeneity) refers to the similarity of results across studies. When all studies are included in the meta-analysis, 'consistency' is defined as absence of statistical heterogeneity. In the case that not all studies are combined in a meta-analysis, 'consistency' is defined when all studies for the specific outcome lead to the same decision or recommendation, and 'inconsistency' is present if the results of two or more studies lead to clinically different decisions or recommendations. Authors use their judgment to decide if there is inconsistency when only one study leads to clinically different decision or recommendation.

Directness (generalizability) refers to the extent to which the people, interventions and outcome measures are similar to those of interest.

Precision of the evidence relates to the number of studies, patients and events for each outcome. Imprecise data is defined as:

- Only one study for an outcome, regardless of the sample size or the confidence interval.
- Multiple studies combined in a meta-analysis: the confidence interval is sufficiently wide that the estimate is consistent with conflicting recommendations. For rare events one should consider the confidence interval around the risk difference rather than the confidence interval around the relative risk.
- Multiple studies not combined in a meta-analysis: the total sample size is underpowered to detect a clinically significant difference between those who received the index intervention compared to those who received the control intervention. In this case, a post-hoc sample size calculation should be performed to determine the adequate sample size for each outcome.

Reporting (publication) bias should only be considered present if there is actual evidence of reporting bias rather than only speculation about reporting bias. The Cochrane Reporting Bias Methods Group describes the following types of Reporting Bias and Definitions:

- Publication Bias: the publication or non publication of research findings, depending on the nature and direction of the results.
- Time Lag Bias: the rapid or delayed publication of research findings, depending on the nature and direction of the results.
- Language Bias: the publication of research findings in a particular language, depending on the nature and direction of the results.
- Funding Bias: the reporting of research findings, depending on how the results accord with the aspirations of the funding body.
- Outcome Variable Selection Bias: the selective reporting of some outcomes but not others, depending on the nature and direction of the research findings.
- Developed Country Biases: the non publication or non indication of findings, depending on whether the authors were based in developed or in developing countries.

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Electrotherapy modalities for adhesive capsulitis (frozen shoulder)

Cochrane Systematic Review - **Intervention** | Version published: 01 October 2014

Am score 39 View article information

Matthew J Page | Sally Green | Sharon Kramer | Renea V Johnston | Brodwen McBain | Rachelle Buchbinder

View authors' declarations of interest

Abstract *available in* English | Español

Background

Adhesive capsulitis (also termed frozen shoulder) is a common condition characterised by spontaneous onset of pain, progressive restriction of movement of the shoulder and disability that restricts activities of daily living, work and leisure. Electrotherapy modalities, which aim to reduce pain and improve function via an increase in energy (electrical, sound, light, thermal) into the body, are often delivered as components of a physical therapy intervention. This review is one in a series of reviews which form an update of the Cochrane review 'Physiotherapy interventions for shoulder pain'.

Objectives

To synthesise the available evidence regarding the benefits and harms of electrotherapy modalities, delivered alone or in combination with other interventions, for the treatment of adhesive capsulitis.

Search methods

We searched CENTRAL, MEDLINE, EMBASE, CINAHL Plus and the ClinicalTrials.gov and World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) clinical trials registries up to May 2014, unrestricted by language, and reviewed the reference lists of review articles and retrieved trials to identify any other potentially relevant trials.

Selection criteria

We included randomised controlled trials (RCTs) and controlled clinical trials using a quasi-randomised method of allocation that included adults with adhesive capsulitis and compared any electrotherapy modality to placebo, no treatment, a different electrotherapy modality, or any other intervention. The two main questions of the review focused on whether electrotherapy modalities are effective compared to placebo or no treatment, or if they are an effective adjunct to manual therapy or exercise (or both). The main outcomes of interest were participant-reported pain relief of 30% or greater, overall pain, function, global assessment of treatment success, active shoulder abduction, quality of life, and the number of participants experiencing any adverse event.

Data collection and analysis

Two review authors independently selected trials for inclusion, extracted the data, performed a risk of bias assessment, and assessed the quality of the body of evidence for the main outcomes using the GRADE approach.

Main results

Nineteen trials (1249 participants) were included in the review. Four trials reported using an adequate method of allocation concealment and six trials blinded participants and personnel. Only two electrotherapy modalities (low-level laser therapy (LLLT) and pulsed electromagnetic field therapy (PEMF)) have been compared to placebo. No trial has compared an electrotherapy modality plus manual therapy and exercise to manual therapy and exercise alone. The two main questions of the review were investigated in nine trials.

Low quality evidence from one trial (40 participants) indicated that LLLT for six days may result in improvement at six days. Eighty per cent (16/20) of participants reported treatment success with LLLT compared with 10% (2/20) of participants receiving placebo (risk ratio (RR) 8.00, 95% confidence interval (CI) 2.11 to 30.34; absolute risk difference 70%, 95% CI 48% to 92%). No participants in either group reported adverse events.

We were uncertain whether PEMF for two weeks improved pain or function more than placebo at two weeks because of the very low quality evidence from one trial (32 participants). Seventy-five per cent (15/20) of participants reported pain relief of 30% or more with PEMF compared with 0% (0/12) of participants receiving placebo (RR 19.19, 95% CI 1.25 to 294.21; absolute risk difference 75%, 95% CI 53% to 97%). Fifty-five per cent (11/20) of participants reported total recovery of joint function with PEMF compared with 0% (0/12) of participants receiving placebo (RR 14.24, 95% CI 0.91 to 221.75; absolute risk difference 55%, 95% CI 31 to 79).

Moderate quality evidence from one trial (63 participants) indicated that LLLT plus exercise for eight weeks probably results in greater improvement when measured at the fourth week of treatment, but a similar number of adverse events, compared with placebo plus exercise. The mean pain score at four weeks was 51

points with placebo plus exercise, while with LLLT plus exercise the mean pain score was 32 points on a 100 point scale (mean difference (MD) 19 points, 95% CI 15 to 23; absolute risk difference 19%, 95% CI 15% to 23%). The mean function impairment score was 48 points with placebo plus exercise, while with LLLT plus exercise the mean function impairment score was 36 points on a 100 point scale (MD 12 points, 95% CI 6 to 18; absolute risk difference 12%, 95% CI 6 to 18). Mean active abduction was 70 degrees with placebo plus exercise, while with LLLT plus exercise mean active abduction was 79 degrees (MD 9 degrees, 95% CI 2 to 16; absolute risk difference 5%, 95% CI 1% to 9%). No participants in either group reported adverse events. LLLT's benefits on function were maintained at four months.

Based on very low quality evidence from six trials, we were uncertain whether therapeutic ultrasound, PEMF, continuous short wave diathermy, Iodex phonophoresis, a combination of Iodex iontophoresis with continuous short wave diathermy, or a combination of therapeutic ultrasound with transcutaneous electrical nerve stimulation (TENS) were effective adjuncts to exercise. Based on low or very low quality evidence from 12 trials, we were uncertain whether a diverse range of electrotherapy modalities (delivered alone or in combination with manual therapy, exercise, or other active interventions) were more or less effective than other active interventions (for example glucocorticoid injection).

Authors' conclusions

Based upon low quality evidence from one trial, LLLT for six days may be more effective than placebo in terms of global treatment success at six days. Based upon moderate quality evidence from one trial, LLLT plus exercise for eight weeks may be more effective than exercise alone in terms of pain up to four weeks, and function up to four months. It is unclear whether PEMF is more or less effective than placebo, or whether other electrotherapy modalities are an effective adjunct to exercise. Further high quality randomised controlled trials are needed to establish the benefits and harms of physical therapy interventions (that comprise electrotherapy modalities, manual therapy and exercise, and are reflective of clinical practice) compared to interventions with evidence of benefit (for example glucocorticoid injection or arthrographic joint distension).

Plain language summary *available in* English | Español | Hrvatski | தமிழ்

Electrotherapy modalities for adhesive capsulitis (frozen shoulder)

Background

Frozen shoulder is a common cause of shoulder pain and stiffness. The pain and stiffness can last up to two to three years before going away, and in the early stages it can be very painful.

Electrotherapy modalities (also known as electrophysical agents) are types of physical therapy that aim to reduce pain and improve function via an increase in energy (electrical, sound, light, thermal) into the body. Examples include therapeutic ultrasound, low-level laser therapy (LLLT), interferential current, transcutaneous electrical nerve stimulation (TENS), and pulsed electromagnetic field therapy (PEMF). Electrotherapy modalities are delivered by various clinicians, including physiotherapists, chiropractors and osteopaths. In practice, patients with frozen shoulder seldom receive a single electrotherapy modality in isolation from other components of physical therapy treatment (for example manual therapy, exercise).

Study characteristics

This summary of an updated Cochrane review presents what we know from research about the benefits and harms of electrotherapy modalities in people with frozen shoulder. After searching for all relevant studies published up to May 2014, we included 19 trials (1249 participants). Of the included participants, 61% were women, the average age was 55 years, and the average duration of the condition was 5.5 months. The average duration of delivery of electrotherapy interventions was four weeks.

Key results - LLLT and exercise compared to placebo and exercise

Pain (higher scores mean worse pain)

People who received LLLT and exercise had less pain than people who had placebo plus exercise - pain was 19 points less (ranging from 15 to 23 points less) at the fourth week of treatment (19% absolute improvement, ranging from 15% to 23% improvement).

- People who had LLLT and exercise rated their pain score as 32 points on a scale of 0 to 100 points.

- People who had placebo and exercise rated their pain score as 51 points on a scale of 0 to 100 points.

Function impairment (higher scores mean worse function impairment)

People who received LLLT and exercise had less function impairment than people who had placebo and exercise - function impairment was 12 points less (ranging from 6 to 18 points less) at the fourth week of treatment (12% absolute improvement, ranging from 6% to 18% improvement).

- People who had LLLT and exercise rated their function impairment as 36 points on a scale of 0 to 100 points.

- People who had placebo and exercise rated their function impairment as 48 points on a scale of 0 to 100 points.

Active shoulder abduction (higher degrees of movement mean greater shoulder abduction)

People who received LLLT and exercise had greater active shoulder abduction than people who had placebo and exercise - active shoulder abduction was 9 degrees more (ranging from 2 to 16 degrees more) at the fourth week of treatment (5% absolute improvement, ranging from 1% to 9% improvement).

- People who had LLLT and exercise had active shoulder abduction of 79 degrees.

- People who had placebo and exercise had active shoulder abduction of 70 degrees.

Side effects

No person in either group reported any side effects.

Participant-reported pain relief of 30% or greater, global assessment of treatment success, and quality of life

These were not measured in this trial.

Quality of the evidence

There was low quality evidence that LLLT for six days may improve global assessment of treatment success more than placebo, when measured at six days. Further research is likely to change the estimate.

We are very uncertain about whether PEMF for two weeks improves pain or function any more than placebo because of the very low quality evidence from one trial.

There was moderate quality evidence that LLLT plus exercise for eight weeks may improve pain, up to four weeks, and function, up to four months, more than placebo plus exercise. Further research may change the estimate.

We are very uncertain about whether therapeutic ultrasound, PEMF, Iodex phonophoresis, continuous short wave diathermy, a combination of Iodex iontophoresis with continuous short wave diathermy, or a combination of therapeutic ultrasound with transcutaneous electrical nerve stimulation (TENS) are effective adjuncts to exercise.

Authors' conclusions

Implications for practice

Of the various electrotherapy modalities, only LLLT and PEMF have been compared to placebo in randomised controlled trials. Also, there are no trials that have compared an electrotherapy modality plus manual therapy to manual therapy alone, or an electrotherapy modality plus manual therapy and exercise to manual therapy and exercise alone. Based on the best currently available data, LLLT may be more effective than placebo in terms of global treatment success at six days; and may be an effective adjunct to exercise in terms of pain up to four weeks, and function up to four months, although its long-term effect has not been investigated. It is unclear whether PEMF is more or less effective than placebo. It is unclear whether

therapeutic ultrasound, PEMF, Iodex phonophoresis, continuous short wave diathermy, a combination of Iodex iontophoresis with continuous short wave diathermy, or a combination of therapeutic ultrasound with TENS are effective adjuncts to exercise.

Implications for research

Further high quality randomised controlled trials are needed to establish the benefits and harms of physical therapy interventions (that comprise electrotherapy modalities, manual therapy and exercise, and are reflective of clinical practice) for adhesive capsulitis. In particular, future trials should compare a combination of LLLT, manual therapy and exercise to interventions with evidence of benefit (for example glucocorticoid injection or arthrographic joint distension). Adhesive capsulitis can last for several years, although most of the previous trials have only assessed outcomes during treatment or in the weeks following treatment cessation. Assessment of longer-term outcomes, for example up to six to 12 months, would be worthwhile in future trials. Trials could also explore the impact of factors such as dosage, wavelength, site and duration of treatment on the effect of electrotherapy modalities (particularly LLLT). Trials should include strategies designed to minimise the potential for bias, including adequate allocation concealment and blinding of participants and outcome assessors. Development of a core set of outcomes for trials of adhesive capsulitis and other shoulder disorders would enhance this endeavour and improve our ability to synthesise the evidence.

Summary of findings

Open in table viewer

Summary of findings for the main comparison. Low-level laser therapy (LLLT) compared to placebo for adhesive capsulitis (frozen shoulder)

Low-level laser therapy (LLLT) compared to placebo for adhesive capsulitis (frozen shoulder)
Patient or population: patients with adhesive capsulitis (frozen shoulder) **Settings:** physical therapy clinic in high-income country **Intervention:** LLLT **Comparison:** placebo

Risk of treatment success in the placebo group in Taverna 1990 used as the assumed control group risk.

Sample size is small, yielding a very wide 95% CI. Outcome measured at the end of six days of treatment, so effect may not be generalisable to a later time point (e.g. up to six weeks).

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo	LLLT				
Participant-reported pain relief ≥ 30%	See comment	See comment	Not estimable	-	See comment	No studies reported this outcome
Overall pain	See comment	See comment	Not estimable	-	See comment	No studies reported this outcome
Function	See comment	See comment	Not estimable	-	See comment	No studies reported this outcome
Global assessment of treatment success 'Excellent' or 'good' result (self-rated) Follow-up: end of 6 days treatment	**Study population**[1]		**RR 8.00** (2.11 to 30.34)	40 (1 study)	⊕⊕⊕⊖ **low**[2]	Absolute risk difference 70% (48% to 92% more); relative per cent change 700% (111% to 2934% more) NNTB = 1 (1 to 2)
	100 per 1000	**800 per 1000** (211 to 1000)				
Active shoulder abduction	See comment	See comment	Not estimable	-	See comment	No studies reported this outcome
Quality of life	See comment	See comment	Not estimable	-	See comment	No studies reported this outcome
Adverse events	See comment	See comment	Not estimable	40 (1 study)	⊕⊕⊕⊖ **low**[2]	No participant in either group reported experiencing any adverse event

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

Risk of treatment success in the placebo group in Taverna 1990 used as the assumed control group risk.

Sample size is small, yielding a very wide 95% CI. Outcome measured at the end of six days of treatment, so effect may not be generalisable to a later time point (e.g. up to six weeks).

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

[1] Risk of treatment success in the placebo group in Taverna 1990 used as the assumed control group risk.

[2] Sample size is small, yielding a very wide 95% CI. Outcome measured at the end of six days of treatment, so effect may not be generalisable to a later time point (e.g. up to six weeks).

Summary of findings 2 Pulsed electromagnetic field therapy (PEMF) compared to placebo for adhesive capsulitis (frozen shoulder)

Open in table viewer

Summary of findings 2. Pulsed electromagnetic field therapy (PEMF) compared to placebo for adhesive capsulitis (frozen shoulder)

Pulsed electromagnetic field therapy (PEMF) compared to placebo for adhesive capsulitis (frozen shoulder)

Patient or population: patients with adhesive capsulitis (frozen shoulder)
Settings: physical therapy clinic in high-income country
Intervention:
Comparison: placebo

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo	PEMF				
Participant-reported pain relief ≥ 30% Complete resolution of SPADI pain	**Study population**[1]		**RR 19.19** (1.25 to 294.21)	32 (1 study)	⊕⊖⊖⊖ **very low**[2]	Absolute risk difference 75% (53% to 97% more); relative per cent change 1819% (25% to 29321% more) NNTB = 1 (1 to 2)

Risk of treatment success in placebo group in Battisti 2007 used as the assumed control group risk.

High risk of attrition bias because a high proportion of the placebo group withdrew due to lack of response to treatment, which is likely to bias the results of the trial in favour of the active treatment group; 95% CI very wide.

Follow-up: end of 15 days treatment	**83 per 1000**	**1000 per 1000** (104 to 1000)				
Overall pain	See comment	See comment	Not estimable	-	See comment	No studies reported this outcome
Function Total recovery of joint function Follow-up: end of 15 days treatment	**Study population**[1]		**RR 14.24** (0.91 to 221.75)	32 (1 study)	⨁⊖⊖⊖ **very low**[2]	Absolute risk difference 55% (31% to 79% more); relative per cent change 1324% (9% fewer to 22075% more) NNTB not applicable.
	83 per 1000	**1000 per 1000** (76 to 1000)				
Global assessment of treatment success	See comment	See comment	Not estimable	-	See comment	No studies reported this outcome
Active shoulder abduction	See comment	See comment	Not estimable	-	See comment	No studies reported this outcome
Quality of life	See comment	See comment	Not estimable	-	See comment	No studies reported this outcome
Adverse events	See comment	See comment	Not estimable	-	See comment	No studies reported this outcome

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Risk of treatment success in placebo group in Battisti 2007 used as the assumed control group risk.
[2] High risk of attrition bias because a high proportion of the placebo group withdrew due to lack of response to treatment, which is likely to bias the results of the trial in favour of the active treatment group; 95% CI very wide.

Summary of findings 3 Low-level laser therapy (LLLT) plus exercise compared to exercise for adhesive capsulitis (frozen shoulder)

Open in table viewer

Summary of findings 3. Low-level laser therapy (LLLT) plus exercise compared to exercise for adhesive capsulitis (frozen shoulder)

Low-level laser therapy (LLLT) plus exercise compared to placebo plus exercise for adhesive capsulitis (frozen shoulder)

Patient or population: patients with adhesive capsulitis (frozen shoulder)
Settings: physical therapy clinic in high-income country
Intervention: LLLT plus exercise
Comparison: placebo laser therapy plus exercise

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo laser therapy plus exercise	LLLT plus exercise				
Participant-reported pain relief ≥ 30%	See comment	See comment	Not estimable	-	See comment	No studies reported this outcome
Overall pain 0-100 visual analogue scale (lower score = less pain) Follow-up: at 4th week of treatment	The mean overall pain in the control group was **51 points**	The mean overall pain in the intervention group was **19 points lower** (23 to 15 lower)		63 (1 study)	⊕⊕⊕⊖ **moderate**[1]	Absolute risk difference 19% (23% to 15% fewer); relative per cent change[2] 28% (34% to 22% fewer) NNTB = 1 (1 to 2)

Sample size is small, yielding wide 95% CIs.

Baseline mean overall pain score of placebo group was 67.

Baseline mean function score of placebo group was 62.

Baseline mean active abduction of placebo group was 59.

Function Shoulder Disabilty Questionnaire 0-100 (lower scores = better function) Follow-up: at 4th week of treatment	The mean function in the control group was **48 points**	The mean function in the intervention group was **12 points lower** (18 to 6 lower)		63 (1 study)	⊕⊕⊕⊖ **moderate**[1]	Absolute risk difference 12% (18% to 6% fewer); relative per cent change[3] 19% (29% to 10% fewer) NNTB = 2 (2 to 5)
Global assessment of treatment success	See comment	See comment	Not estimable	-	See comment	No studies reported this outcome
Active shoulder abduction Degrees Follow-up: 4 weeks	The mean active shoulder abduction in the control group was **70 degrees**	The mean active shoulder abduction in the intervention group was **9 degrees higher** (2 to 16 higher)		63 (1 study)	⊕⊕⊕⊖ **moderate**[1]	Absolute risk difference 5% (1% to 9% more); relative per cent change[4]15% (3% to 27% more)
Quality of life	See comment	See comment	Not estimable	-	See comment	No studies reported this outcome
Adverse events	See comment	See comment	Not estimable	63 (1 study)	⊕⊕⊕⊖ **moderate**[1]	No participant reported experiencing any adverse event

Sample size is small, yielding wide 95% CIs.

Baseline mean overall pain score of placebo group was 67.

Baseline mean function score of placebo group was 62.

Baseline mean active abduction of placebo group was 59.

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Sample size is small, yielding wide 95% CIs.

[2] Baseline mean overall pain score of placebo group was 67.

[3] Baseline mean function score of placebo group was 62.

[4] Baseline mean active abduction of placebo group was 59.

Background

Description of the condition

This review is one in a series of reviews aiming to determine the evidence of the benefits and safety of common interventions for shoulder pain. This series of reviews form the update of an earlier Cochrane review of physiotherapy for shoulder disorders (Green 2003). Since our original review, many new clinical trials studying a diverse range of interventions have been performed. To improve usability of the review, we have subdivided the review by type of shoulder disorder and type of intervention as patients within different diagnostic groupings may respond differently to interventions. This review focuses on electrotherapy modalities for adhesive capsulitis (frozen shoulder). Separate reviews of (i) manual therapy and exercise for adhesive capsulitis (Page 2014), (ii) manual therapy and exercise for rotator cuff disorders, and (iii) electrotherapy modalities for rotator cuff disorders are currently underway.

Adhesive capsulitis (also termed frozen shoulder, painful stiff shoulder or periarthritis) is a common condition characterised by spontaneous onset of pain, progressive restriction of movement of the shoulder, and disability that restricts activities of daily living, work and leisure (Codman 1934; Neviaser 1987; Reeves 1975). There is an acknowledged lack of specific diagnostic criteria for the condition. Reviews of the

diagnostic criteria used in clinical trials of adhesive capsulitis have found that all trialists reported that restricted movement must be present but the amount of restriction, whether the restriction had to be active or passive, or both, and the direction of restriction were inconsistently defined (Green 1998; Schellingerhout 2008). The cumulative incidence of adhesive capsulitis has been reported as 2.4 per 1000 people per year (95% confidence interval (CI) 1.9 to 2.9) based on presentations to Dutch general practice (van der Windt 1995). Adhesive capsulitis has been reported to affect slightly more women than men (Tekavec 2012; Walker 2004) and occurs most commonly in middle age, with an increased frequency in people with diabetes. Most studies indicate that it is a self-limiting condition lasting up to two to three years (Reeves 1975), although some people may have residual clinically detectable restriction of movement and disability beyond this time point (Binder 1984a; Hazelman 1972). The largest case series (269 shoulders in 223 people) found that at a mean follow-up of 4.4 years (range 2 to 20 years) 41% had ongoing symptoms (Hand 2008).

Description of the intervention

Electrotherapy modalities (also known as electrophysical agents) are types of physical therapy that aim to reduce pain and improve function via an increase in energy (electrical, sound, light, thermal) into the body (Watson 2008a; Watson 2010). Several electrotherapy modalities exist, including low-level laser therapy (LLLT), therapeutic ultrasound, interferential current and transcutaneous electrical nerve stimulation (TENS). The use of particular electrotherapy modalities in physical therapy practice has varied over time. Between 1990 and 2010, use of therapeutic ultrasound has increased in several countries, LLLT continues to enjoy consistent use, and use of TENS and interferential current has increased in the UK but declined in Australia (Shah 2012). Patients seeking treatment for musculoskeletal conditions seldom receive a single electrotherapy modality in isolation; other physical therapy interventions such as manual therapy and exercise are commonly delivered as co-interventions (Hanchard 2011). A brief description of the electrotherapy modalities investigated in this review, and their presumed mechanisms of action, are outlined as follows.

Low-level laser therapy (LLLT) generates a beam of light with a particular wavelength which has the potential to deliver light energy to tissue depths below the dermis (Basford 1989; Bjordal 2010; Peplow 2010). Studies suggest that LLLT contributes to pain relief by reducing pro-inflammatory cytokines and increasing anti-inflammatory growth factors and cytokines (Bjordal 2006; Peplow 2010; Sakurai 2000). Systematic reviews of randomised controlled trials (RCTs) have found that LLLT is more effective than placebo in the short-term for neck pain (Chow 2009), although findings are inconclusive for non-specific low-back pain (Yousefi-Nooraie 2008). The effects of LLLT are considered to be dependent on dosage, wavelength, site and duration of treatment, and researchers have argued that previous RCTs of LLLT with inconclusive findings may have delivered dosages that are below that expected to achieve a biological response (Bjordal 2006; Bjordal 2010).

Therapeutic ultrasound delivers energy to deep tissue sites through ultrasonic waves (at 1 or 3 MHz frequency and intensities between 0.1 watts/cm^2 and 3 watts/cm^2) using a crystal sound head. Treatment can be delivered in two forms, continuous (non-stop ultrasonic waves) and pulsed (intermittent ultrasonic waves) (Allen 2006; Watson 2008b). The purpose of treatment is to increase tissue temperature and induce non-thermal physiological changes (such as cell permeability and cell growth), which are believed to promote soft tissue healing and muscle relaxation (O'Brien 2007; Watson 2008b). However, previous Cochrane reviews have found no high quality evidence to support the use of therapeutic ultrasound for chronic low-back pain (Ebadi 2014), osteoarthritis (Rutjes 2010), carpal tunnel syndrome (Page 2013b) or acute ankle sprains (van den Bekerom 2011).

Interferential current involves crossing two medium frequency currents (most commonly 4000 Hz), which reportedly generates a low-frequency 'beating' (amplitude-modulated) effect at between 0 and 150 Hz in the deep tissues (Beatti 2010). These beat frequencies are believed to decrease pain, increase circulation and block nerve conduction. Two recent systematic reviews have found insufficient evidence to support the use of interferential current over placebo, or as an adjunct to other interventions, for a range of musculoskeletal conditions (Beatti 2010; Fuentes 2010).

Transcutaneous electrical nerve stimulation (TENS) delivers electrical stimulation via electrodes placed over the intact skin surface near the source of pain to activate underlying nerves (Jones 2009; Sluka 2003). Several types of TENS applications exist, the most common are conventional TENS (high frequency and low intensity, which is sufficient to produce a comfortable tingling sensation) and acupuncture-like TENS (low frequency and high intensity, which is sufficient to elicit muscle twitching) (Johnson 2008). The development of TENS was based on the Gate Control Theory of Pain (Melzack 1965), which suggests that there is a 'gating' mechanism in the dorsal horn of the spinal cord that regulates the amount of incoming painful stimuli via small diameter afferent nerve fibres and that stimulation of large diameter afferent nerve fibres using other stimuli (such as TENS) can 'close the gate' and reduce the perception of pain (Walsh 2009). Evidence from animal studies suggests that TENS reduces ongoing nociceptive cell activity and inhibits pain facilitatory pathways (DeSantana 2008; Jones 2009). However, previous Cochrane reviews have found no high quality evidence to support the use of TENS for chronic low-back pain (Khadilkar 2008), knee osteoarthritis (Rutjes 2009) or acute pain associated with medical procedures or rib fractures (Walsh 2009).

Pulsed electromagnetic field therapy (PEMF) involves the delivery of pulsing (that is 'on-off') low-frequency magnetic fields through the body, which is believed to provide temporary pain relief by influencing tissue generation and cell proliferation (Gordon 2007; Markov 2007). Moderate quality evidence from a previous Cochrane review suggests that PEMF is more effective than placebo in terms of reducing osteoarthritis pain, but not on function or quality of life (Li 2013).

Continuous short wave diathermy is the delivery of a constant stream of short wave (wavelength 3 to 30 m, frequency 10 to 100 MHz) electromagnetic radiation to produce deep heating within tissues (Allen 2006; Shields 2001). Short wave diathermy is designed to produce heat at deeper tissue levels than superficial

agents (such as a hot pack). The deep tissue heating is believed to induce an increase in metabolic activity, blood flow, collagen extensibility and nerve conduction, which are thought to encourage healing and relieve pain (Allen 2006; Shields 2001). A systematic review of continuous short wave diathermy for knee osteoarthritis found small effects on pain immediately post-treatment but no clinically important effect on function (Laufer 2012).

Two electrotherapy modalities are designed to facilitate delivery of topical medication through the skin (that is transdermal delivery). Phonophoresis is administered using a therapeutic ultrasound device (Machet 2002; Watson 2008b), and iontophoresis is administered using a low-intensity electrical current (Batheja 2006; Roustit 2014). The therapeutic ultrasound device used in phonophoresis is believed to enhance the absorption of the topically applied medication (Machet 2002). The iontophoretic device is believed to induce electromigration and electro-osmosis, which are thought to facilitate the movement of positively and negatively charged drugs into the skin (Roustit 2014). Previous Cochrane reviews have found very low quality evidence suggesting that phonophoresis results in better quality of life scores than therapeutic ultrasound in people with chronic low-back pain (Ebadi 2014), but that iontophoresis is no more effective than placebo for neck pain (Kroeling 2013).

Why it is important to do this review

The previous version of this review (Green 2003) included three trials investigating the efficacy of electrotherapy modalities for adhesive capsulitis (Leclaire 1991; Lee 1973; Taverna 1990). Leclaire 1991 and Lee 1973 concluded that there was little evidence to either support or refute the benefits of PEMF or infrared irradiation, respectively, while Taverna 1990 reported that LLLT was more effective than placebo laser. Other recently published systematic reviews of interventions for adhesive capsulitis (Favejee 2011; Maund 2012) have identified several new trials. Therefore, there is a need to synthesise the most up-to-date evidence on the efficacy of electrotherapy modalities for adhesive capsulitis.

Objectives

To synthesise the available evidence regarding the benefits and harms of electrotherapy modalities, delivered alone or in combination with other interventions, for the treatment of adhesive capsulitis.

Methods

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) of any design (for example parallel, cross-over, factorial) and controlled clinical trials using a quasi-randomised method of allocation, such as by alternation or date of birth. Reports of trials were eligible regardless of the language or date of publication.

Types of participants

We included trials that enrolled adults (> 16 years of age) with adhesive capsulitis (as defined by the trialists) for any duration. We included trials enrolling participants with various soft tissue disorders only if the results for the participants with adhesive capsulitis were presented separately or if 90% or more of participants in the trial had adhesive capsulitis. We excluded trials including participants with a history of significant trauma or systemic inflammatory conditions such as rheumatoid arthritis, osteoarthritis, hemiplegic shoulders, and pain in the shoulder region as part of a complex myofacial neck/shoulder/arm pain condition.

Types of interventions

We included trials comparing any electrotherapy modality to placebo, no treatment, a different electrotherapy modality, or any other intervention. Examples of eligible electrotherapy modalities included therapeutic ultrasound, LLLT, TENS, PEMF, interferential current, phonophoresis, iontophoresis, and continuous short wave diathermy. Trials primarily evaluating the effect of a manual therapy or exercise intervention were excluded and are included in a separate Cochrane review.

Types of outcome measures

We did not consider outcomes as part of the eligibility criteria.

Adhesive capsulitis is characterised by pain and global loss of range of movement. Given the mechanism by which electrotherapy modalities work, we determined reduction of pain to be the main aim of treatment. Considerable variation has been noted in the outcome measures reported in clinical trials of interventions for pain. However, there is general agreement that the outcome measures of greatest importance to patients should be considered. The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) has published consensus recommendations for determining clinically important changes in outcome measures in clinical trials of interventions for chronic pain (Dworkin 2008). Reductions in pain intensity of ≥ 30% and ≥ 50% reflect moderate and substantial clinically important differences, respectively, and it is recommended that the proportion of patients who respond with these degrees of pain relief should be reported.

Continuous outcome measures used in pain trials, such as mean change on a 100 mm visual analogue scale (VAS), may not follow a Gaussian distribution. Often a bimodal distribution is seen instead, where patients tend to report either very good or very poor pain relief (Moore 2010). This creates difficulty in interpreting the meaning of average changes in continuous pain measures. For this reason, a dichotomous outcome measure (the proportion of participants reporting ≥ 30% pain relief) may or may not also be clinically relevant for trials of adhesive capsulitis.

The original review determined that no trials had included a dichotomous outcome for pain, in keeping with the recognition that it has been the practice in most trials of interventions for chronic pain to report continuous measures only. We therefore also included a continuous measure of overall pain.

A global rating of treatment success such as the Patient Global Impression of Change scale (PGIC), which provides an outcome measure that integrates pain relief, changes in function and adverse events into a single, interpretable measure, is also recommended by IMMPACT and was included as a main outcome measure (Dworkin 2008).

Main outcomes

- Participant-reported pain relief of 30% or greater (a moderate clinically important difference)
- Overall pain (mean or mean change measured by VAS, numerical or categorical rating scales)
- Function. Where trialists reported outcome data for more than one function scale we extracted data on the scale that was highest on the following a priori defined list: (1) Shoulder Pain and Disability Index (SPADI); (2) Croft Shoulder Disability Questionnaire; (3) Constant Score; (4) Short Form-36 (SF-36) Physical Component Score; (5) Health Assessment Questionnaire; (6) any other function scale
- Global assessment of treatment success as defined by the trialists (for example proportion of participants with significant overall improvement)
- Active shoulder abduction (measured in degrees or other)
- Quality of life as measured by generic measures (such as components of the SF-36) or disease-specific tools
- Number of participants experiencing any adverse events

Other outcomes

- Night pain measured by VAS, numerical or categorical rating scales
- Pain on motion measured by VAS, numerical or categorical rating scales

- Other range of motion (ROM) measures for example flexion, external rotation and internal rotation (measured in degrees or other such as hand behind back distance in centimetres). Where trialists reported outcome data for both active and passive ROM measures we extracted the data on active ROM only
- Work disability
- Requiring surgery, for example manipulation under anaesthesia, arthroscopy

Timing of outcome assessment

We extracted outcome measures that assessed benefits of treatment (for example pain or function) at the following time points:

- up to three weeks;
- longer than three and up to six weeks (this was the main time point);
- longer than six weeks and up to six months; and
- longer than six months.

If data were available in a trial at multiple time points within each of the above periods (for example at four, five, and six weeks) we only extracted data at the latest possible time point of each period. We extracted adverse events at all time points.

We collated the main results of the review into summary of findings (SoF) tables, which provide key information concerning the quality of evidence and the magnitude and precision of the effect of the interventions. We included the main outcomes (see above) in the SoF tables with results at, or nearest, the main time point (six weeks) presented.

Search methods for identification of studies

Electronic searches

We searched CENTRAL (to Issue 4, 2014 in *The Cochrane Library*), MEDLINE (January 1966 to May 2014), EMBASE (January 1980 to May 2014), and CINAHL Plus (January 1937 to May 2014). The complete search strategies are presented in Appendix 1. The search terms used included clinical terms relevant to adhesive capsulitis, rotator cuff disorders and manual therapy and exercise interventions as the current review and Cochrane reviews of (i) manual therapy and exercise for adhesive capsulitis, (ii) manual therapy and exercise for rotator cuff disorders, and (iii) electrotherapy modalities for rotator cuff disorders were conducted simultaneously.

Searching other resources

We searched for ongoing trials and protocols of published trials in the clinical trials register that is maintained by the US National Institute of Health (http://clinicaltrials.gov) and the World Health Organization (WHO) International Clinical Trials Registry Platform (http://www.who.int/ictrp/). We also reviewed the reference lists of the included trials and any relevant review articles retrieved from the electronic searches to identify any other potentially relevant trials.

Data collection and analysis

Selection of studies

Two review authors (MJP and BM) independently selected trials for possible inclusion against a predetermined checklist of inclusion criteria (see Criteria for considering studies for this review). We screened titles and abstracts and initially categorised studies into the following groups.

- Possibly relevant: studies that met the inclusion criteria and studies from which it was not possible to determine whether they met the criteria either from their title or abstract.
- Excluded: studies clearly not meeting the inclusion criteria.

If a title or abstract suggested that the study was eligible for inclusion, or we could not tell, we obtained a full text version of the article and two review authors (MJP and BM) independently assessed it to determine whether the study met the inclusion criteria. The review authors resolved discrepancies through discussion or adjudication by a third author (SG or RB).

Data extraction and management

Two review authors (MJP and either SK or RJ) independently extracted data using a standard data extraction form developed for this review. The authors resolved any discrepancies through discussion or adjudication by a third author (SG or RB) until consensus was reached. We pilot tested the data extraction form and modified it accordingly before use. In addition to items for assessing risk of bias and numerical outcome data, we also recorded the following characteristics:

- trial characteristics, including type (for example parallel or cross-over), country, source of funding, and trial registration status (with registration number recorded if available);
- participant characteristics, including age, sex, duration of symptoms, and inclusion and exclusion criteria;
- intervention characteristics, including type of electrotherapy modality, duration of treatment, use of co-interventions;
- outcomes reported, including the measurement instrument used and timing of outcome assessment.

One author (MJP) compiled all comparisons and entered the outcome data into Review Manager 5.2.

For a particular systematic review outcome there may be a multiplicity of results available in the trial reports (for example multiple scales, time points and analyses). To prevent selective inclusion of data based on the results (Page 2013a), we used the following a priori defined decision rules to select data from trials:

- where trialists reported both final values and change from baseline values for the same outcome, we extracted final values;
- where trialists reported both unadjusted and adjusted values for the same outcome, we extracted unadjusted values;
- where trialists reported data analysed based on the intention-to-treat (ITT) sample and another sample (for example per-protocol, as-treated), we extracted ITT-analysed data;
- for cross-over RCTs, we preferentially extracted data from the first period only.

Where trials did not include a measure of overall pain but included one or more other measures of pain, for the purpose of combining data for the primary analysis of overall pain we combined overall pain with other types of pain in the following hierarchy: unspecified pain; pain with activity; daytime pain.

Assessment of risk of bias in included studies

Two review authors (MJP and either SK or RJ) independently assessed the risk of bias in the included trials using The Cochrane Collaboration's tool for assessing risk of bias, as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). The following domains were assessed:

- random sequence generation;
- allocation concealment;
- blinding of participants and personnel;
- blinding of outcome assessment (assessed separately for self-reported and objectively assessed outcomes);
- incomplete outcome data;
- selective reporting;
- other sources of bias (for example baseline imbalance).

Each item was rated as being at 'Low risk', 'Unclear risk' or 'High risk' of bias. We resolved any discrepancies through discussion or adjudication by a third author (SG or RB).

Measures of treatment effect

We used The Cochrane Collaboration's statistical software, Review Manager 5.2, to perform data analysis. We expressed dichotomous outcomes as risk ratios (RRs) with 95% confidence intervals (CIs) and continuous outcomes as mean differences (MDs) with 95% CIs if different trials used the same measurement instrument to measure the same outcome. Alternatively, we analysed continuous outcomes using the standardised mean difference (SMD) when trials measured the same outcome but employed different measurement instruments. To enhance interpretability of dichotomous outcomes, risk differences and the number needed to treat to benefit (NNTB) or the number needed to treat to harm (NNTH) were calculated. To enhance interpretability of continuous outcomes, pooled SMDs of overall pain and function were back-transformed to an original 0 to 100 mm VAS by multiplying the SMD and 95% CI by a representative pooled standard deviation (SD) at the baseline of one of the included trials.

Unit of analysis issues

The unit of analysis was the participant. Two trials included a small number of participants with bilateral adhesive capsulitis. In these trials we analysed data based on the number of participants, not the number of shoulders, in order to produce conservative estimates of effect.

Dealing with missing data

Where required, we contacted trialists via email (twice, separated by three weeks) to retrieve missing information about trial design, outcome data, or attrition rates such as dropouts, losses to follow-up and post-randomisation exclusions in the included trials. For continuous outcomes with no standard deviations (SD) reported, we calculated SDs from standard errors (SEs), 95% CIs or P values. If no measures of variation were reported and SDs could not be calculated, we planned to impute SDs from other trials in the same meta-analysis, using the median of the other SDs available (Ebrahim 2013). Where data were imputed or calculated (for example SDs calculated from SEs, 95% CIs or P values, or imputed from graphs or from SDs in other trials) we reported this in the tables Characteristics of included studies.

Assessment of heterogeneity

We assessed clinical heterogeneity by determining whether the characteristics of participants, interventions, outcome measures and timing of outcome measurement were similar across trials. We assessed statistical heterogeneity using the Chi^2 statistic and the I^2 statistic (Higgins 2002). We interpreted the I^2 statistic using the following as an approximate guide:

- 0% to 40% may not be important heterogeneity;
- 30% to 60% may represent moderate heterogeneity;
- 50% to 90% may represent substantial heterogeneity;
- 75% to 100% may represent considerable heterogeneity (Deeks 2011).

Assessment of reporting biases

To assess publication bias, we planned to generate funnel plots if at least 10 trials examining the same intervention comparison were included in the review, and comment on whether any asymmetry in the funnel plot was due to publication bias or methodological or clinical heterogeneity of the trials (Sterne 2011). To assess outcome reporting bias, we compared the outcomes specified in trial protocols with the outcomes reported in the corresponding trial publications; if trial protocols were unavailable, we compared the outcomes reported in the methods and results sections of the trial publications (Dwan 2011; Norris 2013). We generated an Outcome Reporting Bias In Trials (ORBIT) Matrix (http://ctrc.liv.ac.uk/orbit/) using the ORBIT classification system (Kirkham 2010). We compared the fixed-effect model estimate against the random-effects model estimate to assess the possible presence of small sample bias in the published literature (that is where the intervention effect is more beneficial in smaller studies). In the presence of small sample bias, the random-effects model estimate of the intervention effect is generally more beneficial than the fixed-effect model estimate (Sterne 2011).

Data synthesis

For this review update, a large number of trials that investigated a diverse range of interventions were identified. To define the most clinically important questions to investigate in the review, after completing data extraction one author (MJP) sent the list of all possible trial comparisons to both of the original primary authors of this review, who are both clinicians (SG, physiotherapist and RB, rheumatologist). After reviewing the list of possible trial comparisons, both authors discussed and drafted a list of clinically important review questions and categorised each trial comparison under the review question to which it fitted best. This process was conducted iteratively until all trial comparisons were allocated to a review question and was conducted without knowledge of the results of any outcomes. The following questions were defined.

1. Is an electrotherapy modality effective compared to placebo or no treatment?
2. Is an electrotherapy modality combined with manual therapy or exercise (or both) effective compared to manual therapy or exercise (or both) alone?
3. Is an electrotherapy modality effective compared to another active intervention (for example glucocorticoid injection, oral non-steroidal anti-inflammatory drugs (NSAIDs))?
4. Is one type of electrotherapy modality more effective than another?
5. Is a combination of an electrotherapy modality with manual therapy or exercise (or both) effective compared to placebo, no treatment, or another active intervention?
6. Is a combination of an electrotherapy modality with manual therapy or exercise (or both) and another active intervention more effective than the other active intervention alone?

7. Is a combination of an electrotherapy modality with manual therapy or exercise (or both) and another active intervention more effective than placebo or no treatment?

The first two questions were considered the main questions of the review.

We combined the results of trials with similar characteristics (participants, interventions, outcome measures and timing of outcome measurement) to provide estimates of benefits and harms. Where we could not combine data, we have summarised effect estimates and 95% CIs of each trial narratively. We planned to combine results using a random-effects meta-analysis model based on the assumption that clinical and methodological heterogeneity was likely to exist and to have an impact on the results.

Subgroup analysis and investigation of heterogeneity

We did not undertake any subgroup analyses.

Sensitivity analysis

We planned to perform a sensitivity analysis to investigate the robustness of the treatment effect (of the main outcomes) to allocation concealment and participant blinding by removing the trials that reported inadequate or unclear allocation concealment and lack of participant blinding from the meta-analysis to see if this changed the overall treatment effect.

Summary of findings tables

We presented the results of the most important comparisons of the review in summary of findings (SoF) tables, which summarise the quality of evidence, the magnitude of effect of the interventions examined, and the sum of the available data on the outcomes as recommended by The Cochrane Collaboration (Schünemann 2011a). The SoF tables include an overall grading of the evidence related to each of the main outcomes, using the GRADE approach (Schünemann 2011b).

In the comments column of the SoF tables, we reported the absolute per cent difference, the relative per cent change from baseline, and the number needed to treat (NNT) (the NNT was only provided when the outcome showed a statistically significant difference).

For dichotomous outcomes (pain relief of 30% or greater, global assessment, adverse events) the absolute risk difference was calculated using the risk difference statistic in RevMan. The result was expressed as a percentage, and the relative per cent change was calculated as the risk ratio (RR) - 1 and expressed as a percentage. For continuous outcomes (overall pain, function, active shoulder abduction, quality of life) the absolute risk difference was calculated as the improvement in the intervention group minus the improvement in the control group, in the original units (that is MD from RevMan divided by the units in the original scale), expressed as a percentage. The relative per cent change was calculated as the absolute change (or MD) divided by the baseline mean of the control group, expressed as a percentage.

In addition to the absolute and relative magnitude of effect provided in the SoF tables, for dichotomous outcomes the number needed to treat to benefit (NNTB) or the number needed to treat to harm (NNTH) was calculated from the control group event rate and the RR using the Visual Rx NNT calculator (Cates 2004). For the continuous outcomes, overall pain and function, the NNT was calculated using the Wells calculator software available at the Cochrane Musculoskeletal Review Group (CMSG) editorial office (www.cochranemsk.org). We assumed a minimal clinically important difference (MCID) of 1.5 points on a 10 point scale (or 15 points on a 100 point scale) for pain (Hawker 2011), and 10 points on a 100 point scale for function or disability (for example SPADI, Constant-Murley, Disabilities of the Arm, Shoulder and Hand (DASH)) for input into the calculator (Angst 2011; Roy 2009; Roy 2010).

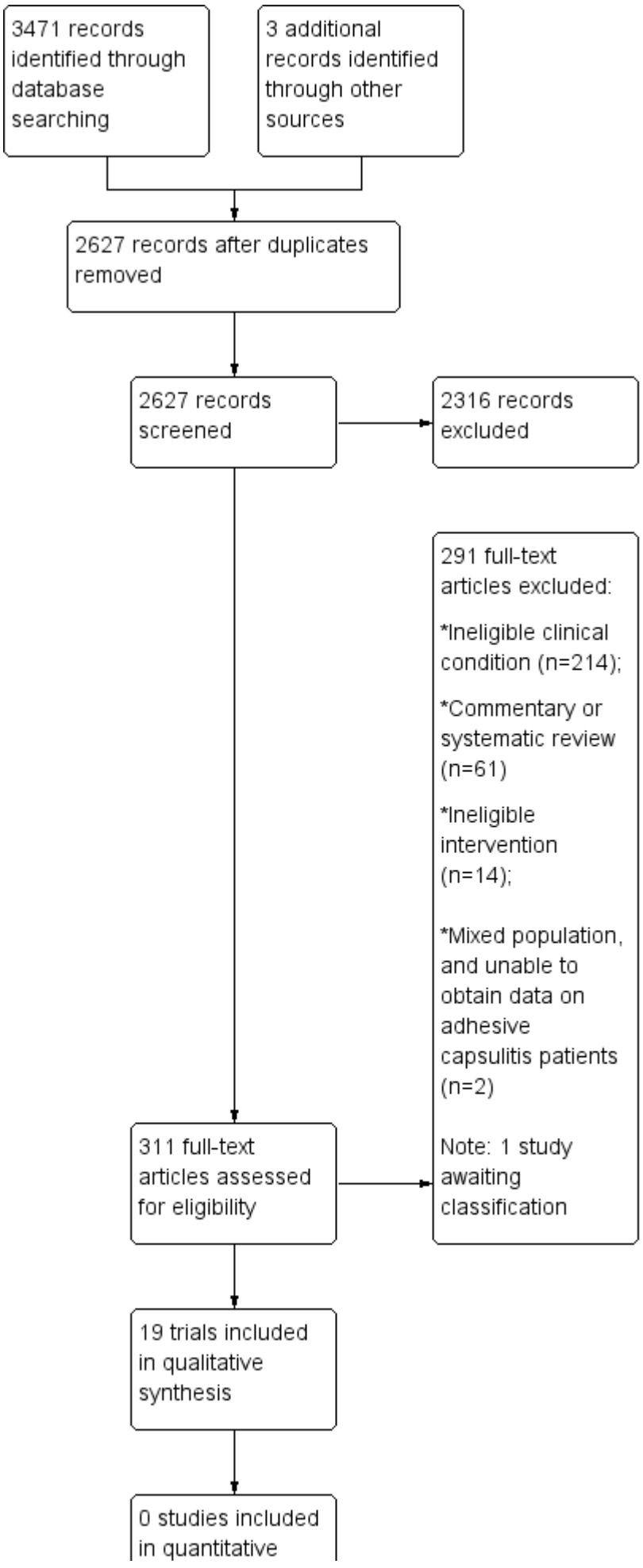
Results

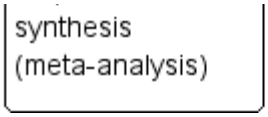
Description of studies

Results of the search

The search, conducted up to May 2014, yielded 3471 records across the four databases. Three additional records were identified from other sources (for example screening reference lists of previous systematic reviews and included trials). After removal of duplicates, 2627 unique records remained. Of these, 311 were retrieved for further scrutiny based on the title and abstract. Based on full text screening, 19 trials were deemed eligible for inclusion (Battisti 2007; Bumin 2001; Calis 2006; Carette 2003; Cheing 2008; Dewan 2011; Dogru 2008; Ghosh 2012; Guler-Uysal 2004; Kanai 2006; Leclaire 1991; Lee 1973; Leung 2008; Maryam 2012; Pajareya 2004; Rigato 2002; Ryans 2005; Stergioulas 2008; Taverna 1990). One trial was only available as a conference abstract and is awaiting assessment (Alicicco 2000), and one ongoing trial was identified in a clinical trials registry (ACTRN12611000680965). A flow diagram of the study selection process is presented in Figure 1.

Figure 1 Open in figure viewer | Download as PowerPoint


3471 records identified through database searching
3 additional records identified through other sources
2627 records after duplicates removed
2627 records screened
2316 records excluded
291 full-text articles excluded:
*Ineligible clinical condition (n=214);
*Commentary or systematic review (n=61)
*Ineligible intervention (n=14);
*Mixed population, and unable to obtain data on adhesive capsulitis patients (n=2)
Note: 1 study awaiting classification
311 full-text articles assessed for eligibility
19 trials included in qualitative synthesis
0 studies included in quantitative



Study flow diagram.

Included studies

A full description of all included trials is provided in the table of Characteristics of included studies. We contacted the authors of 17 trials to retrieve either (a) information about the study design, participants, interventions, and outcomes in the trial; (b) information required to complete the risk of bias assessments; or (c) missing data for unreported or partially reported outcomes. We received replies from six trialists (Carette 2003; Dogru 2008; Maryam 2012; Pajareya 2004; Ryans 2005; Stergioulas 2008).

Design

All trials were described as RCTs, and all trials used a parallel group design. Eight trials included two intervention arms (Dewan 2011; Dogru 2008; Guler-Uysal 2004; Kanai 2006; Leclaire 1991; Pajareya 2004; Stergioulas 2008; Taverna 1990), seven included three arms (Battisti 2007; Bumin 2001; Cheing 2008; Ghosh 2012; Leung 2008; Maryam 2012; Rigato 2002), and four included four arms (Calis 2006; Carette 2003; Lee 1973; Ryans 2005).

Participants

A total of 1249 participants were included in the 19 trials, with the number of participants per trial ranging from 30 to 122. The median of the mean age of participants in each trial was 55 years, and the median of the mean duration of symptoms was 5.5 months. Sixty-one per cent of participants were female. Diagnostic criteria or definitions of adhesive capsulitis varied in regards to the type, amount and direction of shoulder restriction, and ranged from undefined (Taverna 1990) to very specific (for example painful and limited passive glenohumeral mobility, with more restricted lateral rotation (< 8 °) relative to abduction and medial rotation) (Stergioulas 2008). Trials were conducted in Turkey (n = 4); Italy (n = 3); Canada, Hong Kong, India and United Kingdom (n = 2 each); and Greece, Iran, Japan and Thailand (n = 1 each).

Interventions

The characteristics of the electrotherapy modalities are summarised in Table 1. The trials evaluated physical therapy interventions comprising therapeutic ultrasound (four trials: Calis 2006; Carette 2003; Dogru 2008; Ghosh 2012), TENS (four trials: Calis 2006; Carette 2003; Dewan 2011; Maryam 2012), continuous short wave diathermy (four trials: Bumin 2001; Guler-Uysal 2004; Leung 2008; Pajareya 2004), PEMF (three trials: Battisti

2007; Leclaire 1991; Rigato 2002), interferential current (three trials: Cheing 2008; Dewan 2011; Ryans 2005), LLLT (two trials: Stergioulas 2008; Taverna 1990), Iodex phonophoresis (one trial: Bumin 2001), Iodex iontophoresis (one trial: Bumin 2001), polarity exchangeable permanent magnet (one trial: Kanai 2006), and infrared irradiation (one trial: Lee 1973). The median duration of electrotherapy was four weeks (range 1 to 12) with a median of three treatment sessions delivered per week (range 1 to 15) and a median of 10 treatment sessions provided in total across the treatment period (range 1 to 36). Several trials did not report important components of the electrotherapy modality, including duration of each treatment session, and frequency and intensity of the intervention. Five trials evaluated the efficacy of an electrotherapy modality delivered in isolation, testing: PEMF (Battisti 2007; Rigato 2002), LLLT (Taverna 1990), TENS (Dewan 2011), interferential current (Dewan 2011), and polarity exchangeable permanent magnet (Kanai 2006). The comparators also varied considerably comprising no treatment, placebo electrotherapy, glucocorticoid injection, manual therapy, exercises, hot pack, and oral NSAIDs.

Table 1. Electrotherapy intervention characteristics **Open in table viewer**

Electrotherapy modality	Study ID	Frequency/Intensity	Session duration	# electrotherapy sessions per week	# weeks of electrotherapy	Total # electrotherapy sessions
Therapeutic ultrasound	Calis 2006	Frequency: not reported; Intensity: 1.5 W/cm^2	5 mins	5	2	10
	Carette 2003	Not reported	Not reported	3	4	12
	Dogru 2008	Frequency: 3 MHz; Intensity: 1.5 W/cm^2	10 mins	5	2	10
	Ghosh 2012	Not reported	Not reported	Not reported	Not reported	Not reported
Continuous short wave diathermy	Bumin 2001	Not reported	20 mins	1	10	10
	Guler-Uysal 2004	Frequency: 27.12 MHz	20 mins	5	2	10
	Leung 2008	Frequency: 27.12 MHz; Intensity: adjusted to patient's feeling of comfortable warmth	20 mins	3	4	12

	Pajareya 2004	Not reported	20 mins	3	3	9
Pulsed electromagnetic field therapy	Battisti 2007	Frequency: 100 Hz	30 mins	7	2	14
	Leclaire 1991	Frequency: range from 10 to 30 Hz	30 mins	3	12	36
	Rigato 2002	Frequency: 100 Hz	30 mins	7	2	14
Interferential current	Cheing 2008	Current swept from 80 to 120 Hz	20 mins	2.5	4	10
	Dewan 2011	Current swept from 80 to 120 Hz	20 mins	2.5	4	10
	Ryans 2005	Not reported	Not reported	2	4	8
TENS	Calis 2006	Intensity: patient's tolerance	20 mins	5	2	10
	Carette 2003	Not reported	Not reported	3	4	12
	Dewan 2011	Frequency: High; Intensity: tolerance level just below pain threshold	20 mins	2.5	4	10
	Maryam 2012	Not reported	Not reported	1	6	6
Low-level laser therapy	Stergioulas 2008	810-nm Galium-Aluminum-Arsenide (Ga-Al-As) laser with a continuous output of 60 mW applied to eight of the most painful points for 30 seconds each	4 mins	1.5	8	12
	Taverna 1990	Frequency 1000 Hz and power 24 mW applied to painful points, points of greater access, and trigger points	15 to 20 mins	15	1	15

Iodex iontophoresis	Bumin 2001	Intensity: 2 mA	20 mins	1	10	10
Iodex phonophoresis	Bumin 2001	Intensity: 1.5 W/cm^2	5 mins	1	10	10
Polarity exchangeable permanent magnet	Kanai 2006	Not reported	24 hours	1	1	1
Infra-red irradiation	Lee 1973	Not reported	10 mins	1	6	6

Outcomes

An Outcome Reporting Bias In Trials (ORBIT) matrix, which presents the level of reporting of each outcome in each trial (rated as fully reported, partially reported, measured but not reported, unclear if measured, or not measured), is presented in Table 2. Of the main outcomes, two trials measured participant-reported pain relief of 30% or greater, 14 measured overall pain (mean or mean change), 13 measured function, four measured global assessment of treatment success, four measured active shoulder abduction, three measured quality of life, and five measured adverse events. Overall pain was most commonly measured using a 0 to 10 or 0 to 100 VAS. Function was most commonly measured using the SPADI, followed by the Constant Score. Of the other outcomes, 12 trials measured other measures of range of motion (ROM), two measured night pain, and four measured pain on motion. No trial explicitly measured work disability or requiring surgery. Partial reporting of outcomes occurred in eight trials. We contacted the authors of these eight trials to retrieve missing outcome data, and we obtained data from one (Stergioulas 2008).

Table 2. Outcome Reporting Bias In Trials (ORBIT) matrix **Open in table viewer**

Study ID	Main outcomes							Other outcomes	
	Participant-reported pain relief ≥30%	Overall pain	Function	Global assessment	Active shoulder abduction	QoL	Adverse events	Night pain	Pain o motio
Battisti 2007	Full	Full	Full	?	?	?	?	?	?
Bumin 2001	?	Full	?	?	?	?	?	?	?
Calis 2006	?	Partial	Full	?	?	?	?	?	?

Carette 2003	?	Full	Full	?	Measured	Full	?	?	?
Cheing 2008	?	Full	Full	?	?	?	?	?	?
Dewan 2011	?	Partial	Partial	?	?	?	?	?	?
Dogru 2008	?	Full	Full	?	?	Full	?	?	Full
Ghosh 2012	?	?	?	Full	?	?	?	?	?
Guler-Uysal 2004	?	Full	?	Full	?	?	?	Full	Full
Kanai 2006	?	Partial	?	?	?	?	?	?	?
Leclaire 1991	?	Measured	Measured	?	?	?	Full	?	Full
Lee 1973	?	?	?	?	Partial	?	?	?	?
Leung 2008	?	?	Full	?	?	?	?	?	?
Maryam 2012	Not measured	Full	Full	Not measured	Not measured	Not measured	Not measured	Not measured	Not measu
Pajareya 2004	?	?	Full	Full	?	?	Full	?	?
Rigato 2002	Partial	Full	Full	?	?	?	Full	?	?
Ryans 2005	?	Full	Full	?	Measured	Measured	?	?	?
Stergioulas 2008	?	Full	Full	?	Full	?	Full	Full	Full
Taverna 1990	?	?	?	Full	?	?	Full	?	?

'Full'= sufficient data for inclusion in a meta-analysis was reported (e.g. mean, standard deviation, and sample size per group for continuous outcomes)

'Partial' = insufficient data for inclusion in a meta-analysis was reported (e.g. means only, with no measures of variation)

'Measured' = outcome was measured but no outcome data was reported

'Not measured' = outcome was not measured by the trialists

'?' = unclear whether the outcome was measured or not (as a trial protocol was unavailable)

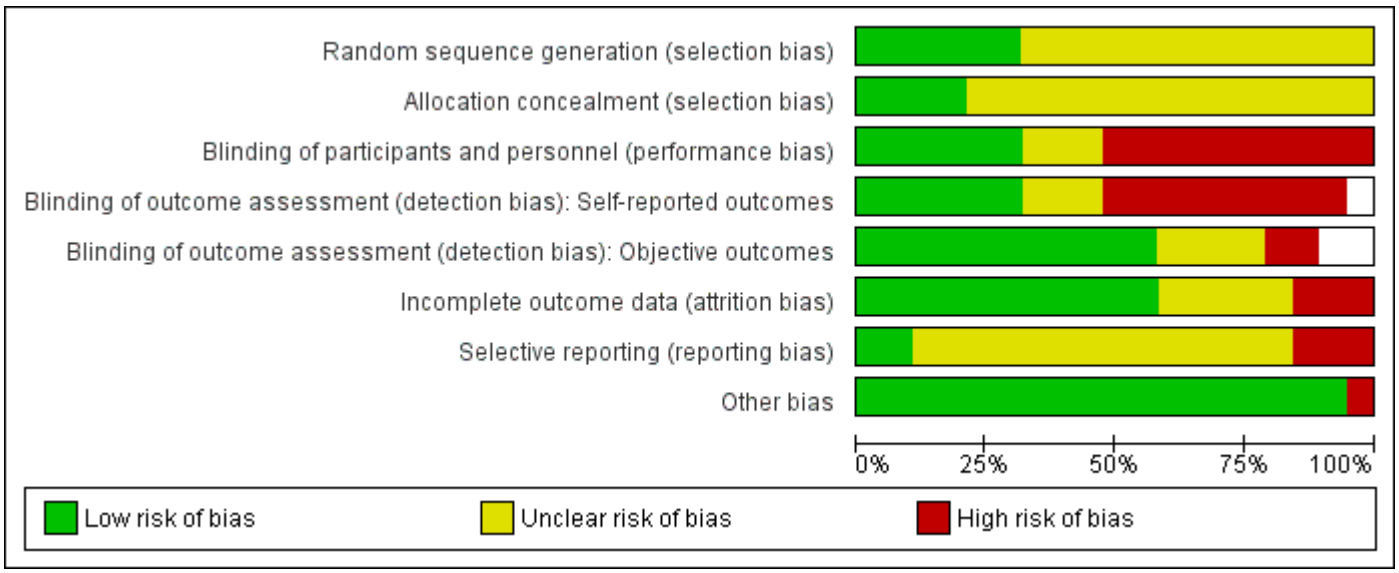
Excluded studies

Of the 311 full text records retrieved for further scrutiny, the majority (n = 275) were excluded because they were studies or commentaries focused on shoulder pain due to conditions other than adhesive capsulitis (that is rotator cuff disorders or mixed shoulder pain conditions). We have listed 16 adhesive capsulitis studies in the table Characteristics of excluded studies. The reasons for their exclusion were that the intervention was ineligible (for example an electrotherapy modality was provided to all groups with or without a co-intervention (n = 14)), or the trial included a mixed population of participants with either adhesive capsulitis or lateral epicondylitis and data could not be obtained on the subgroup of adhesive capsulitis participants (n = 2).

Risk of bias in included studies

A summary of the risk of bias in the included trials is presented in Figure 2 and Figure 3.

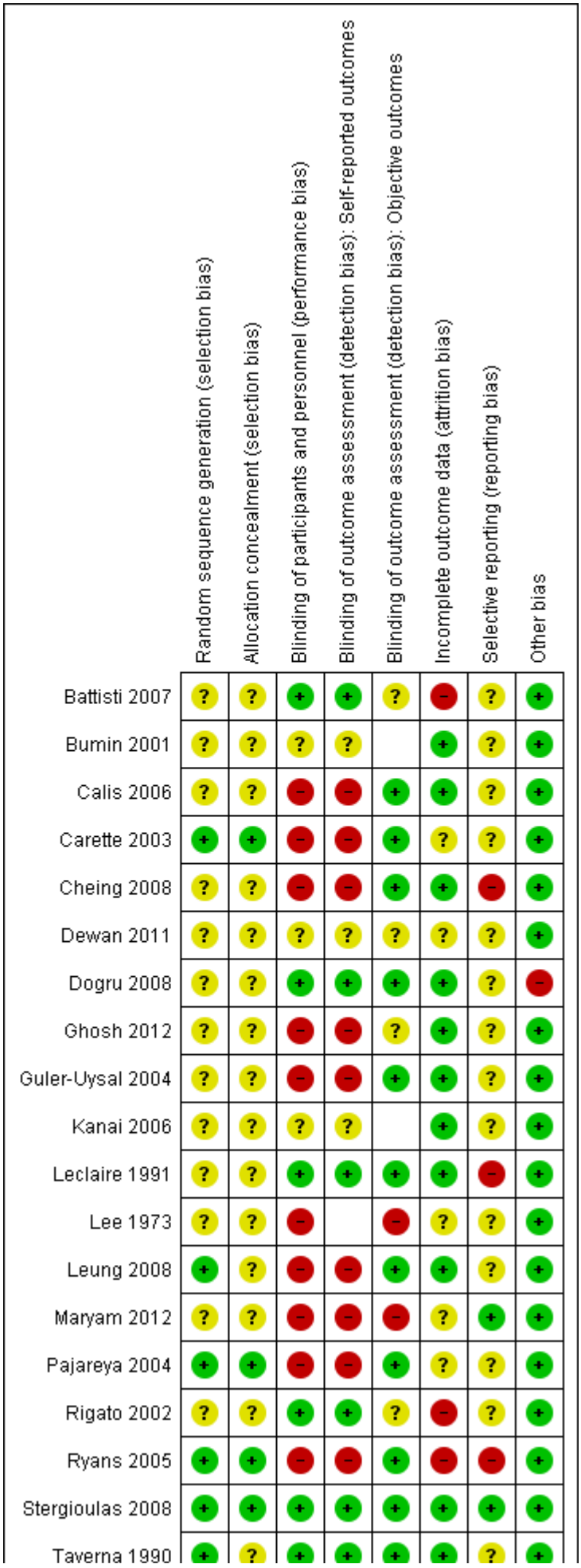
Figure 2 **Open in figure viewer** | **Download as PowerPoint**

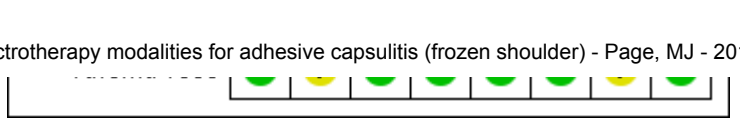


Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 3

Open in figure viewer | Download as PowerPoint


Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias): Self-reported outcomes
Blinding of outcome assessment (detection bias): Objective outcomes
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
Battisti 2007
Bumin 2001
Calis 2006
Carette 2003
Cheing 2008
Dewan 2011
Dogru 2008
Ghosh 2012
Guler-Uysal 2004
Kanai 2006
Leclaire 1991
Lee 1973
Leung 2008
Maryam 2012
Pajareya 2004
Rigato 2002
Ryans 2005
Stergioulas 2008
Taverna 1990



Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Allocation

Six trials (Carette 2003; Leung 2008; Pajareya 2004; Ryans 2005; Stergioulas 2008; Taverna 1990) reported using an adequate method to generate a random allocation sequence, while only four trials (Carette 2003; Pajareya 2004; Ryans 2005; Stergioulas 2008) reported using an adequate method of allocation concealment. Thirteen trials did not report how the allocation sequence was generated, and 15 trials did not report how the allocation sequence was concealed, so the risk of selection bias in these trials was unclear.

Blinding

Six trials (Battisti 2007; Dogru 2008; Leclaire 1991; Rigato 2002; Stergioulas 2008; Taverna 1990) were rated at low risk of performance bias due to successful blinding of participants. This was achieved by delivering a placebo intervention to the control group or not informing participants of the type of electrotherapy they would receive. Three trials were rated at unclear risk of performance bias because participants received different types of electrotherapy, but it was unclear whether they were provided with any information that would make them perceive the type of electrotherapy they received as superior or inferior to the alternative type of electrotherapy (Bumin 2001; Dewan 2011; Kanai 2006). The remaining 10 trials were rated at high risk of performance bias as the participants were not blinded and may have had different expectations about the benefits of each intervention. Of 18 trials assessing self-reported outcomes, the same six trials that blinded participants were rated at low risk of detection bias for self-reported outcomes, three were rated at unclear risk of detection bias due to unclear participant blinding (Bumin 2001; Dewan 2011; Kanai 2006), and the remaining nine trials were rated at high risk of detection bias for self-reported outcomes due to lack of participant blinding. Of 17 trials measuring objectively-rated outcomes (for example ROM), 11 trials (Calis 2006; Carette 2003; Cheing 2008; Dogru 2008; Guler-Uysal 2004; Leclaire 1991; Leung 2008; Pajareya 2004; Ryans 2005; Stergioulas 2008; Taverna 1990) reported blinding of outcome assessors and were thus rated at low risk of detection bias for objective outcomes. Two trials (Lee 1973; Maryam 2012) failed to blind the assessors of objective outcomes, so the risk of detection bias for objective outcomes was high; whereas four trials (Battisti 2007; Dewan 2011; Ghosh 2012; Rigato 2002) did not report whether such blinding was done, so the risk of detection bias for objective outcomes was unclear.

Incomplete outcome data

Eleven trials (Bumin 2001; Calis 2006; Cheing 2008; Dogru 2008; Ghosh 2012; Guler-Uysal 2004; Kanai 2006; Leclaire 1991; Leung 2008; Stergioulas 2008; Taverna 1990) either had no dropouts, losses to follow-up or exclusions, or had a small amount of incomplete data that was deemed unlikely to bias the results. These trials were rated at low risk of attrition bias. Three trials (Battisti 2007; Rigato 2002; Ryans 2005) reported differential dropouts across the groups, with the reasons appearing to be related to the treatments received, and were thus rated at high risk of attrition bias. The remaining five trials did not report either the amount of or the reasons for incomplete outcome data and so had an unclear risk of attrition bias (Carette 2003; Dewan 2011; Lee 1973; Maryam 2012; Pajareya 2004).

Selective reporting

Two trials (Maryam 2012; Stergioulas 2008) were rated at low risk of selective reporting bias because all outcomes specified in the trial registry entry were fully reported in the trial publications or were provided by the trialist on request. Three trials were rated at high risk of selective reporting bias because some of the outcomes that were reported in either the trial registry entry or in the methods section of the publication were not reported at all in the results section (Cheing 2008; Leclaire 1991; Ryans 2005). The remaining 14 trials were rated at unclear risk of selective reporting bias because either (a) the outcome data were completely reported for all outcomes specified in the methods section of the publication, but none of these trials were registered in a trials registry or had an available trial protocol so it was unclear whether other outcomes were measured but not reported based on the results; or (b) the outcome data were incompletely reported (for example reporting means without any measures of variation) but it was unclear whether the data were incompletely reported based on the statistical significance, magnitude or direction of the results, or not.

Other potential sources of bias

All trials except one (Dogru 2008) were rated as being free from other potential sources of bias. Dogru 2008 reported that participants in the therapeutic ultrasound plus home exercises group had worse pre-treatment values and lower compliance with the home exercises than participants in the placebo ultrasound plus home exercises group, which may have biased the results towards the null.

Effects of interventions

See: **Summary of findings for the main comparison** Low-level laser therapy (LLLT) compared to placebo for adhesive capsulitis (frozen shoulder); **Summary of findings 2** Pulsed electromagnetic field therapy (PEMF) compared to placebo for adhesive capsulitis (frozen shoulder); **Summary of findings 3** Low-level laser therapy (LLLT) plus exercise compared to exercise for adhesive capsulitis (frozen shoulder)

Due to heterogeneity of the interventions, comparators and outcomes, we were unable to conduct any meta-analyses. Non-synthesised summary data and effect estimates (with 95% CIs) of all outcomes were presented either in the Data and analyses or Additional tables sections (we have also reported effect estimates and 95% CIs for the main outcomes at all time points for comparisons falling under questions 1 and 2 in the following section). We have reported all time points as post-randomisation. Unless otherwise stated, differences between groups in overall pain and function that were reported as 'significant' meant that the effect estimate met our criteria for a minimal clinically important difference and the 95% CI did not include the null value.

1) Is an electrotherapy modality effective compared to placebo or no treatment?

No trial compared therapeutic ultrasound, interferential current, infrared irradiation, continuous short wave diathermy, iontophoresis, TENS or multiple electrotherapy modalities to placebo or no treatment. Three trials compared an electrotherapy modality to placebo: one trial compared LLLT to placebo (Taverna 1990), and two trials compared PEMF to placebo (Battisti 2007; Rigato 2002).

LLLT

See Table 3; summary of findings Table for the main comparison. Taverna 1990 compared LLLT to placebo for six days in 40 participants. Apart from an unclear risk of selection bias (the trialists did not report the method of allocation sequence) all other risk of bias domains were at low risk. The trialists found that participants receiving LLLT were statistically significantly more likely to be rated as having global treatment success at six days than participants receiving placebo (RR 8.00, 95% CI 2.11 to 30.34). No participant in either group reported any adverse events. Overall, based on low quality evidence, LLLT may be more effective than placebo at the end of six days of treatment.

Table 3. Taverna 1990: LLLT (intervention) versus placebo (control) **Open in table viewer**

OUTCOME	INTERVENTION		CONTROL		EFFECT ESTIMATE
	Events	Total	Events	Total	Risk ratio (95% CI)
Global assessment of treatment success ("excellent" or "good" result) at 6 days	16	20	2	20	8.00 [2.11, 30.34]

PEMF

See Table 4; summary of findings Table 2. Two trials compared PEMF to placebo for two weeks (Battisti 2007; Rigato 2002), but no outcome data were available for the placebo group in Rigato 2002 (none were reported in the publication and the trialist no longer had access to the data). Battisti 2007 (60 participants) was a three-arm trial comparing low-frequency (100 MHz) PEMF to Therapeutic Application of a Musically Modulated Electromagnetic Field (TAMMEF) and to placebo, and assessed outcomes at two weeks. The TAMMEF intervention is not a standard type of PEMF that can be applied by physical therapists, so no data for this group were included in the review. Participants and outcome assessors were blinded but there was a high risk of attrition bias because a high proportion of the placebo group withdrew due to lack of response to treatment, which was likely to bias the results of the trial in favour of the active treatment groups. The trialists found that statistically significantly more participants receiving low-frequency (100 Hz) PEMF reported pain relief of 30% or greater compared to participants receiving placebo, at two weeks (RR 19.19, 95% CI 1.25 to 294.21) but there was no statistically significant difference between groups in terms of total recovery of joint function (RR 14.24, 95% CI 0.91 to 221.75). The precision of these effect estimates was very low, so there was a large degree of uncertainty in these results. Overall, based on very low quality evidence, we are uncertain whether PEMF is more or less effective than placebo.

Table 4. Battisti 2007: PEMF (low frequency 100 Hz) (intervention) versus placebo (control) **Open in table viewer**

OUTCOME	INTERVENTION		CONTROL		EFFECT ESTIMATE
	Events	Total	Events	Total	Risk ratio (95% CI)
Overall pain (complete resolution of SPADI pain) at 15 days	15	20	0	12	19.19 [1.25, 294.21]
Function (total recovery of joint function) at 15 days	11	20	0	12	14.24 [0.91, 221.75]

2) Is an electrotherapy modality combined with manual therapy or exercise (or both) effective compared to manual therapy or exercise (or both) alone?

No trial compared an electrotherapy modality plus manual therapy to manual therapy alone. No trial compared an electrotherapy modality plus manual therapy and exercise to manual therapy and exercise alone. Six trials compared an electrotherapy modality plus exercise to exercise alone (Bumin 2001; Calis 2006; Dogru 2008; Leclaire 1991; Leung 2008; Stergioulas 2008). Figure 4 presents non-synthesised data for all trials reporting overall pain, and Figure 5 presents non-synthesised data for all trials reporting function (the data were presented as SMDs because the trials used different measurement instruments). Data for other outcomes are reported in the tables indicated below. A SoF table was created for the comparison LLLT plus exercise versus placebo plus exercise because, of all the trials falling under this review question, the trial investigating this comparison reported the largest number of our main review outcomes.

Figure 4

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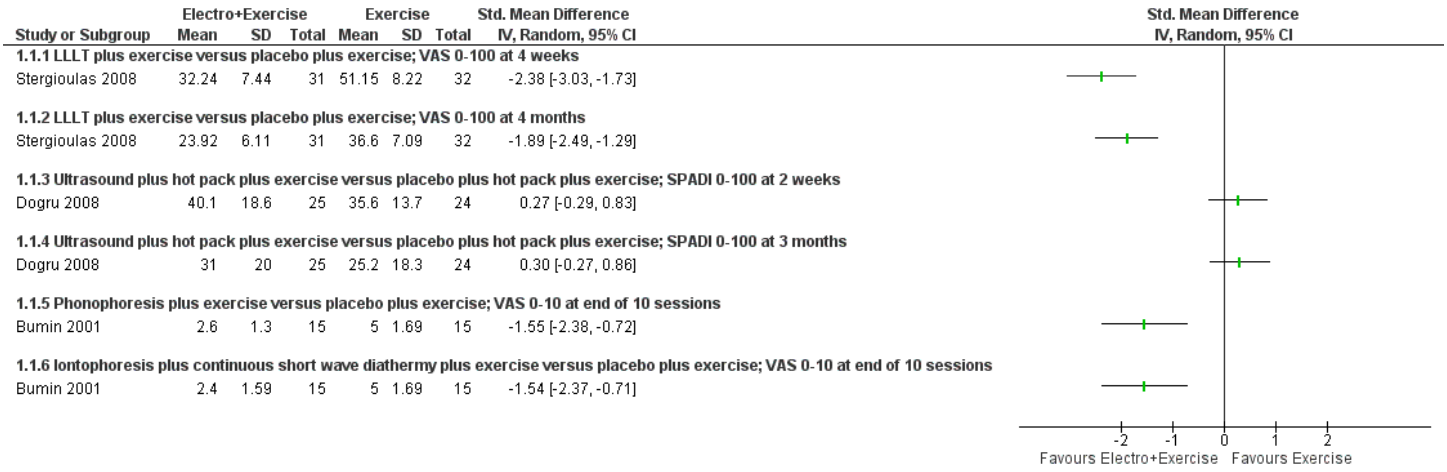
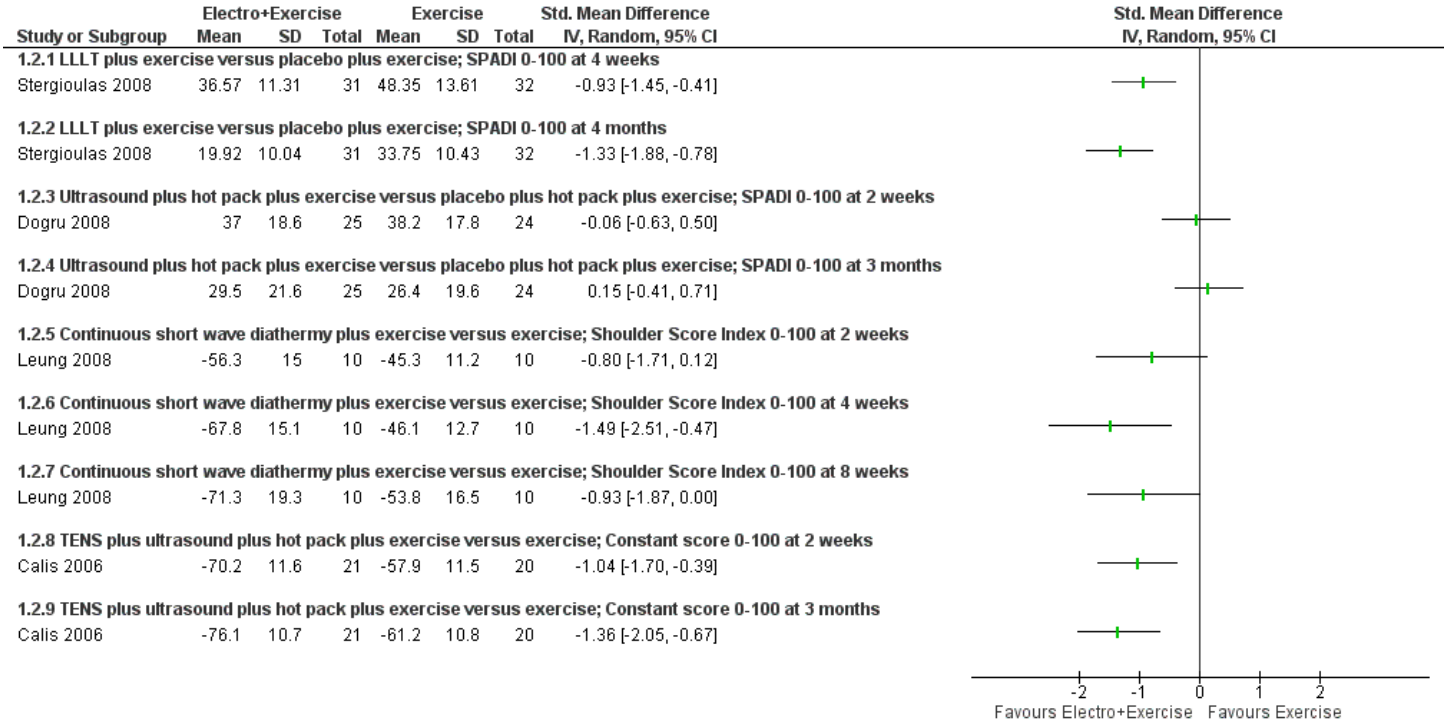


Forest plot of comparison: 1 Electrotherapy modality plus manual therapy or exercise (or both) versus manual therapy or exercise (or both), outcome: 1.1 Overall pain.

Figure 5

Open in figure viewer | Download as PowerPoint



Forest plot of comparison: 1 Electrotherapy modality plus manual therapy or exercise (or both) versus manual therapy or exercise (or both), outcome: 1.2 Function.

LLLT

See Table 5; summary of findings Table 3. One trial (63 participants) compared LLLT plus home exercises to placebo plus home exercises for eight weeks (Stergioulas 2008). All risk of bias domains were rated at low risk. The trialists found that, compared to placebo plus exercise, participants receiving LLLT plus exercise had clinically and statistically significantly lower overall pain at the fourth week of treatment (MD -18.81, 95% CI -22.68 to -14.94, 100 point scale) and statistically (but not clinically) significantly lower pain at four months (MD -12.68, 95% CI -15.95 to -9.41, 100 point scale); clinically and statistically significantly less disability at four weeks (MD -11.78, 95% CI -17.95 to -5.61, 100 point scale) and four months (MD -13.83, 95% CI -18.88 to -8.78, 100 point scale); and greater active abduction at four weeks (MD 8.99, 95% CI 2.41 to 15.57) but not at four months (MD 5.20, 95% CI -1.60 to 12.00). All these 95% CIs included non-clinically important differences as possible estimates of effect. In terms of other outcomes, the LLLT group had statistically significantly lower night pain and pain on motion at four weeks and four months, but other measures of active ROM (flexion and external rotation) did not significantly differ between groups at either time point. No participant in either group reported any adverse events. Overall, based on moderate quality evidence, LLLT is probably an effective adjunct to home exercises in terms of pain up to four weeks and function up to four months.

Table 5. Stergioulas 2008: LLLT plus exercise (intervention) versus placebo plus exercise (control) **Open in table viewer**

OUTCOME	INTERVENTION			CONTROL			EFFECT ESTIMATE
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-100) at 4 weeks	32.34	7.44	31	51.15	8.22	32	-18.81 [-22.68, -14.94]
Overall pain (VAS 0-100) at 4 months	23.92	6.11	31	36.6	7.09	32	-12.68 [-15.95, -9.41]
Function (SPADI 0-100) at 4 weeks	36.57	11.31	31	48.35	13.61	32	-11.78 [-17.95, -5.61]
Function (SPADI 0-100) at 4 months	19.92	10.04	31	33.75	10.43	32	-13.83 [-18.88, -8.78]
Night pain (VAS 0-100) at 4 weeks	41.42	7.69	31	55.67	8.49	32	-14.25 [-18.25, -10.25]
Night pain (VAS 0-100) at 4 months	19.38	5.77	31	42.35	7.57	32	-22.97 [-26.29, -19.65]
Pain on motion (VAS 0-100) at 4 weeks	45.57	8.27	31	67.75	8.03	32	-22.18 [-26.21, -18.15]
Pain on motion (VAS 0-100) at 4 months	22.54	6.02	31	39.78	7.65	32	-17.24 [-20.63, -13.85]
Active flexion (degrees) at 4 weeks	101.07	14.42	31	98.22	14.14	32	2.85 [-4.20, 9.90]
Active flexion (degrees) at 4 months	102.55	14.78	31	97.72	14.01	32	4.83 [-2.29, 11.95]

Active abduction (degrees) at 4 weeks	78.67	13.76	31	69.68	12.87	32	8.99 [2.41, 15.57]
Active abduction (degrees) at 4 months	85.63	13.95	31	80.43	13.58	32	5.20 [-1.60, 12.00]
Active external rotation (degrees) at 4 weeks	35.33	9.91	31	33.56	9.12	32	1.77 [-2.94, 6.48]
Active external rotation (degrees) at 4 months	42.72	10.05	31	38.53	9.9	32	4.19 [-0.74, 9.12]

Therapeutic ultrasound

See Table 6. One trial (49 participants) compared therapeutic ultrasound plus hot pack and exercise to placebo ultrasound plus hot pack and exercise for two weeks (Dogru 2008). Participants and outcome assessors were blinded but those in the ultrasound group had worse pre-treatment values and lower compliance with home exercises than participants in the placebo ultrasound group, which may have biased results towards the null. Therapeutic ultrasound plus hot pack and exercise was not significantly different to placebo ultrasound plus hot pack and exercise in terms of overall pain at two weeks (MD 4.50, 95% CI -4.62 to 13.62, 100 point scale) and three months (MD 5.80, 95% CI -4.93 to 16.53, 100 point scale), function at two weeks (MD -1.20, 95% CI -11.39 to 8.99, 100 point scale) and three months (MD 3.10, 95% CI -8.44 to 14.64, 100 point scale), quality of life at three months (SF-36 Physical Component Summary (PCS) MD -0.40, 95% CI -5.22 to 4.42, 100 point scale; SF-36 Mental Component Sumamry (MCS) MD 1.00, 95% CI -5.19 to 7.19, 100 point scale), or pain on motion and passive ROM at two weeks and three months. Overall, based on very low quality evidence, we are uncertain whether therapeutic ultrasound is an effective adjunct to hot packs and exercise.

Open in table viewer

Table 6. Dogru 2008: Therapeutic ultrasound plus hot pack plus exercise (intervention) versus placebo ultrasound plus hot pack plus exercise (control)

OUTCOME	INTERVENTION			CONTROL			EFFECT ESTIMATE
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (SPADI 0-100) at 2 weeks	40.1	18.6	25	35.6	13.7	24	4.50 [-4.62, 13.62]
Overall pain (SPADI 0-100) at 3 months	31	20	25	25.2	18.3	24	5.80 [-4.93, 16.53]
Function (SPADI 0-100) at 2 weeks	37	18.6	25	38.2	17.8	24	-1.20 [-11.39, 8.99]
Function (SPADI 0-100) at 3 months	29.5	21.6	25	26.4	19.6	24	3.10 [-8.44, 14.64]
Pain on motion (VAS 0-100) at 2 weeks	39.6	25.3	25	40.7	20.3	24	-1.10 [-13.92, 11.72]
Pain on motion (VAS 0-100) at 3 months	24.8	29.9	25	23.6	25.5	24	1.20 [-14.34, 16.74]

Passive abduction (degrees) at 2 weeks	142.8	25.9	25	146	26.2	24	-3.20 [-17.79, 11.39]
Passive abduction (degrees) at 3 months	147.8	30.1	25	148	26.5	24	-0.20 [-16.06, 15.66]
Passive flexion (degrees) at 2 weeks	162.6	12.4	25	165.4	15	24	-2.80 [-10.52, 4.92]
Passive flexion (degrees) at 3 months	163.7	16.5	25	168.5	13	24	-4.80 [-13.10, 3.50]
Passive internal rotation (degrees) at 2 weeks	52.2	15.7	25	58.3	15.5	24	-6.10 [-14.84, 2.64]
Passive internal rotation (degrees) at 3 months	57.4	13.8	25	60.9	15.3	24	-3.50 [-11.67, 4.67]
Passive external rotation (degrees) at 2 weeks	58	16.6	25	71.3	14.9	24	-13.30 [-22.12, -4.48]
Passive external rotation (degrees) at 3 months	65.7	19.4	25	75.4	15.5	24	-9.70 [-19.51, 0.11]
Quality of life (SF-36 PCS 0-100) at 3 months	44.2	8.4	25	44.6	8.8	24	-0.40 [-5.22, 4.42]
Quality of life (SF-36 MCS 0-100) at 3 months	44.8	11.5	25	43.8	10.6	24	1.00 [-5.19, 7.19]

Phonophoresis

See Table 7. One trial (30 participants) compared Iodex phonophoresis plus exercise to placebo ultrasound plus exercise (Bumin 2001). Participants and outcome assessors were blinded but the risk of selection bias was unclear. Iodex phonophoresis plus exercise resulted in significantly less overall pain at the end of 10 treatment sessions than placebo ultrasound plus exercise (MD -2.40, 95% CI -3.48 to -1.32, 10 point scale), though the time point was unclear as the trialists did not report how many sessions were delivered per week. Overall, based on very low quality evidence, we are uncertain whether Iodex phonophoresis is an effective adjunct to exercise.

Open in table viewer

Table 7. Bumin 2001: Phonophoresis plus exercise (intervention) versus placebo ultrasound plus exercise (control)

OUTCOME	INTERVENTION			CONTROL			EFFECT ESTIMATE
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-10) at the end of 10 sessions	2.6	1.3	15	5	1.69	15	-2.40 [-3.48, -1.32]

PEMF

See Table 8. One trial (47 participants) compared PEMF plus hot pack and exercise to placebo electrotherapy plus hot pack and exercise for 12 weeks (Leclaire 1991). The participants and outcome assessors were blinded but there was an unclear risk of selection bias. There was no significant difference between groups

in pain on motion or ROM (unclear if active or passive) at four or eight weeks. Overall, based on very low quality evidence, we are uncertain whether PEMF is an effective adjunct to hot packs and exercise.

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Table 8. Leclaire 1991: PEMF plus hot pack plus exercise (intervention) versus placebo plus hot pack plus exercise (control)

OUTCOME	INTERVENTION			CONTROL			EFFECT ESTIMATE
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Pain at rest (4-point ordinal scale) ar 12 weeks	1.5	0.61	22	1.4	0.65	25	Not estimable (outcome is not continuous)
Pain on movement (4-point ordinal scale) ar 12 weeks	2.2	0.76	22	2.2	0.7	25	Not estimable (outcome is not continuous)
Flexion (degrees) at 4 weeks (unclear if active or passive)	149	15.4	22	154	9.8	25	-5.00 [-12.49, 2.49]
Flexion (degrees) at 8 weeks (unclear if active or passive)	163	17.1	22	171	11.9	25	-8.00 [-16.53, 0.53]
Abduction (degrees) at 4 weeks (unclear if active or passive)	115	17.3	22	120	13.2	25	-5.00 [-13.89, 3.89]
Abduction (degrees) at 8 weeks (unclear if active or passive)	135	19.8	22	142	13.1	25	-7.00 [-16.74, 2.74]
External rotation (degrees) at 4 weeks (unclear if active or passive)	57	22.4	22	62	16.8	25	-5.00 [-16.44, 6.44]
External rotation (degrees) at 8 weeks (unclear if active or passive)	71	20.3	22	80	14.5	25	-9.00 [-19.21, 1.21]
Internal rotation (degrees) at 4 weeks (unclear if active or passive)	33	10.3	22	36	10	25	-3.00 [-8.82, 2.82]
Internal rotation (degrees) at 8 weeks (unclear if active or passive)	38	9.9	22	40	4	25	-2.00 [-6.42, 2.42]

Continuous short wave diathermy

See Table 9. One trial (30 participants) compared continuous short wave diathermy plus exercise to exercise alone for four weeks (Leung 2008). Given the inability to blind participants and personnel, the trial had a high risk of performance bias and detection bias for the self-reported outcomes. The participants in the continuous short wave diathermy and exercise group had significantly better function scores than

participants receiving exercise alone at four weeks (MD 21.70, 95% CI 9.47 to 33.93, 100 point scale) and eight weeks (MD 17.50, 95% CI 1.76 to 33.24, 100 point scale) and had statistically significantly greater external rotation and less hand-behind-back distance than the exercise alone group, though flexion did not significantly differ between the groups. Overall, based on very low quality evidence, we are uncertain whether continuous short wave diathermy is an effective adjunct to exercise.

Table 9. Leung 2008: Short wave diathermy plus exercise (intervention) versus exercise (control) **Open in table viewer**

OUTCOME	INTERVENTION			CONTROL			EFFECT ESTIMATE
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Function (Shoulder Score Index 0-100) at 2 weeks	56.3	15	10	45.3	11.2	10	11.00 [-0.60, 22.60]
Function (Shoulder Score Index 0-100) at 4 weeks	67.8	15.1	10	46.1	12.7	10	21.70 [9.47, 33.93]
Function (Shoulder Score Index 0-100) at 8 weeks	71.3	19.3	10	53.8	16.5	10	17.50 [1.76, 33.24]
Flexion (degrees) at 2 weeks (unclear if active or passive)	146.9	13.5	10	134.7	16.6	10	12.20 [-1.06, 25.46]
Flexion (degrees) at 4 weeks (unclear if active or passive)	146.9	14.2	10	132.1	25.7	10	14.80 [-3.40, 33.00]
Flexion (degrees) at 8 weeks (unclear if active or passive)	148.2	14.4	10	137.6	20.8	10	10.60 [-5.08, 26.28]
External rotation (degrees) at 2 weeks (unclear if active or passive)	59.3	19.8	10	39.5	20.6	10	19.80 [2.09, 37.51]
External rotation (degrees) at 4 weeks (unclear if active or passive)	60.9	14.5	10	43.3	22.6	10	17.60 [0.96, 34.24]
External rotation (degrees) at 8 weeks (unclear if active or passive)	62.1	11.5	10	41.1	23.2	10	21.00 [4.95, 37.05]
Hand behind back distance (cm) at 2 weeks (unclear if active or passive)	7.2	6.1	10	14.7	8.1	10	-7.50 [-13.78, -1.22]
Hand behind back distance (cm) at 4 weeks (unclear if active or passive)	7.6	5.7	10	14.7	8	10	-7.10 [-13.19, -1.01]
Hand behind back distance (cm) at 8 weeks (unclear if active or passive)	6	7.3	10	13	6.7	10	-7.00 [-13.14, -0.86]

Multiple electrotherapy modalities

See Table 10. One trial (30 participants) compared Iodex iontophoresis plus continuous short wave diathermy plus exercise to placebo ultrasound plus exercise (Bumin 2001). Participants and outcome assessors were blinded but the risk of selection bias was unclear. The trialists found that Iodex iontophoresis plus continuous short wave diathermy plus exercise resulted in significantly lower overall pain at the end of 10 treatment sessions compared to placebo ultrasound and exercise (MD -2.60, 95% CI -3.77 to -1.43, 10 point scale), though the time point was unclear as the trialists did not report how many sessions were delivered per week. Overall, based on very low quality evidence, we are uncertain whether Iodex iontophoresis plus continuous short wave diathermy is an effective adjunct to exercise.

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Table 10. Bumin 2001: Iontophoresis plus short wave diathermy plus exercise (intervention) versus placebo ultrasound plus exercise (control)

OUTCOME	INTERVENTION			CONTROL			EFFECT ESTIMATE
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-10) at the end of 10 sessions	2.4	1.59	15	5	1.69	15	-2.60 [-3.77, -1.43]

See Table 11. One trial (41 participants) compared a combination of therapeutic ultrasound, TENS, hot pack and home exercises to home exercises alone for two weeks (Calis 2006). Given the inability to blind participants and personnel, the trial had a high risk of performance bias and detection bias for the self-reported outcomes. In the multiple electrotherapies group, functional ability scores were significantly higher (that is better) than the home exercises alone group at two weeks (MD 12.30, 95% CI 5.23 to 19.37, 100 point scale) and three months (MD 14.90, 95% CI 8.32 to 21.48, 100 point scale). However, the 95% CIs included non-clinically important differences as possible estimates of effect. In addition, the multiple electrotherapies group had statistically significantly greater passive abduction and external rotation than the home exercise alone group. Overall, based on very low quality evidence, we are uncertain whether a combination of therapeutic ultrasound, TENS and hot packs is an effective adjunct to exercise.

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Table 11. Calis 2006: Therapeutic ultrasound plus TENS plus hot pack plus home exercises (intervention) versus home exercises (control)

OUTCOME	INTERVENTION			CONTROL			EFFECT ESTIMATE
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Function (Constant score 0-100) at 2 weeks	70.2	11.6	21	57.9	11.5	20	12.30 [5.23, 19.37]
Function (Constant score 0-100) at 3 months	76.1	10.7	21	61.2	10.8	20	14.90 [8.32, 21.48]
Passive abduction (degrees) at 2 weeks	145.4	19.2	21	125	20.1	20	20.40 [8.36, 32.44]

Passive abduction (degrees) at 3 months	158.4	18.3	21	133.5	15.3	20	24.90 [14.59, 35.21]
Passive external rotation (degrees) at 2 weeks	63.8	11.7	21	52.7	9.3	20	11.10 [4.65, 17.55]
Passive external rotation (degrees) at 3 months	73.8	10.4	21	55	8.1	20	18.80 [13.11, 24.49]

3) Is an electrotherapy modality effective compared to another active intervention, for example glucocorticoid injection, oral non-steroidal anti-inflammatory drugs (NSAIDs)?

Five trials compared an electrotherapy modality to another active intervention (Calis 2006; Cheing 2008; Guler-Uysal 2004; Lee 1973; Leung 2008).

Interferential current

See Table 12. One trial (47 participants) compared interferential current plus home exercises to electroacupuncture plus home exercises and to home exercises alone for four weeks (Cheing 2008). Given the inability to blind participants and personnel, the trial had a high risk of performance bias and detection bias for the self-reported outcomes. Also, no outcome data were reported for the group receiving home exercises alone. There was no statistically significant difference between interferential current plus exercise and electroacupuncture plus exercise in terms of overall pain at four weeks (MD -0.10, 95% CI -1.19 to 0.99, 10 point scale), four months, or seven months; or function at four weeks (MD -1.10, 95% CI -5.85 to 3.65, 100 point scale), four months, or seven months. Overall, based on very low quality evidence, we are uncertain whether interferential current is more or less effective than electroacupuncture.

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Table 12. Cheing 2008: Interferential current plus exercise (intervention) versus electroacupuncture plus exercise (control)

OUTCOME	INTERVENTION			CONTROL			EFFECT ESTIMATE
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-10) at 4 weeks	3.4	1.9	23	3.5	1.9	24	-0.10 [-1.19, 0.99]
Overall pain (VAS 0-10) at 4 months	2	1.5	23	2.4	2.2	24	-0.40 [-1.47, 0.67]
Overall pain (VAS 0-10) at 7 months	1.3	1.4	23	1.7	2.3	24	-0.40 [-1.48, 0.68]
Function (Constant score 0-100) at 4 weeks	84.9	8.4	23	86	8.2	24	-1.10 [-5.85, 3.65]
Function (Constant score 0-100) at 4 months	90.2	9.7	23	93.3	6	24	-3.10 [-7.73, 1.53]
Function (Constant score 0-100) at 7 months	95.5	4.1	23	93.8	6.4	24	1.70 [-1.36, 4.76]

Infrared irradiation

One trial (80 participants) compared infrared irradiation plus home exercises to glucocorticoid injection plus home exercises and to analgesics plus home exercises for six weeks (Lee 1973). Insufficient data were reported for the only outcome reported in the trial paper, ROM.

Continuous short wave diathermy

Two trials compared continuous short wave diathermy to another active intervention (Guler-Uysal 2004; Leung 2008). Given the inability to blind participants and personnel, both trials had a high risk of performance bias and detection bias for the self-reported outcomes.

See Table 13. One trial (30 participants) compared continuous short wave diathermy plus exercise to hot pack plus exercise for four weeks (Leung 2008). There was no significant difference between continuous short wave diathermy and exercise compared to hot pack and exercise in terms of function at four weeks (MD 11.30, 95% CI -1.50 to 24.10, 100 point scale) or eight weeks. However, in terms of ROM, the continuous short wave diathermy and exercise group had statistically significantly greater flexion and external rotation and less hand-behind-back distance than the hot pack and exercise group (it was unclear whether the ROM was active or passive in this trial).

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Table 13. Leung 2008: Short wave diathermy plus exercise (intervention) versus hot pack plus exercise (control)

OUTCOME	INTERVENTION			CONTROL			EFFECT ESTIMATE
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Function (Shoulder Score Index 0-100) at 2 weeks	56.3	15	10	54.2	15.4	10	2.10 [-11.22, 15.42]
Function (Shoulder Score Index 0-100) at 4 weeks	67.8	15.1	10	56.5	14.1	10	11.30 [-1.50, 24.10]
Function (Shoulder Score Index 0-100) at 8 weeks	71.3	19.3	10	57.8	16.3	10	13.50 [-2.16, 29.16]
Flexion (degrees) at 2 weeks (unclear if active or passive)	146.9	13.5	10	120.2	21	10	26.70 [11.23, 42.17]
Flexion (degrees) at 4 weeks (unclear if active or passive)	146.9	14.2	10	122	20.9	10	24.90 [9.24, 40.56]
Flexion (degrees) at 8 weeks (unclear if active or passive)	148.2	14.4	10	124.7	20.3	10	23.50 [8.07, 38.93]
External rotation (degrees) at 2 weeks (unclear if active or passive)	59.3	19.8	10	27.6	18.7	10	31.70 [14.82, 48.58]
External rotation (degrees) at 4 weeks (unclear if active or passive)	60.9	14.5	10	32.6	21.1	10	28.30 [12.43, 44.17]

External rotation (degrees) at 8 weeks (unclear if active or passive)	62.1	11.5	10	32.6	21.7	10	29.50 [14.28, 44.72]
Hand behind back distance (cm) at 2 weeks (unclear if active or passive)	7.2	6.1	10	22.2	11.5	10	-15.00 [-23.07, -6.93]
Hand behind back distance (cm) at 4 weeks (unclear if active or passive)	7.6	5.7	10	18.5	8.9	10	-10.90 [-17.45, -4.35]
Hand behind back distance (cm) at 8 weeks (unclear if active or passive)	6	7.3	10	18.3	7.5	10	-12.30 [-18.79, -5.81]

See Table 14. One trial (42 participants) compared continuous short wave diathermy, hot pack and exercise to deep friction massage (Cyriax approach) and exercise for two weeks (Guler-Uysal 2004). There was no significant difference between groups in terms of overall pain at two weeks. In contrast, those receiving continuous short wave diathermy were statistically significantly less likely to be rated as global treatment successes, had higher pain on motion, and had less passive internal and external rotation at two weeks. Differences in night pain and passive abduction and flexion at two weeks were not statistically significant.

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Table 14. Guler-Uysal 2004: Short wave diathermy plus exercises (intervention) versus manual therapy plus exercises (control)

OUTCOME	INTERVENTION			CONTROL			EFFECT ESTIMATE
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-100) at 2 weeks	21.2	17.9	20	15.2	18.5	20	6.00 [-5.28, 17.28]
Night pain (VAS 0-100) at 2 weeks	42	25.6	20	39.1	28.1	20	2.90 [-13.76, 19.56]
Pain on motion (VAS 0-100) at 2 weeks	62.5	12.6	20	50.4	24.5	20	12.10 [0.03, 24.17]
Passive internal rotation (degrees) at 2 weeks	56.1	14.7	20	66.7	10	20	-10.60 [-18.39, -2.81]
Passive external rotation (degrees) at 2 weeks	52.8	24.3	20	74.4	14.2	20	-21.60 [-33.93, -9.27]

Passive abduction (degrees) at 2 weeks	145.3	28.5	20	157.7	21.6	20	-12.40 [-28.07, 3.27]
Passive flexion (degrees) at 2 weeks	146.4	22.7	20	155.5	14.2	20	-9.10 [-20.83, 2.63]
	Events	**Total**		**Events**	**Total**		**Risk ratio (95% CI)**
Global assessment of treatment success (reaching 80% of normal ROM) at 2 weeks	13	20		19	20		0.68 [0.49, 0.96]

Overall, based on low quality evidence from two small trials, continuous short wave diathermy may not be more effective than hot packs or deep friction massage.

Multiple electrotherapy modalities

See Table 15 and Table 16. One trial (70 participants) compared a combination of therapeutic ultrasound, TENS, hot pack and home exercises to (1) sodium hyaluronate injection plus home exercises, and (2) glucocorticoid injection plus home exercises for two weeks (Calis 2006). Given the inability to blind participants and personnel, the trial had a high risk of performance bias and detection bias for self-reported outcomes. In the multiple electrotherapies group, functional ability scores (100 point scale) were significantly higher (that is better) than the sodium hyaluronate injection group at two weeks but not at three months, and were not significantly different to the glucocorticoid injection group at either time point. However, the 95% CIs for the significant differences included non-clinically important differences as possible estimates of effect. In addition, the multiple electrotherapies group had statistically significantly greater passive abduction and external rotation than the sodium hyaluronate injection group but, compared to glucocorticoid injection, only passive external rotation was greater in the multiple electrotherapies group. Overall, based on the very low quality evidence, we are uncertain whether a combination of therapeutic ultrasound, TENS and hot pack is more or less effective than sodium hyaluronate injection or glucocorticoid injection.

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Table 15. Calis 2006: Therapeutic ultrasound plus TENS plus hot pack plus home exercises (intervention) versus sodium hyaluronate injection plus home exercises (control)

OUTCOME	**INTERVENTION**			**CONTROL**			**EFFECT ESTIMATE**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Function (Constant score 0-100) at 2 weeks	70.2	11.6	21	58.4	11	24	11.80 [5.17, 18.43]
Function (Constant score 0-100) at 3 months	76.1	10.7	21	70.1	10.3	24	6.00 [-0.16, 12.16]

Passive abduction (degrees) at 2 weeks	145.4	19.2	21	127.2	19	24	18.20 [7.01, 29.39]
Passive abduction (degrees) at 3 months	158.4	18.3	21	145.9	21	24	12.50 [1.02, 23.98]
Passive external rotation (degrees) at 2 weeks	63.8	11.7	21	52.9	10.7	24	10.90 [4.31, 17.49]
Passive external rotation (degrees) at 3 months	73.8	10.4	21	63.3	11.4	24	10.50 [4.13, 16.87]

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Table 16. Calis 2006: Therapeutic ultrasound plus TENS plus hot pack plus home exercises (intervention) versus glucocorticoid injection plus home exercises (control)

OUTCOME	INTERVENTION			CONTROL			EFFECT ESTIMATE
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Function (Constant score 0-100) at 2 weeks	70.2	11.6	21	66.5	11.6	25	3.70 [-3.03, 10.43]
Function (Constant score 0-100) at 3 months	76.1	10.7	21	70.3	9.9	25	5.80 [-0.20, 11.80]
Passive abduction (degrees) at 2 weeks	145.4	19.2	21	135.1	23.4	25	10.30 [-2.01, 22.61]
Passive abduction (degrees) at 3 months	158.4	18.3	21	150.3	19.6	25	8.10 [-2.87, 19.07]
Passive external rotation (degrees) at 2 weeks	63.8	11.7	21	54.8	10.5	25	9.00 [2.52, 15.48]
Passive external rotation (degrees) at 3 months	73.8	10.4	21	63	10.8	25	10.80 [4.66, 16.94]

4) Is one type of electrotherapy modality more effective than another?

Two trials compared one type of electrotherapy modality to another (Bumin 2001; Dewan 2011).

See Table 17. One trial (30 participants) compared Iodex iontophoresis plus continuous short wave diathermy plus exercise to Iodex phonophoresis plus exercise (Bumin 2001). It was unclear whether participants would be able to tell the difference between the electrotherapy modalities, and the risk of selection bias was unclear. The trialists found that participants receiving Iodex iontophoresis plus continuous short wave diathermy plus exercise did not have statistically significantly lower overall pain at the end of 10 treatment sessions compared to the Iodex phonophoresis and exercise group (though the time point was unclear as the trialists did not report how many sessions were delivered per week). Based on very low quality evidence, we are uncertain whether Iodex iontophoresis plus continuous short wave diathermy is more or less effective than Iodex phonophoresis (when delivered with exercise).

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Table 17. Bumin 2001: Iontophoresis plus short wave diathermy plus exercise (intervention) versus phonophoresis plus exercise (control)

OUTCOME	INTERVENTION			CONTROL			EFFECT ESTIMATE
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-10) at the end of 10 sessions	2.4	1.59	15	2.6	1.3	15	-0.20 [-1.24, 0.84]

See Table 18. One trial (50 participants) compared interferential current to TENS for four weeks (Dewan 2011). The sample size on which each analysis was based was unclear, so no effect sizes were estimable.

Table 18. Dewan 2011: Interferential current (intervention) versus TENS (control) **Open in table viewer**

OUTCOME	INTERVENTION			CONTROL			EFFECT ESTIMATE
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-10) at 4 weeks	2.15	0.75	?	5.1	0.85	?	Not estimable (sample size unknown)
Range of flexion (degrees) at 4 weeks (unclear if active or passive)	148.5	12.99	?	99	18.04	?	Not estimable (sample size unknown)
Range of abduction (degrees) at 4 weeks (unclear if active or passive)	154	14.29	?	104	16.35	?	Not estimable (sample size unknown)
Range of external rotation (degrees) at 4 weeks (unclear if active or passive)	65.5	8.09	?	34	12.42	?	Not estimable (sample size unknown)

One trial (64 participants) compared a polarity exchangeable permanent magnet to a non-polarity exchangeable permanent magnet for 24 hours (Kanai 2006). No effect estimates were reported in a format that was suitable for extraction and analysis.

5) Is a combination of an electrotherapy modality with manual therapy or exercise (or both) effective compared to placebo, no intervention or another active intervention?

No trial compared a combination of an electrotherapy modality with manual therapy or exercise (or both) to placebo or no treatment. Four trials compared a combination of an electrotherapy modality with manual therapy or exercise (or both) to another active intervention (Carette 2003; Ghosh 2012; Maryam 2012; Ryans 2005). All trials had a high risk of performance and detection bias for the self-reported outcomes. The

outcome data for these trials are presented in the companion review of manual therapy and exercise for adhesive capsulitis (Page 2014). Overall, based on low quality evidence from these four trials, we are uncertain whether a combination of an electrotherapy modality with manual therapy or exercise (or both) is more or less effective than glucocorticoid injection, placebo injection or manipulation under anaesthesia.

6) Is a combination of an electrotherapy modality with manual therapy or exercise (or both) and another active intervention more effective than the other active intervention alone?

Four trials compared a combination of an electrotherapy modality with manual therapy or exercise (or both) and another active intervention to the other active intervention alone (Carette 2003; Maryam 2012; Pajareya 2004; Ryans 2005). All trials had a high risk of performance and detection bias for the self-reported outcomes. The outcome data for these trials are presented in the companion review of manual therapy and exercise for adhesive capsulitis (Page 2014). Overall, based on low quality evidence from these four trials, we are uncertain whether a combination of an electrotherapy modality with manual therapy or exercise (or both) is an effective adjunct to glucocorticoid injection or oral NSAIDs.

7) Is a combination of an electrotherapy modality with manual therapy or exercise (or both) and another active intervention more effective than placebo or no treatment?

Two trials compared a combination of an electrotherapy modality with manual therapy, exercise and glucocorticoid injection to placebo injection (Carette 2003; Ryans 2005). Both trials had a high risk of performance bias and detection bias for the self-reported outcomes. The outcome data for these trials are presented in the companion review of manual therapy and exercise for adhesive capsulitis (Page 2014). Overall, based on low quality evidence from these two trials, the multi-component intervention may be more effective than placebo injection at six weeks, but not at six or 12 months.

Sensitivity analyses and assessment of publication bias

Due to the inability to conduct any meta-analyses, we did not undertake any of our planned sensitivity analyses or formal investigations of publication bias (that is using funnel plots).

Discussion

Summary of main results

Overall, based on the results of 19 trials involving 1249 participants, there is limited evidence from which to draw firm conclusions about the efficacy or safety of several electrotherapy modalities, delivered either in isolation, with manual therapy or exercise, or with manual therapy, exercise and another active intervention (for example glucocorticoid injection), in terms of patient-relevant outcomes such as pain, function, global assessment of treatment success, active shoulder abduction and quality of life. Only five trials measured adverse events, with one reporting statistically non-significant differences between groups (Pajareya 2004) and four reporting no adverse events in any group (Leclaire 1991; Rigato 2002; Stergioulas 2008; Taverna 1990).

The two main questions of the review, which focus on whether electrotherapy modalities are (1) effective compared to placebo or no treatment, or (2) an effective adjunct to manual therapy or exercise (or both), were investigated in nine trials (Battisti 2007; Bumin 2001; Calis 2006; Dogru 2008; Leclaire 1991; Leung 2008; Rigato 2002; Stergioulas 2008; Taverna 1990). The overall impression from these trials is that only one electrotherapy modality, LLLT, has evidence of benefit when compared to placebo or when used as an adjunct to exercise. Low quality evidence from one trial suggests that LLLT was more effective than placebo in terms of global assessment of treatment success at the end of six days of treatment (Taverna 1990). Moderate quality evidence from another trial suggests that LLLT plus exercise was more effective than placebo plus exercise in terms of overall pain reduction and active abduction at four weeks and improved function at four weeks and four months (Stergioulas 2008). Very low quality evidence from another trial suggests that PEMF was more effective than placebo in terms of participant-reported pain relief of 30% or greater and function at two weeks, but the 95% CIs were very wide leading to uncertainty in this result. Based on single trials, it is unclear whether therapeutic ultrasound (Dogru 2008), PEMF (Leclaire 1991), Iodex phonophoresis (Bumin 2001), continuous short wave diathermy (Leung 2008), a combination of Iodex iontophoresis with continuous short wave diathermy (Bumin 2001) or a combination of therapeutic ultrasound with TENS (Calis 2006) are an effective adjunct to exercise.

Regarding the other questions of the review, the majority of the differences between groups were not statistically or clinically significant. Any statistically significant differences (favouring either the electrotherapy or other intervention group) that were detected in these trials are likely to be exaggerated due to the high risk of performance and detection bias resulting from non-blinding of participants and personnel.

Overall completeness and applicability of evidence

The diagnostic criteria for (or definitions of) adhesive capsulitis varied across the trials in regards to the type, amount and direction of shoulder restriction (as has been found in previous reviews, for example Green 1998; Schellingerhout 2008). Despite this variation in diagnosis, the study populations in all trials appeared to be representative of patients seen in routine care, and the age, gender ratio and symptom duration were similar across trials. Also, trials were conducted in a range of high and low-middle income

countries. The median duration of electrotherapy was four weeks (range 1 to 12), with a median of three treatment sessions delivered per week (range 1 to 15), though this differed by type of modality (see Table 1). Several trials did not report important components of the electrotherapy modality, such as the frequency and intensity of the intervention and the duration of the session, which makes it difficult to draw implications for clinical practice from these trials. For example, the trial comparing LLLT to placebo (Taverna 1990) reported the power of the laser (24 mW) but not the wavelength or device used (for example Gallium-Arsenide (GaAs) or Galium-Aluminum-Arsenide (GaAlAs)).

There are several comparisons that are relevant to clinical practice which have not yet been undertaken in this field. Only two electrotherapy modalities (LLLT and PEMF) have been compared to placebo. No trial has compared an electrotherapy modality plus manual therapy to manual therapy alone. No trial has compared an electrotherapy modality plus manual therapy and exercise to manual therapy and exercise alone. The only modality with evidence of benefit when compared to placebo (that is LLLT) has not been compared to any active intervention with evidence of benefit, for example glucocorticoid injection or arthrographic joint distension (Buchbinder 2008; Favejee 2011). No trial has compared any electrotherapy modality to arthrographic joint distension, oral steroids or NSAIDs. Few trials have compared different electrotherapy modalities to one another, and no trial has compared different variants of the same modality (for example LLLT at one dosage versus another dosage). It is unclear whether factors such as dosage, wavelength, site and duration of treatment impact on the effect of specific electrotherapy modalities for adhesive capsulitis.

There was considerable variation in the outcomes measured across the included trials. Only two trials (11%) measured pain using a dichotomous measure, as recommended by IMMPACT (Dworkin 2008). The proportion of trials measuring other main outcomes of the review were overall pain (mean or mean change) (74%), function (68%), global assessment of treatment success (21%), active shoulder abduction (21%), quality of life (16%) and adverse events (26%). Development of a core set of outcomes for trials of adhesive capsulitis and other shoulder disorders would improve our ability to synthesise the evidence.

Quality of the evidence

We used the GRADE approach to assess the quality of all included trials (Schünemann 2011b). Most trials were downgraded to low or very low quality based on three factors: (1) the risk of selection bias was unclear because trialists did not report whether the allocation sequence was concealed, (2) the risk of performance and detection bias was high for self-reported outcomes because participants were not blinded, and (3) the 95% CIs of the effect estimates were imprecise (due to small sample sizes). Trials with unclear allocation concealment have been found to overestimate treatment effects by 7% (ratio of odds ratios 0.93, 95% credible interval 0.87 to 0.99), and unblinded assessment of self-reported outcomes (such as pain and function) is estimated to exaggerate the treatment benefit by about 22% (ratio of odds ratios 0.78, 95% credible interval 0.65 to 0.92) (Savovic 2012). Thus, given that most trials included in our review had unclear allocation concealment and unblinded assessment of self-reported outcomes, further high quality trials may

show even smaller effect estimates than those summarised in this review. Only one trial was not downgraded to low or very low quality, Stergioulas 2008 was downgraded to moderate quality due to imprecision.

Potential biases in the review process

Upon completion of a thorough search of all major databases with no language restrictions, it is likely that all relevant trials were identified. Two review authors independently assessed the trials for inclusion in the review, extracted data and assessed the risk of bias, and a third review author adjudicated whenever there was any discrepancy. Defining of review comparisons of interest was conducted with full knowledge of all comparisons undertaken within the trials but no knowledge of the results. We used a priori defined decision rules to select data from trials when multiple measurement scales, time points and analyses were reported to prevent selective inclusion of results (Page 2013a).

Agreements and disagreements with other studies or reviews

Our companion review of manual therapy and exercise for adhesive capsulitis reached the conclusion that the effects of physical therapy interventions for adhesive capsulitis are uncertain (Page 2014). Based on 32 clinically heterogeneous trials, the companion review found that a combination of manual therapy and exercise may not be as effective as glucocorticoid injection at seven weeks. However, it is unclear whether (a) a combination of manual therapy, exercise and electrotherapy is an effective adjunct to glucocorticoid injection or oral NSAIDs, (b) manual therapy or exercise are effective compared to other active interventions when not delivered together, and (c) one type of manual therapy or exercise is more effective than another.

We are aware of two other relevant systematic reviews of interventions for adhesive capsulitis published within the last five years (Favejee 2011; Maund 2012). Both reviews examined a range of conservative and surgical interventions. Of the 14 trials included in our review that investigated the primary or adjunct effect of an electrotherapy modality (that is trials not falling under questions five to seven), Favejee 2011 included seven (Calis 2006; Cheing 2008; Guler-Uysal 2004; Kanai 2006; Lee 1973; Stergioulas 2008; Taverna 1990) and Maund 2012 included four (Calis 2006; Dogru 2008; Leung 2008; Stergioulas 2008). Despite including more trials, we reached a similar conclusion to both reviews, that there is no or only limited evidence to determine the effectiveness of a range of electrotherapy modalities.

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Jump to: **included studies** | **excluded studies** | **studies awaiting assessment** | **ongoing studies** | **additional references**

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Characteristics of studies

Characteristics of included studies [ordered by study ID]

Battisti 2007

Methods	**Design:** Parallel group, three-arm, single-blind randomised controlled trial (Italy) **Interventions:** Low-frequency (100 Hz) pulsed electromagnetic field therapy (PEMF) or Therapeutic Application of a Musically Modulated Electromagnetic Field (TAMMEF) or simulated (placebo) electromagnetic field, each while listening to music **Sample size calculation:** Not reported **Analysis:** Per protocol analysis **Source of funding:** Fondazione Monte dei Paschi di Siena (non-industry)
Participants	**Number of participants:** 60 (20 per group) **Baseline characteristics:** Basline characteristics by group were not reported Mean (SD; range) age = 47.6 (7.3; 37-66) years; Male:Female = 32:28 Mean (SD) duration of symptoms = 1.4 (1.9) months **Inclusion criteria:** 1. Affected by shoulder periarthritis for less than three months 2. Stopped taking analgesic anti-inflammatory drugs 15 days prior to electromagnetic therapy 3. Had never had infiltrative steroid therapy **Exclusion criteria:** Not reported

Interventions	**Low-frequency (100 Hz)** pulsed **electromagnetic field therapy while listening to music (N=20)** *Components of intervention :* Extremely low-frequency (100 Hz) electromagnetic field therapy was delivered by applying magnets to the shoulder while the participant listened to music *Dosage :* 30 minutes *Frequency of administration :* Daily for 15 days (15 sessions) *Provider :* Physicist **Therapeutic Application of a Musically Modulated Electromagnetic Field (TAMMEF) while listening to music (N=20)*** *Components of intervention :* TAMMEF was delivered by applying magnets to the shoulder while the participant listened to music. The electromagnetic field parameters (frequency, intensity, waveform) were modified in time, randomly varying within the respective ranges, so that all the possible codes can occur during a single application *Dosage :* 30 minutes *Frequency of administration :* Daily for 15 days (15 sessions) *Provider :* Physicist **Simulated (placebo) electromagnetic field while listening to music (N=20)** *Components of intervention :* A simulated (placebo) electromagnetic field was delivered by applying magnets to the shoulder while the participant listened to music *Dosage :* 30 minutes *Frequency of administration :* Daily for 15 days (15 sessions) *Provider :* Physicist
Outcomes	Outcomes measured at baseline, day 7, day 15 (end of treatment), and day 45 (30 days post-treatment cessation). No primary outcome was specified by the trialists 1. Shoulder pain and disability index (SPADI) (0-100 scale where a higher score indicates worse pain and/or disability) 2. Joint function, rated as 0 = absence of functional limitation; 1 = slight limitation; 2 = moderate limitation; 3 = severe limitation
Notes	*This intervention is not a standard type of pulsed electromagnetic field therapy that can be applied by physical therapists, so no data for this group was included in the review. Article is in Italian. MP used Google Translate to translate into English.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "We examined 60 subjects, aged between 37 and 66 years, 28 women and 32 men, suffering from painful shoulder easier to less than 3 months, who were randomly divided into three groups: A = 20 patients undergoing TAMMEF, B = 20 patients undergoing ELF and C = 20 patients undergoing simulated field, listening to music" (Google Translate translation of Italian article) Comment: No information about how the allocation sequence was generated was reported
Allocation concealment (selection bias)	Unclear risk	Comment: No information about how the allocation sequence was concealed was reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"This study was conducted in a blinded fashion" (Google Translate translation of Italian article) Comment: The trialists did not specify who was blind to treatment in this study (participants, personnel, or outcome assessors, or more than one of these parties), but given the nature of the interventions, it is likely that participants were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	"This study was conducted in a blinded fashion" (Google Translate translation of Italian article) Comment: Participants self-reported pain and disability, and were probably blind to treatment
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	"This study was conducted in a blinded fashion" (Google Translate translation of Italian article) Comment: The trialists did not specify who was blind to treatment in this study (participants, personnel, or outcome assessors, or more than one of these parties), and while participants were likely to have been blinded, it is unclear whether assessors of joint function were
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "All patients in groups A and B have completed the course of therapy, without the occurrence of noteworthy local or systemic effects that would require the suspension of such treatment" (Google Translate translation of Italian article) Quote: "After the first week of treatment, 8 patients (40%) in group C had to stop treatment because of ineffective applications. The remaining 12 patients (60%) completed the cycle in the manner already described" (Google Translate translation of Italian article) Comment: A high proportion of the placebo group withdrew due to lack of response to treatment, which is likely to bias the results of the study in favour of the two active treatment groups

Selective reporting (reporting bias)	Unclear risk	Comment: Data for most outcomes listed in the methods section were present in the results section of the report (except for improvement at day 45, in which data was not reported for the simulated electromagnetic field therapy group). Also, without a trial protocol it is unclear whether other outcomes were assessed but not reported based on the results
Other bias	Low risk	Comment: No other sources of bias identified

Bumin 2001

Methods	**Design:** Parallel group, three-arm randomised controlled trial (Turkey) **Interventions:** Iodex iontophoresis plus continuous short wave diathermy plus exercise or iodex phonophoresis plus exercise or placebo ultrasound plus exercise **Sample size calculation:** Not reported **Analysis:** Intention-to-treat analysis **Source of funding:** Not reported
Participants	**Number of participants:** 45 (15 per group) **Baseline characteristics:** Duration of symptoms was not reported *Iodex iontophoresis, continuous short wave diathermy and exercise group:* Mean (SD) age = 53.67 (3.03) years; Male:Female = 6:9 *Iodex phonophoresis and exercise group:* Mean (SD) age = 51.8 (3.86) years; Male:Female = 7:8 *Placebo ultrasound and exercise group:* Mean (SD) age = 50.93 (3.87) years; Male:Female = 10:5 **Inclusion criteria:** 1. Diagnosis of shoulder periarthritis **Exclusion criteria:** Not reported

Interventions	Ten sessions of exercises (not specified) were done by all groups **Iodex iontophoresis plus continuous short wave diathermy (N=15)** *Components of intervention:* The pomade used was a mixture of 4.8% methyl salicylate and 4.7% iodine. In order to increase ion penetration, continuous short wave diathermy application with three dosages was applied for 20 minutes following the iontophoresis application. Direct current with a maximum intensity of 2 mA was applied for 20 minutes *Dosage:* 20 minutes *Frequency of administration:* 10 sessions (number of sessions per week not reported) *Provider:* Physical therapist **Iodex phonophoresis (N=15)** *Components of intervention:* Before application, iodex pomade was applied to the area and then direct ultrasound was applied with a 1.5 watt/cm^2 dosage for five minutes *Dosage:* 5 minutes *Frequency of administration:* 10 sessions (number of sessions per week not reported) *Provider:* Physical therapist **Placebo ultrasound (N=15)** *Components of intervention:* Placebo ultrasound application *Dosage:* 5 minutes *Frequency of administration:* 10 sessions (number of sessions per week not reported) *Provider:* Physical therapist
Outcomes	Outcome assessed before and at the end of 10 sessions of treatment. No primary outcome was reported by the trialists 1. Pain measured using a visual analogue scale (10 point scale from 0 = no pain to 10 = severe pain)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Unclear risk	Quote: "Forty five cases who had shoulder periarthritis were randomly divided into three equal groups (n = 15)." Comment: No information about how the allocation sequence was generated was reported
Allocation concealment (selection bias)	Unclear risk	Comment: No information about how the allocation sequence concealed was reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: Participants received different electrotherapy modalities, but it is unclear whether they were provided any information that would make them perceive the type of electrotherapy they received as superior or inferior to the alternative type of electrotherapy
Blinding of outcome assessment (detection bias) Self-reported outcomes	Unclear risk	Comment: Participants self-reported pain, but it is unclear whether they were provided any information that would make them perceive the electrotherapy they received as superior or inferior to the alternative type of electrotherapy
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: No drop-outs or losses to follow-up were reported, and the analysis is reported as being based on the total number of participants randomised
Selective reporting (reporting bias)	Unclear risk	Comment: Pain was the only reported outcome. Without a trial protocol it is unclear whether other outcomes were measured but not reported based on the results
Other bias	Low risk	Comment: No other sources of bias identified

Calis 2006

Methods	**Design:** Parallel group, four-arm randomised controlled trial (Turkey) **Interventions:** Electrotherapy modalities (ultrasound, transcutaneous electrical nerve stimulation) plus hot pack plus exercises or sodium hyaluronate injection plus exercises or triamsinolone acetonide injection plus exercises or exercises alone **Sample size calculation:** Not reported **Analysis:** Intention-to-treat analysis **Source of funding:** Not reported

Participants	**Number of participants:** 90 (21, 24, 25 and 20 in each respective group) **Baseline characteristics:** Duration of symptoms was not reported *Electrotherapy modalities (ultrasound, TENS) plus hot pack group:* Mean (SD) age = 52.33 (10.1) years; Male:Female = 8:13 *Sodium hyaluronate injection group:* Mean (SD) age = 59.7 (9.81) years; Male:Female = 10:14 *Triamsinolone acetonide injection group:* Mean (SD) age = 56.36 (11.3) years; Male:Female = 9:16 *Stretching and Codman exercises alone group:* Mean (SD) age = 59.25 (6.8) years; Male:Female = 6:14 **Inclusion criteria:** 1. At least a one-month history of pain 2. Limited active and passive shoulder movement 3. Decreased passive range of motion of 20% or more, in at least three movements, according to the American Medical Association guide for the evaluation of permanent impairment 4. No previous injection in the involved shoulder 5. No history of allergy to local anaesthetics, steroids or sodium hyaluronate 6. Absence of coagulation disease 7. Absence of cervical radiculopathy, fracture, dislocation, and rotator cuff laceration 8. Absence of hematological, infectious, endocrine, neurological, and malignant disease, severe osteoporosis, cardiovascular disease, hepatic, and renal disorders 9. Subacromial impingement injection test negativity **Exclusion criteria:** See inclusion criteria

Interventions	All groups were recommended stretching and Codman exercises to do at home for two weeks **Electrotherapy modalities (ultrasound, TENS) plus hot pack group (N=21)** *Components of intervention :* - Electrotherapy: Ultrasonic therapy at 1.5 W/cm^2, and TENS at the patient's tolerance - Other: hot pack *Dosage :* - Electrotherapy: Ultrasonic therapy for five minutes; TENS for 20 minutes - Hot pack: 20 minutes *Frequency of administration :* Daily for 10 days (10 sessions) *Provider :* Physiatrist **Sodium hyaluronate injection (N=24)** *Components of intervention :* Sodium hyaluronate 30 mg (Orthovisc 30 mg) was injected into the shoulder joint by the posterior approach. The injection was done with a 22-gauge needle as follows: while the participant was sitting, the index finger of the operator's free hand was placed on the tip of the coracoid process with the thumb at the angle of the acromion and the spine of the scapula. The needle punctured the skin near operator's thumb and was aimed just laterally to the tip of the index finger *Dosage :* N/A *Frequency of administration :* Once a week for two weeks *Provider :* Rheumatologist **Triamsinolone acetonide injection (N=25)** *Components of intervention :* A 40 mg dose of triamsinolone asetonide (Kenakort-A) was injected into the shoulder joint by the posterior approach. The injection was done with a 22-gauge needle as follows: while the participant was sitting, the index finger of the operator's free hand was placed on the tip of the coracoid process with the thumb at the angle of the acromion and the spine of the scapula. The needle punctured the skin near operator's thumb and was aimed just laterally to the tip of the index finger *Dosage :* N/A *Frequency of administration :* Once *Provider :* Rheumatologist **Stretching and Codman exercises alone (N=20)**

Outcomes	Outcomes assessed at baseline, day 15, and the third month after the initial visit. No primary outcome was reported by the trialists 1. Pain using a horizontal visual analogue scale (scale units not reported) 2. Passive range of motion in abduction and external rotation using a goniometry 3. Constant score (0-100 scale where a higher score indicates better functional ability)
Notes	One participant in the electrotherapy modalities group, three in the sodium hyaluronate injection group, and one in the triamsinolone asetonide injection group had bilateral adhesive capsulitis and contributed both shoulders to the trial. The unit of analysis reported was shoulders, not participants. Trialists did not report adjusting for the bilateral involvement, or how bilateral shoulders were randomised (i.e. whether both shoulders received the same or different interventions is unclear). As a conservative estimate of the treatment effect, we entered the number of participants per group as the sample sizes.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly allocated to one of the four treatment groups" Comment: No information about how the allocation sequence was generated was reported
Allocation concealment (selection bias)	Unclear risk	Comment: No information about how the allocation sequence was concealed was reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported pain and some components of the Constant score

Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "The same specialist (MC) determined the diagnosis and treatment protocol in all patients. All the patients were evaluated by another physiatrist (SU) who was blinded to groups" Comment: The outcome assessor of range of motion was blind to treatment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: No dropouts or losses to follow-up reported, and the analyses are reported as being based on the total number of randomised shoulders
Selective reporting (reporting bias)	Unclear risk	Comment: No numerical outcome data was reported for pain. Instead, mean endpoint values (with no measures of variation) were presented in Figure format. However, it is not clear whether data were incompletely reported based on the statistical significance or magnitude of the results. Also, without a trial protocol, it is unclear whether other outcomes were assessed but not reported based on the results
Other bias	Low risk	Comment: No other sources of bias identified

Carette 2003

Methods	**Design:** Parallel group, four-arm, single-blind randomised controlled trial (Canada) **Interventions:** Supervised physiotherapy (transcutaneous electrical nerve stimulation or ultrasound, mobilisation techniques, active ROM exercises, ice application) plus corticosteroid injection (triamcinolone hexacetonide 40 mg) or corticosteroid injection alone or supervised physiotherapy plus saline injection or saline injection alone **Sample size calculation:** 36 participants per group were estimated to be needed based upon detecting a clinically relevant difference of ≥10 points in the Shoulder Pain and Disability Index (SPADI) (SD≤15) at the 5% level of statistical significance with 80% power **Analysis:** Intention-to-treat analysis (analysing all participants randomised, using a last observation carried forward analysis) **Source of funding:** Arthritis Society of Canada (non-industry)

Participants	**Number of participants:** 93 (21, 23, 26, and 23 in each respective group) **Baseline characteristics:** *Supervised physiotherapy plus corticosteroid injection group:* Mean (SD) age = 54.9 (10.5) years; Male:Female = 7:14 Mean (SD) duration of symptoms: 22.1 (14.9) weeks *Corticosteroid injection alone group:* Mean (SD) age = 55.4 (10) years; Male:Female = 8:15 Mean (SD) duration of symptoms: 21.2 (11) weeks *Supervised physiotherapy plus saline injection group:* Mean (SD) age = 54.2 (8.3) years; Male:Female = 14:12 Mean (SD) duration of symptoms: 20.8 (11.2) weeks *Saline injection alone group:* Mean (SD) age = 56.5 (9.4) years; Male:Female = 9:14 Mean (SD) duration of symptoms: 20.3 (7.3) weeks **Inclusion criteria:** 1. Age 18 years or older 2. Had been symptomatic for <1 year (defined as the presence of shoulder pain with limitation of both active and passive movements of the glenohumeral joint of ≥25% in at least 2 directions (abduction, flexion, external rotation, internal rotation), as compared with the contralateral shoulder or with normal values 3. A total score of ≥30 on the Shoulder Pain and Disability Index (SPADI) **Exclusion criteria:** 1. Adhesive capsulitis was secondary to another cause, including inflammatory, degenerative, metabolic, or infectious arthritis, cerebrovascular accident, or fracture 2. Had a known blood coagulation disorder or an allergy to radiologic contrast material

Interventions	All participants were taught a 10-minute exercise program consisting of active and auto-assisted ROM exercises in the planes of flexion, abduction, external rotation, and internal rotation (hand behind back) to be done at home twice daily for 3 months **Supervised physiotherapy plus glucocorticoid injection (N=21)** *Components of physiotherapy intervention :* - Electrotherapy: TENS (for acute adhesive capsulitis); therapeutic ultrasound (for chronic adhesive capsulitis) - Manual therapy: Mobilisation techniques (not specified) - Supervised exercise: Active ROM exercises (for acute adhesive capsulitis); active and auto-assisted ROM exercises and isometric strengthening exercises (for chronic adhesive capsulitis) - Other: Ice application *Dosage :* 1 hour overall *Frequency of administration :* Three times a week for four weeks (12 sessions) *Provider :* Physiotherapist *Components of glucocorticoid injection :* Under fluoroscopic guidance, a 21-gauge needle, 2.5–3" long, was directed into the shoulder joint space. Aqueous contrast material (Omnipaque; Sanofi-Winthrop, Markham, Ontario, Canada) was injected to confirm the correct location of the needle in the joint. This was followed by injection of 40 mg triamcinolone hexacetonide (2 ml) **Glucocorticoid injection alone (N=23)** The same injection method as described above was delivered **Supervised physiotherapy plus placebo injection (N=26)** The same injection and supervised physiotherapy methods as described above were delivered, except that isotonic saline (2 ml) was injected into the shoulder joint space **Placebo injection alone (N=23)** The same injection method as described above was delivered, except that isotonic saline (2 ml) was injected into the shoulder joint space

Outcomes	Outcomes assessed at 6 weeks, 3 months, 6 months and 1 year post-randomisation **Primary outcome:** 1. Shoulder pain and disability index (SPADI) (0-100 scale where a higher score indicates worse pain and/or disability) **Secondary outcomes:** 2. General health status measured using the SF-36 3. Active and passive range of motion in flexion, abduction, and external rotation, assessed using a goniometer with the participant in a supine position
Notes	Trialists reported the following protocol violation: "Five patients (2 in the combination group and 1 in each of the other groups) received, in addition to their assigned injection, a glucocorticoid injection (triamcinolone hexacetonide, 20 mg) after randomization, and 1 patient in the saline group underwent rotator cuff repair 8 months after enrolment. All of these injections were prescribed by study investigators who were blinded to the original treatment assignment, and all were done under fluoroscopic guidance. The patient in the placebo group and the patient in the physiotherapy group each received the injection after the 6-week visit; the 3 patients in the corticosteroid and combination group received it after the 3-month or 6-month visits". Unpublished data regarding study design (required for risk of bias assessment) provided by trialist on request.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The assignment scheme was generated from a table of random numbers. Random assignments to the treatment groups were stratified according to study center and balanced after every 12 assignments" Comment: An adequate method to generate the allocation sequence was used
Allocation concealment (selection bias)	Low risk	Quote: "The opaque prenumbered envelopes containing the assignments were kept by the hospital pharmacist at each center" Comment: An adequate method to conceal the allocation sequence was probably used
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The syringes containing the triamcinolone hexacetonide or saline were prepared by the hospital pharmacist and covered with aluminum foil so the radiologist administering the injections and the patient were not aware of the treatment" Comment: Participants and personnel were blind to the injection component of the intervention, but not the physiotherapy component. Participants may have had different expectations about the benefits of each intervention

Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Participants self-reported their SPADI and general health scores, and were not blind to whether they had received physiotherapy or not. Participants may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "Each subject was assessed by the same physiotherapist throughout the trial, with a few exceptions. The physiotherapists involved in these assessments were unaware of the treatment allocation and did not normally work in the clinics where the physiotherapy was administered" Comment: Outcome assessors of objective outcomes were blind to treatment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "The primary analysis was based on an intent-to-treat principle, and all subjects were included in the analysis. In the case of subjects lost to followup, the data from the last available assessment were imputed to all subsequent evaluations." Quote: "Of the remaining 93 patients, 2 in the combination group, 9 in the corticosteroid group, 4 in the physiotherapy group, and 1 in the placebo group did not return for all visits." Comment: There was a higher amount of loss to follow-up in the glucocorticoid injection group compared to the other three groups, but it is unclear if the reasons for loss to follow-up were related to treatment received (or whether they were balanced across the groups)
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the results
Other bias	Low risk	Comment: No other sources of bias identified

Cheing 2008

Methods	**Design:** Parallel group, three-arm, single-blind randomised controlled trial (Hong Kong) **Interventions:** Interferential current plus home exercises or electroacupuncture plus home exercises or no treatment **Sample size calculation:** Not reported **Analysis:** Per protocol analysis **Source of funding:** Not reported

Participants	**Number of participants:** 74 (25, 24, and 25 in each respective group) **Baseline characteristics:** Sex of participants was reported as 22 males and 48 females. Age range for all participants was reported as 33-90 years *Interferential current plus home exercises group:* Mean (SD) duration of treatment = 6.7 (6.05) months *Electroacupuncture plus home exercises group:* Mean (SD) duration of treatment = 6.71 (6.5) months *No treatment group:* Mean (SD) duration of treatment = 8.26 (7.94) months **Inclusion criteria:** 1. Patients who reported localized pain over one shoulder, experienced night pain and had restricted active and passive shoulder motions **Exclusion criteria:** 1. History of trauma, fractures, previous shoulder surgery, cervical or thoracic pain syndrome, complex regional pain syndrome, malignancies, on anti-coagulant therapy 2. Had received acupuncture treatment to the painful shoulder in the past six months
Interventions	**Interferential current plus home exercises (N=25)** *Components of intervention :* - Interferential current: An interferential electrotherapy machine (a Phyaction Guidance E unit) delivered a current swept from 80 to 120 Hz, and 4 suction-type electrodes were placed around the shoulder region in a coplanar arrangement. The intensity of the stimulation was adjusted to just below the pain threshold and the stimulation lasted for 20 minutes - Home exercises: Participants were instructed to follow a chart and perform a standard set of shoulder mobilisation exercises five times a day, which included four directions: (i) forward flexion – with the help of an overhead pulley system; (ii) external rotation – keeping the arm close to trunk, using a small bamboo to externally rotate the shoulder through pushing against the palm; (iii) horizontal adduction – pressing a horizontally adducted arm against the chest with the other arm to achieve horizontal adduction; and (iv) internal rotation – placing the affected arm behind the back and grasping one end of a towel, the other hand then pulling the opposite end of the towel to achieve maximum internal rotation *Dosage :* - Interferential current: 20 minutes - Home exercises: Not reported

	Frequency of administration : - Interferential current: 10 sessions over four weeks - Home exercises: Five times a day for six months *Provider :* Physiotherapist **Electroacupuncture plus home exercises (N=25)** *Components of intervention :* - Electrotheracupuncture: Sterile stainless steel acupuncture needles were inserted 15–25 mm intramuscularly into three acupoints including one trigger point, one local point (LI 15: Jianyu), and one distal point (ST38: Tiaokou) (14). Trigger points were identified by areas of greatest tenderness around the painful shoulder that were determined on an individual basis. The two needles in the shoulder region (trigger point and LI 15) were connected to an electroacupuncture device (Model: ES-160, ITO Co. Ltd, 3-3-3 Tpupta, al-M inami, Nerima-ku, Tokyo 176-86 05, Japan) and stimulated with an alternating frequency of 2–100 Hz at a pulse duration of 100– 400 μs for 20 minutes. The intensity of the stimulation was adjusted to a tolerance level of just below the pain threshold. The needle that was applied at the distal point S T38 (Tiaokou) was retained for 20 minutes and was manually lifted and thrusted every 10 minutes - Home exercises: See above *Dosage :* - Electroacupuncture: 40 minutes - Home exercises: Not reported *Frequency of administration :* - Electroacupuncture: Two to three times a week for four weeks (10 sessions in total) - Home exercises: Five times a day for six months *Provider :* Physiotherapist **No treatment (N=25)**
Outcomes	Outcomes assessed at the end of 4 weeks treatment and at 1, 3 and 6 months follow-up for Group 1 and 2, but only at the end of 4 weeks treatment for Group 3 No primary outcome was reported by the trialists 1. Constant score (0-100 scale where a higher score indicates better functional ability) 2. Pain severity at the moment of assessment, measured using a 10cm visual analogue scale, with "No pain" anchored at the left and "Pain as bad as it could be" anchored at the right
Notes	No outcome data for the no treatment group was reported in the trial publication, so we could not analyse the comparison between interferential current and home exercises versus no treatment.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The subjects were randomly allocated into: (i) the EA group (n = 24); (ii) IFE group (n = 23); or (iii) control group (n = 23)" Comment: No information on how the allocation sequence was generated was reported
Allocation concealment (selection bias)	Unclear risk	Comment: No information on how the allocation sequence was concealed was reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The study was a double-blind, randomized, controlled clinical trial. An independent assessor was blind to the group allocation." Comment: Despite reporting this trial as "double-blind", given the nature of the interventions (electrotherapy versus no treatment), participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported pain and some components of the Constant score
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "The study was a double-blind, randomized, controlled clinical trial. An independent assessor was blind to the group allocation." Comment: Outcome assessors of some components of the Constant score were probably blind to treatment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "One participant dropped out of each of the electroacupuncture group and interferential electrotherapy group, both because of time conflict, and two participants dropped out of the no treatment group because they experienced no improvement." Comment: While drop-out is related to treatment in the no treatment group, the number of dropouts is small and unlikely to affect the function and pain outcomes

Selective reporting (reporting bias)	High risk	Comment: The trialists reported the mean (SD) scores for the Constant Murley Assessment scale and VAS pain at the end of four weeks treatment for the electroacupuncture and interferential current groups, but not for the no treatment group, because the no treatment group did not have a statistically significant improvement from baseline. Also, without a trial protocol it is unclear whether other outcomes were measured but not reported based on the results
Other bias	Low risk	Comment: No other sources of bias identified

Dewan 2011

Methods	**Design:** Parallel group, two-arm, randomised controlled trial (India) **Interventions:** Interferential current or TENS **Sample size calculation:** Not reported **Analysis:** Intention-to-treat analysis **Source of funding:** Not reported
Participants	**Number of participants:** 50 (25 per group) **Baseline characteristics:** No baseline characteristics reported **Inclusion criteria:** 1. Aged 40-60 years 2. Reported localised pain over one shoulder, experienced night pain and had restricted active and passive shoulder motions **Exclusion criteria:** 1. Aged below 40 or above 60 years; 2. History of trauma, fractures, previous shoulder surgery, cervical or thoracic pain syndrome, complex regional pain syndrome, malignancies, on anticoagulant therapy, psychic patient, hypermobile joint, or had received acupuncture treatment to the painful shoulder in the past six months.

Interventions	**Interferential current (N=25)** *Components of intervention:* The participant was positioned comfortably and the skin was prepared, washed and any skin lesion insulated with petroleum jelly. An interferential electrotherapy machine delivered current swept from 80 to 120 Hz, and 4 suction-type electrodes were placed around the shoulder region used in two pairs (quadripolar technique was applied), each pair being indicated by the colorings of the wire from the machine. The electrodes of each pair were placed diagonally opposite one another in such a way that the interference effect was produced in the tissues where it was required, which was very deep. The participant was warned that he or she would feel a tingling sensation which should not be too uncomfortable or burning. The intensity of the stimulation was adjusted to just below the pain threshold *Dosage:* 20 minutes *Frequency of administration:* Two to three sessions per week for four weeks (10 sessions) *Provider:* Physiotherapist **Transcutaneous electrical nerve stimulation (TENS) (N=25)** *Components of intervention:* The skin in the treatment area was first sterilized with an isopropyl alcohol skin wipe. Conductive rubber electrodes covered with a conductive gel in order to gain good skin contact were placed on the participant's skin. The electrodes could be bandaged onto the participant or fixed with adhesive tape. Four electrodes were placed. High frequency TENS was used. The intensity of the stimulation was adjusted to a tolerance level of just below the pain threshold. Pulses of around 0.2 ms at about 100Hz were given at intensities that provoke gentle contraction. The participant should have felt a tingling pins and needle sensation. It was applied to acupuncture points but was sometimes applied to motor points of muscles. The intensity of the stimulation was adjusted to a tolerance level of just below the pain threshold. The needle was retained for 20 minutes, and was manually lifted and thrusted every 10 minutes *Dosage:* 20 minutes *Frequency of administration:* Two to three sessions per week for four weeks (10 sessions) *Provider:* Physiotherapist
Outcomes	Outcomes assessed at the end of four weeks treatment. No primary outcome was reported by the trialists 1. Range of motion in flexion, abduction and external ration, using a goniometer (not reported whether active or passive) 2. Constant score (0-100 scale where a higher score indicates better functional ability) 3. Pain using a 10cm visual analogue scale, anchored as 1="No pain" and 10="Severe pain"
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Unclear risk	Quote: "The subjects were randomly allocated into: (i) the IFE group (n = 25); (ii) TENS group (n = 25)" Comment: No information on how the allocation sequence was generated was reported
Allocation concealment (selection bias)	Unclear risk	Comment: No information on how the allocation sequence was concealed was reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: Participants received different electrotherapy modalities, but it is unclear whether they were provided any information that would make them perceive the type of electrotherapy they received as superior or inferior to the alternative type of electrotherapy
Blinding of outcome assessment (detection bias) Self-reported outcomes	Unclear risk	Comment: Participants self-reported pain and function, but it is unclear whether they were provided any information that would make them perceive the electrotherapy they received as superior or inferior to the alternative type of electrotherapy
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Comment: Trialists did not report whether assessors of range of motion were blind to treatment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: Twenty-five participants were randomly allocated to each group. No drop-outs, losses to follow-up or exclusions were reported, but it is clear that the outcome data reported was not based on the total number of randomised participants. The sample sizes on which each outcome was based were not reported in tables. However SDs and SEs per group for each outcome were. When calculating the sample size (based on the SD and SE), none of the SEs matched the SDs when a sample size of 25 per group was assumed (in some cases, an assumed sample size of 16 lead to the calculation of the correct SE and SD. Therefore, data was not collected on all participants, and the number of dropouts and reasons for drop-out were unclear

Selective reporting (reporting bias)	Unclear risk	Comment: Trialists fully reported post-treatment data for both groups for pain and range of motion, but reported post-treatment Constant Score means and SDs for the interferential current group only (no measures of variation were reported for the Constant Score in the TENS group). However, it is not clear whether data were incompletely reported based on the statistical significance or magnitude of the results. Also, without a trial protocol, it is unclear whether other outcomes were assessed but not reported based on the results
Other bias	Low risk	Comment: No other sources of bias identified

Dogru 2008

Methods	**Design:** Parallel group, two-arm, double-blind randomised controlled trial (Turkey) **Interventions:** Ultrasound plus hot pack and exercise or placebo ultrasound plus hot pack and exercise **Sample size calculation:** 34 participants per group were estimated to be needed based upon detecting a clinically relevant difference of 10.7 points in the Shoulder Pain and Disability Index (SPADI) (SD=14) at the 5% level of statistical significance with 80% power including a 15% rate of loss at follow-up **Analysis:** Per protocol analysis **Source of funding:** Not reported

Participants	**Number of participants:** 50 (25 per group) **Baseline characteristics:** *Ultrasound plus hot pack plus exercise group:* Mean (SD; range) age = 53.9 (7.8; 41-72) years; Male:Female = 11:14 Mean (SD; range) duration of symptoms = 6.3 (3.5; 3-12) months *Placebo ultrasound plus hot pack plus exercise group:* Mean (SD; range) age = 56.8 (7.3; 46-70) years; Male:Female = 10:14 Mean (SD; range) duration of symptoms = 5.2 (2.9; 3-12) months **Inclusion criteria:** 1. Shoulder pain of minimum three months duration with no major trauma 2. ≥25% loss of shoulder motion in all planes 3. Pain with motion with a minimum visual analogue scale (VAS) score of 40 mm 4. Normal findings on radiographs of the glenohumeral joint 5. Absence of arthritis, malignancy, and medical conditions such as cardiac diseases, infections and coagulation disorders **Exclusion criteria:** 1. Patients with adhesive capsulitis due to rotator cuff tears, fractures, dislocations and reflex sympathetic dystrophy

Interventions	**Ultrasound plus hot pack plus exercise (N=25)** *Components of intervention :* - Ultrasound: Continuous ultrasound with 3 MHz frequency and 1.5 W/cm2 intensity (Intelect® Mobile Ultrasound device, Chattanooga Group) with a transducer head of 5 cm^2 was delivered. After coating the skin with an aquasonic gel, ultrasound was delivered by moving the applicator over the anterior, superior and posterior regions of the target joint in slow, overlapping strokes - Hot pack: Superficial heat was administered by use of hot packs (60 °C) - Supervised exercise: The exercise program consisted of Codman's exercises and wall climbing followed by glenohumeral joint stretching exercises to the patient's tolerance - Home exercise: Consisting of Codman's exercises, active range of motion and stretching exercises *Dosage :* - Ultrasound: 10 minutes - Hot pack: 20 minutes - Supervised exercise: 20 minutes - Home exercise: Not reported *Frequency of administration :* Every day for two weeks except weekends (10 sessions) for the ultrasound, hot pack and supervised exercise program; after these two weeks, home exercises were conducted for three months *Provider :* Physical therapist **Placebo ultrasound plus hot pack plus exercise (N=25)** Participants received the same interventions as described above, except that for the ultrasound component, the skin was covered with an aquasonic gel and ultrasound was applied in the same manner except the device was not switched to "on"

Outcomes	Outcomes assessed at the end of two weeks treatment, and at three months from baseline **Primary outcome** 1. Shoulder pain and disability index (SPADI) (0-100 scale where a higher score indicates worse pain and/or disability) **Secondary outcomes:** 2. Passive range of motion in abduction, flexion, inner and outer rotation using a goniometer 3. Pain on motion using a 0-100 visual analogue scale 4. General health status using the SF-36. Both the Physical Component Score and Mental Component score were reported (scores range between 0 and 100 and lower scores represent worse health status)
Notes	Unpublished data regarding study design (required for risk of bias assessment) provided by trialist on request

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Fifty patients were numbered sequentially and assigned to either the ultrasound (US) group or placebo (sham US) group by another physician (second author)." Comment: No information about how the allocation sequence was generated was reported
Allocation concealment (selection bias)	Unclear risk	Comment: No information about how the allocation sequence was concealed was reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: Participants were likely blind to treatment
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported pain, SPADI and SF-36

Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "All patients were assessed by the same physician who was blind to the treatment groups (first author)." Quote: "The first author was blind to the treatment groups. She only evaluated the patients according to a standardized form including physical examination and supervised patients while they are filling in the questionnaires" (personal communication) Comment: Trialists reported via personal communication that the outcome assessor was blind to treatment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Fifty patients were numbered sequentially and assigned to either the ultrasound (US) group or placebo (sham US) group by another physician (second author). One patient from the sham US group discontinued the intervention at the beginning of the first week due to personnel reasons. Twenty-five patients in the US group and 24 patients in the sham US group were assessed for final evaluation." Comment: Only one participant dropped out (from the control group) for personal reasons. This is unlikely to have affected the outcomes
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the results
Other bias	High risk	Quote: "Effectiveness of US might be masked by worse pre-treatment values of the US group and higher exercise compliance of the sham US group." Quote: "The percentage of exercise compliance was calculated from the charts given to the patients on the control evaluation. Exercise compliance of the sham US group was significantly higher than the US group (76.6±15.2 vs. 67.1±14.9 respectively, p = 0.04)." Comment: Participants in the ultrasound group had worse pre-treatment values and lower compliance with home exercises than participants in the sham ultrasound group. These may have biased results towards the null

Ghosh 2012

Methods	**Design:** Parallel group, three-arm randomised controlled trial (India) **Interventions:** Ultrasound plus active and passive mobilisation exercises plus shoulder wheel and pulley exercises or manipulation under anaesthesia or glucocorticoid injection (all received home exercises) **Sample size calculation:** Not reported **Analysis:** Per-protocol analysis **Source of funding:** Not reported

Participants	**Number of participants:** 72 (24 per group) **Baseline characteristics:** Baseline characteristics by group were not reported. Sex was not reported Age range: 40-73 years Duration of symptoms: 0-2 months (N=33), 2-4 months (N=23), 4-6 months (N=16) **Inclusion criteria:** 1. Pain and stiffness of shoulder for six months or less 2. Mild osteoporosis **Exclusion criteria:** 1. Diabetes mellitus, rheumatoid arthritis, hyperthyroidism, locked posterior and anterior dislocation, sub-acromial impingement syndrome or rotator cuff lesion 2. Disease duration more than 6 months

Interventions	All participants were advised to perform active shoulder mobilisation exercises at home **Therapeutic ultrasound plus mobilisation exercises plus shoulder wheel and pulley exercises (N=24)** *Components of intervention :* - Electrotherapy: Ultrasound - Supervised exercises: Active and passive shoulder mobilisation exercises plus shoulder wheel and pulley exercises *Dosage :* Not reported *Frequency of administration :* For six months (number of sessions per week not reported) *Provider :* Physiotherapist **Manipulation under anaesthesia (N=24)** *Components of intervention :* After general anaesthesia manipulations were done in the sequence of flexion, extension, abduction, adduction, external rotation and internal rotation. Analgesics were given post-manipulation period for two to three days and shoulder mobilisation exercises started three to four days after manipulation which were taught previously *Dosage :* Not reported *Frequency of administration :* Once *Provider :* Not reported **Glucocorticoid injection (N=24)** *Components of intervention :* An injection of methylprednisolone in 40 mg dosage was given intra-articularly by the anterior approach under strict aseptic preparation *Dosage :* See above *Frequency of administration :* An average of three doses with three week interval *Provider :* Not reported
Outcomes	Outcome assessed at the end of six months treatment 1. Clinical improvement rated as "Good" (no pain, no tenderness present, ROM is equal or comparable with normal limb, and no muscle wasting present), "Fair" (mild pain and tenderness may or may not be present, mild restriction of ROM still present even after 6 months, and muscle wasting may or may not be present), or "Poor" (gross restriction of movement is still present, with or without pain).

Notes	To analyse the "treatment success" outcome we dichotomised participants into those who had a clinical improvement rating of "Good" versus those who had a rating of "Fair" or "Poor". Trialists reported that participants in the study had "almost equal right and left sided affection with one having bilateral affection". However, the group that the bilaterally affected participant was allocated to was not reported, nor was any mention of controlling for the correlation between shoulders (but this is unlikely to have affected the results substantially given the dichotomous 'clinical improvement' outcome used).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "These patients were randomly allocated in 3 groups" Comment: No information about how the allocation sequence was generated was reported
Allocation concealment (selection bias)	Unclear risk	Comment: No information about how the allocation sequence was concealed was reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported pain and tenderness
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Comment: No information about whether assessors of muscle atrophy and range of motion were blind to treatment was reported

Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: Only one participant was lost to follow-up (in the glucocorticoid injection group). This is unlikely to have biased the results
Selective reporting (reporting bias)	Unclear risk	Comment: The results of the single outcome reported in the methods section of the publication (treatment success) were fully reported, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the results
Other bias	Low risk	Comment: No other sources of bias identified

Guler-Uysal 2004

Methods	**Design:** Parallel group, two-arm, single blind randomised controlled trial (Turkey) **Interventions:** Continuous short wave diathermy application, hot pack, stretching exercises and home exercises or Cyriax approach of deep friction massage, stretching exercises and home exercises **Sample size calculation:** 20 participants per group were estimated to be needed based upon detecting a 40% increase in the number of patients treated successfully in the Cyriax group at the 5% level of statistical significance with 80% power **Analysis:** Per protocol analysis **Source of funding:** Not reported

Participants	**Number of participants:** 42 (21 per group) **Baseline characteristics:** *Continuous short wave diathermy application and hot pack group:* Mean (SD; range) age = 58.4 (9.7; 44-82) years; Male:Female = 7:13 Median (SD; range) duration of symptoms: 5.6 (3.9; 2-12) months *Cyriax approach of deep friction massage group:* Mean (SD; range) age = 53.6 (6.9; 43-70) years; Male:Female = 5:15 Median (SD; range) duration of symptoms: 7.6 (3.9; 2-12) months **Inclusion criteria:** 1. Shoulder pain of minimum 2 months duration with no major shoulder trauma 2. Marked loss of active and passive shoulder motion 3. Pain with motion with a minimum visual analogue scale (VAS) score of 30 mm 4. Normal findings on anteroposterior and axillary lateral radiographs of the glenohumeral joint 5. Absence of polyarthritis or neurological diseases or cervical neuropathy 6. Absence of medical conditions such as cardiac disease, Infections, coagulation disorders **Exclusion criteria:** 1**.** Patients who had adhesive capsulitis secondary to shoulder dislocation, fractures, reflex sympathetic dystrophy and rotator cuff tears

Interventions	Both groups received active stretching and pendulum exercises at the end of each treatment session, and were also instructed in a standardised home exercise program consisting of passive ROM and pendulum exercises to be performed every day **Continuous short wave diathermy application and hot pack (N=21)** *Components of intervention :* - Continuous short wave diathermy: Continuous short wave diathermy with 220 V/50 Hz power source and 27.12 MHz oscillation frequency was applied to the therapy region for deep heating while the participants were lying supine (Short wave Diathermy KSF Model equipment ITO, Tokyo-Japan) - Hot pack: Wrapped in towelling and placed on the target shoulder for superficial heating *Dosage :* - Continuous short wave diathermy: 20 minutes - Hot pack: 20 minutes *Frequency of administration :* Every day except weekends for two weeks (10 sessions) *Provider :* Physiotherapist **Cyriax approach of deep friction massage (N=21)** *Components of intervention :* - Manual therapy: Cyriax approach of deep friction massage - Supervised exercises: Mobilisation exercises *Dosage :* One hour *Frequency of administration :* Three times per week for two weeks (six sessions) *Provider :* Physiotherapist
Outcomes	Outcomes assessed at the end of the first and second week of treatment **Primary outcome:** 1. Number of participants who reached 80% of normal range of motion of the shoulder at the end of the second week of treatment **Secondary outcomes:** 2. Pain (spontaneous pain, night pain, and pain with motion) using a 100mm visual analogue scale 3. Passive range of motion in flexion, abduction, inner rotation, outer rotation using a goniometer
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "42 patients were randomised for enrolment in the study. The patients were numbered sequentially and allocated to two groups (the Cyriax group and the physical therapy group)." Comment: No information on how the allocation sequence was generated was reported
Allocation concealment (selection bias)	Unclear risk	Quote: "42 patients were randomised for enrolment in the study. The patients were numbered sequentially and allocated to two groups (the Cyriax group and the physical therapy group)." Comment: No information on how the allocation sequence was concealed was reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported pain
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "The pre-treatment evaluation of shoulder pain and ROM was carried out by a blinded observer at the beginning of the study." Comment: Outcome assessors of range of motion were probably blind to treatment (though it is unclear how blinding of pain was achieved, given it was self-reported by unblinded participants)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "One patient in the CYR group were excluded from the study due to poor compliance and one from the PT group discontinued the intervention due to attacks of unstable hypertension in the first week." Comment: The number of drop-outs or exclusions was low and equal between groups, and reasons are unlikely to influence the results
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data was fully reported for all outcomes specified in the methods section. However, without a trial protocol it is unclear whether other outcomes were measured but not reported based on the results
Other bias	Low risk	Comment: No other sources of bias identified

Kanai 2006

Methods	**Design:** Parallel group, two-arm, randomised controlled trial (Japan) **Interventions:** Polarity exchangeable permanent magnet (PEPM) device (which emits a magnetic field with an alternating north and south pole) or a non-polarity exchangeable permanent magnet (N-PEPM) device **Sample size calculation:** Not reported **Analysis:** Intention-to-treat analysis **Source of funding:** Not reported
Participants	**Number of participants:** 64 (32 per group) **Baseline characteristics:** *Polarity exchangeable permanent magnet (PEPM) group:* Mean (SD) age not reported, but 3 were aged between 20-29, 7 between 30-39, 13 between 40-49, 5 between 50-59, and 4 between 60-69 years; Male:Female = 16:16 Mean (SD duration of symptoms not reported, but 21 had a contraction period between 1-6 months, 5 between 7-12 months, 2 between 13-24 months, 3 between 25-48 months, and 1 >49 months *Non-polarity exchangeable permanent magnet (N-PEPM) group:* Mean (SD) age not reported, but 4 were aged between 20-29, 8 between 30-39, 12 between 40-49, 6 between 50-59, and 2 between 60-69 years; Male:Female = 16:16 Mean (SD duration of symptoms not reported, but 14 had a contraction period between 1-6 months, 7 between 7-12 months, 7 between 13-24 months, 3 between 25-48 months, and 1 >49 months **Inclusion criteria:** 1. Had frozen shoulder 2. Had not received any medication to reduce pain within the week before enrolment **Exclusion criteria:** 1. Were concurrently being treated for hyperthermia, massage or acupuncture 2. Presence of a severe disorder such as cancer, hypertension, diabetes mellitus, an inflammatory disease or a cardiac disease 3. Presence of a cardiac pacemaker or other metallic implants

Interventions	**Polarity exchangeable permanent magnet (PEPM) (N=32)** *Components of intervention:* Polarity exchangeable permanent magnet (PEPM) device applied to the area of frozen shoulder pain for 24 hours. The device consisted of a cylindrical magnet that rotated 180 degrees every second and had north and south poles that came into contact with the patient's skin in an alternating fashion. The area that was exposed to the magnetic field from the PEPM device was four times wider than that from the N-PEPM device *Dosage:* 24 hours *Frequency of administration:* One day *Provider:* Not reported **Non-polarity exchangeable permanent magnet (N-PEPM) (N=32)** *Components of intervention:* Non-polarity exchangeable permanent magnet (N-PEPM) device applied to the area of frozen shoulder pain for 24 hours. The device consisted of a cylindrical magnet of the same size as that in the PEPM device but the magnet in the N-PEPM device did not rotate *Dosage:* 24 hours *Frequency of administration:* One day *Provider:* Not reported
Outcomes	Outcomes assessed at three hours after treatment started, at the end of 24 hours treatment and at 24 hours follow-up (i.e. 48 hours from baseline). No primary outcome was reported by the trialists 1. Overall pain, calculated by summing the score of four 0-10 visual analogue scales (measuring spontaneous pain, limited range of motion, pain to palpation, and night pain)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The subjects were randomly assigned to receive treatment with a PEPM device (n = 32) or an N-PEPM device (n = 32)" Comment: No information about how the allocation sequence was generated was reported
Allocation concealment (selection bias)	Unclear risk	Comment: No information about how the allocation sequence was concealed was reported

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: In contrast to the N-PEPM device, the PEPM device rotated and the area of the shoulder that was covered by the PEPM device was four times larger than the area covered by the N-PEPM device. However, it is unclear whether participants were provided any information that would make them perceive the type of electrotherapy they received as superior or inferior to the alternative type of electrotherapy
Blinding of outcome assessment (detection bias) Self-reported outcomes	Unclear risk	Comment: Participants self-reported pain, but it is unclear whether they were provided any information that would make them perceive the type of electrotherapy they received as superior or inferior to the alternative type of electrotherapy
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: There were no dropouts, losses to follow-up or exclusions reported, and outcome data was reported as being based on the number of randomised participants
Selective reporting (reporting bias)	Unclear risk	Comment: Trialists reported percentage change from baseline (with no measures of variation) in overall pain at 3 and 24 hours. Trialists also reported percentage change from baseline (with standard errors) in overall pain at 3, 24, and 48 hours in Figure format. Therefore, no data suitable for meta-analysis was reported. However, it is not clear whether data were incompletely reported based on the statistical significance or magnitude of the results. Also, without a trial protocol, it is unclear whether other outcomes were assessed but not reported based on the results
Other bias	Low risk	Comment: No other sources of bias were identified

Leclaire 1991

Methods	**Design:** Parallel group, two-arm, triple blind randomised controlled trial (Canada) **Interventions:** Pulsed electromagnetic field therapy (PEMF) plus hot pack applications plus passive manual stretching and pulley exercises or placebo electromagnetic field therapy plus hot pack applications plus passive manual stretching and pulley exercises **Sample size calculation:** Trialists reported that "…the power of this study was 90% to show a change of 37 degrees in mean total range of motion recorded for the placebo group" (pg 286). However, this was reported in the Discussion section and could be a post hoc power calculation **Analysis:** Intention-to-treat analysis **Source of funding:** Not reported

Participants	**Number of participants:** 47 (22 and 25 in each respective group) **Baseline characteristics:** Baseline characteristics by group were not reported Mean (SD) age = 58 (6.9) years; Male:Female = 18:29 Mean (SD) duration of symptoms = 17 (4.1) weeks **Inclusion criteria:** 1. Shoulder pain for more than two months 2. Limited active and passive shoulder movement 3. Pain on resisted abduction, internal and external rotation, and impaired glenohumeral joint motion 4. Decreased passive range of motion of 20% or more, in at least three movements, according to the American Medical Association guide for the evaluation of permanent impairment, i.e. flexion <144 degrees, extension <32 degrees, abduction <120 degrees, adduction <24 degrees, external rotation <72 degrees, and internal rotation <32 degrees **Exclusion criteria:** 1. Have arthritis, bone or neurologic disease, unstable heart disease, or haemostatic disorder 2. Have rotator cuff rupture, x-ray calcification >2mm, or severe adhesive capsulitis defined as a limitation of flexion to 100 degrees, abduction to 90 degrees, or global rotations by 20 degrees or more 3. Currently receiving anticoagulants or anti-inflammatory drugs, or have received steroid injection in the shoulder previously

Interventions	**Pulsed electromagnetic field therapy (PEMF) plus hot pack plus exercise (N=22)** *Components of intervention :* - PEMF: The schedule was: 30 Gauss, 10 Hz for sessions 1 to 6; 40 Gauss, 15 Hz for sessions 7 to 16; and 60 Gauss, 30 Hz for sessions 17 and beyond - Hot pack - Supervised exercise: Passive glenohumeral joint stretching exercises to the participants tolerance plus standardised pulley exercises - Home exercise: Active non-assisted exercises using a wooden stick *Dosage :* - PEMF: 30 minutes - Hot pack: 30 minutes - Supervised exercise: 5 minutes (stretching) and 10 minutes (pulley) - Home exercise: 20 minutes *Frequency of administration :* Three times a week up to a maximum of 12 weeks (36 sessions); home exercises only conducted on the days in which physical therapy was not received *Provider :* Not reported **Placebo electromagnetic field therapy (N=25)** Participants received the same interventions as described above except that placebo electromagnetic field therapy was applied
Outcomes	Outcomes assessed weekly for 12 weeks. No primary outcome was reported by the trialists 1. Range of motion in flexion, extension, abduction, adduction, external rotation, internal rotation measured at week 4, 8 and 12 (not reported whether passive or active) 2. Pain intensity at rest, on motion, and lying down, using a 4-point ordinal scale rated as 1=absence of pain, 2=light pain, 3=moderate pain, and 4=severe pain 3. Pain intensity using a 100mm visual analogue scale 4. Disability (interference with daily activities) using a 100mm visual analogue scale 5. Adverse events
Notes	Trialists did not report any outcome data for VAS pain and VAS disability.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Consenting participants were then randomised". Comment: No information on how the allocation sequence was generated was reported
Allocation concealment (selection bias)	Unclear risk	Quote: "A separate individual was provided the randomization code and controlled the concealed switch." Comment: No information on how the allocation sequence was concealed was reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The study used a triple-blind parallel group design. Subjects received either (1) electromagnetic field therapy or sham therapy…The patient, therapist, and investigator were blind to the procedure. A separate individual was provided the randomization code and controlled the concealed switch." Comment: Participants and personnel were blind to treatment
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Quote: "The patient, therapist, and investigator were blind to the procedure." Comment: Blinded participants self-reported pain and disability
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "The patient, therapist, and investigator were blind to the procedure." Comment: Range of motion was assessed by blinded a outcome assessor
Incomplete outcome data (attrition bias) All outcomes	Low risk	"…and all completed the study according to the protocol." Comment: There were no dropouts, exclusions, or losses to follow-up

Selective reporting (reporting bias)	High risk	Comment: Outcome data was fully reported for all outcomes specified in the methods section of the publication, except for VAS pain and VAS disability (which appear to have been incompletely reported because there was no statistically significant difference between groups on these outcomes). Also, without a trial protocol it is unclear whether other outcomes were measured but not reported based on the results
Other bias	Low risk	Comment: No other sources of bias identified

Lee 1973

Methods	**Design:** Parallel group, four-arm randomised controlled trial (United Kingdom) **Interventions:** Infrared irradiation plus active exercises or intra-articular injection of hydrocortisone acetate 25 mg (anterior approach, below the coracoid process) plus active exercises or intra-articular injection of hydrocortisone acetate 25 mg into the synovial sheath surrounding the bicipital tendon of the bicipital groove of the humerus plus active exercises or analgesics only **Sample size calculation:** Not reported **Analysis:** Intention-to-treat analysis **Source of funding:** Not reported
Participants	**Number of participants:** 80 (20 per group) **Baseline characteristics:** Age, sex, and duration of symptoms not reported **Inclusion criteria:** 1. Pain in the shoulder associated with limitation of passive movement of the shoulder joint **Exclusion criteria:** 1. Participants with a known cause of arthritis, bone or neurological disease, determined by full clinical, haematological, and radiographic examination

Interventions	All participants received a program of graduated active exercises according to the participants tolerance for six weeks. The exercises were divided into two categories: (1) Free active exercises, which were given to work the flexors and extensors of the shoulder joint, the abductors, and the medial and lateral rotators. A progression was followed using gravity, firstly to assist the movement, then with its effect eliminated, and finally with its effect resisting the action. The participants were asked to practice these exercises three times daily for 10 minutes each session, specifically in the morning, at midday, and in the evening; (2) Manual resistance, using proprioceptive neuromuscular facilitation techniques **Infrared irradiation (N=20)** *Components of intervention:* Infrared irradiation to both the anterior and posterior aspects of the shoulder region *Dosage:* 10 minutes *Frequency of administration:* Not reported *Provider:* Physiotherapist **Intra-articular injection of hydrocortisone acetate 25 mg (anterior approach, below the coracoid process) (N=20)** *Components of intervention:* Intra-articular injection of hydrocortisone acetate 25 mg (anterior approach, below the coracoid process) *Dosage:* N/A *Frequency of administration:* Not reported *Provider:* Rheumatologist **Intra-articular injection of hydrocortisone acetate 25 mg into the synovial sheath surrounding the bicipital tendon of the bicipital groove of the humerus (N=20)** *Components of intervention:* Intra-articular injection of hydrocortisone acetate 25 mg into the synovial sheath surrounding the bicipital tendon of the bicipital groove of the humerus *Dosage:* N/A *Frequency of administration:* Not reported *Provider:* Rheumatologist **Analgesics (N=20)** *Components of intervention:* Analgesics such as paracetamol, aspirin, codeine, or dihydrocodeine *Dosage:* As required *Frequency of administration:* Six weeks *Provider:* N/A

Outcomes	Outcomes assessed weekly for six weeks. No primary outcome was reported by the trialists 1. Range of motion (active abduction of the coronal plane, passive abduction of the coronal plane, active lateral rotation with the arm by the side, active medial rotation with the arm by the side) using a goniometer
Notes	Trialists reported that since there was high positive correlation between the four range of motion measures, component analysis was used to produce a single measure. The results of this measure were presented in Figure format as means with no measures of variation.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Consecutive patients were allocated to one of the four treatment groups according to a randomised plan unknown to the referring clinician" Comment: No information on how the allocation sequence was generated was reported
Allocation concealment (selection bias)	Unclear risk	Comment: No information on how the allocation sequence was concealed was reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Due to the nature of the trial it was impossible for it to be double blind in construction, but it was strictly controlled" Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Objective outcomes	High risk	Quote: "Due to the nature of the trial it was impossible for it to be double blind in construction, but it was strictly controlled" Comment: Outcome assessors were not blind to treatment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: No dropouts, losses to follow-up or exclusions were reported, but it was unclear whether the outcome data reported was based on the total number of randomised participants (as sample sizes were not reported in data tables)

Selective reporting (reporting bias)	Unclear risk	Comment: Trialists reported that since there was high positive correlation between the four range of motion measures, component analysis was used to produce a single measure. The results of this measure were presented in Figure format as means with no measures of variation. However, it is not clear whether data were incompletely reported based on the statistical significance or magnitude of the results. Also, without a trial protocol, it is unclear whether other outcomes were assessed but not reported based on the results
Other bias	Low risk	Comment: No other sources of bias identified

Leung 2008

Methods	**Design:** Parallel group, three-arm, single-blind randomised controlled trial (Hong Kong) **Interventions:** Continuous short wave diathermy plus stretching exercises or superficial heating (hot pack) plus stretching exercises or stretching exercises alone **Sample size calculation:** Not reported **Analysis:** Intention-to-treat analysis **Source of funding:** Not reported

Participants	**Number of participants:** 30 (10 per group) **Baseline characteristics:** Duration of symptoms not reported *Continuous short wave diathermy plus stretching exercises group:* Mean (SD) age = 59.8 (12.87) years; Male:Female = 5:5 *Hot pack plus stretching exercises group:* Mean (SD) age = 62.5 (12.13) years; Male:Female = 2:8 *Stretching exercises alone group:* Mean (SD) age = 57.3 (13.1) years; Male:Female = 2:8 **Inclusion criteria:** 1. Experienced shoulder pain and limited shoulder movement for at least eight weeks **Exclusion criteria:** 1. History of trauma to the shoulder 2. Acute signs of inflammation over the shoulder 3. Intrinsic shoulder pathology 4. Taking analgesic or anti-inflammatory drugs 5. Had metal implants 6. Impaired sensation of hot and cold 7. Pregnant 8. Had a cardiac pacemaker

Interventions	All participants received four stretching exercises in the following fixed sequence: stretching in external rotation, in flexion, followed by stretching in hand behind the back and cross-body abduction. Participants were asked to repeat the stretches four times. Each stretch was sustained for 30 seconds, with 10 seconds rest between each stretch. The participants were asked to perform the stretching exercises at home every day for four weeks **Continuous short wave diathermy (N=10)** *Components of intervention:* A continuous shortwave diathermy machine (Curapuls 419, Enraf Nonius, the Netherlands) with an operating frequency of 27.12 MHz was used to deliver deep heating treatment. A pair of disc electrodes was placed on the anterior–posterior aspects of the affected glenohumeral joint, separated by a hand's-breadth from the surface of the body. The intensity of the current was adjusted according to the participants' subjective feeling of comfortable warmth. If the level of perceived heating changed during the application, the machine's output was adjusted to maintain the sensation of comfortable warmth throughout the treatment *Dosage:* 20 minutes *Frequency of administration:* Three times a week for four weeks (12 sessions) *Provider:* Physiotherapist **Hot pack (N=10)** *Components of intervention:* An electrical hot pack sized 35.5 x 68.5 cm was used to deliver superficial heating. The temperature was set to 63 degrees Centigrade. The participants were informed that the only purpose of the heating was to produce a feeling of comfortable warmth. If they felt that the heat was excessive, the temperature of the electrical hot pack was adjusted immediately to ensure that the heat remained at a comfortably warm level only throughout the treatment *Dosage:* 20 minutes *Frequency of administration:* Three times a week for four weeks (12 sessions) *Provider:* Physiotherapist **Stretching exercises only (N=10)** See description of exercises above

Outcomes	Outcomes assessed before the intervention at sessions 6 (week 2) and 12 (end of 4 weeks treatment), and at four weeks post-treatment cessation. No primary outcome was reported by the trialists 1. Shoulder score index, which combines self-reported scores for pain (using a 10cm visual analogue scale) and function (using a 10-item questionnaire addressing activities of daily living, each scored on a 4-point ordinal scale of level of difficulty: 0=unable to do; 1=very difficult to do; 2=somewhat difficult; 3=not difficult). Both the pain and function score were weighted equally (50 points each) and combined for a total score of 100 points, which a higher score indicating better function. This combined score is calculated as (10 – VAS pain score) x 5 + (5/3 x cumulative activities of daily living score) 2. Range of motion in flexion, cross-body adduction, external rotation with the arm by the side, external rotation with the arm in 90 degrees abduction, and hand-behind-back using a goniometer (not reported whether passive or active)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was performed using an online randomization plane (http:/www.randomization.com)" Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	Comment: No information about how the allocation sequence was concealed was reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	"A single-blinded, randomized controlled study was conducted. The rater was blinded to the group allocation" Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported pain and function

Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "A single-blinded, randomized controlled study was conducted. The rater was blinded to the group allocation" Comment: Assessors of range of motion were blind to treatment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "None of the participants in any of the treatment groups dropped out throughout the study period." Comment: Data for the complete sample of randomised participants was reported for each outcome
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data was fully reported for all outcomes specified in the methods section of the publication, but it is unclear why pain and function sub-scores of the shoulder index were not reported, and without a trial protocol it is unclear whether any other outcomes were measured but not reported based on the results
Other bias	Low risk	Comment: No other sources of bias identified

Maryam 2012

Methods	**Design:** Parallel group, three-arm, single blind randomised controlled trial (Iran) **Interventions:** Physiotherapy (transcutaneous electrical nerve stimulation, active range of motion exercises, and ice application) or glucocorticoid injection or physiotherapy plus glucocorticoid injection **Sample size calculation:** 35 participants per group were estimated to be needed based upon detecting a clinically relevant difference at the 5% level of statistical significance with 80% power (outcome used in power calculation not reported) **Analysis:** Per-protocol analysis **Source of funding:** Not reported

Participants	**Number of participants:** 87 (27, 31, and 29 in each respective group) **Baseline characteristics:** *Physiotherapy group:* Mean (SD) age = 53.73 (7.49) years; Male:Female = 1:26 Mean (SD) duration of symptoms: 4.48 (3.37) months *Glucocorticoid injection group:* Mean (SD) age = 53.33 (7.49) years; Male:Female = 4:25 Mean (SD) duration of symptoms: 6.83 (3.75) months *Physiotherapy plus glucocorticoid injection group:* Mean (SD) age = 53.71 (6.69) years; Male:Female = 4:27 Mean (SD) duration of symptoms: 6.21 (3.95) months **Inclusion criteria:** 1. 18 years or older 2. Duration of symptoms were <1 year 3. Frozen shoulder defined as the presence of shoulder pain with limitation of both active and passive range of motion in glenohumeral joint ≤ 25% in at least 2 directions: flexion, abduction, external and internal rotation, as compared with normal values or contra lateral shoulder 4. Total score of ≥30 on Shoulder Pain and Disability Index (SPADI) **Exclusion criteria:** 1. Disorder was secondary to inflammatory, degenerative, metabolic (except for diabetes mellitus), trauma, septic arthritis and cerebrovascular accident 2. Had been treated with injection or physiotherapy in last six months

Interventions	**Physiotherapy (N=27)** *Components of intervention :* - Electrotherapy: TENS - Supervised exercises: Active range of motion exercises - Other: Ice application *Dosage :* Not reported *Frequency of administration :* 10 sessions (number of sessions per week not reported) *Provider :* Physiotherapist **Glucocorticoid injection (N=31)** *Components of intervention :* Cortiosteroid injection included as 60 milligrams triamcinolone acetonide and 3 cc lidocaine in shoulder joint with posterior approach and 20 milligrams triamcinolone acetonide and 1.5 cc lidocaine in subacromial bursa *Dosage :* See above *Frequency of administration :* Once *Provider :* Rheumatologist **Physiotherapy plus glucocorticoid injection (N=29)** Physiotherapy (as above) one week after glucocorticoid injection (as above)
Outcomes	Outcomes assessed at six weeks and six months. No primary outcome was reported by the trialists 1. Shoulder pain and disability index (SPADI) (0-100 scale where a higher score indicates worse pain and/or disability) 2. Passive range of motion in flexion, abduction, external rotation, and distance of hand behind back using a goniometer
Notes	Unpublished data regarding study design (required for risk of bias assessment) provided by trialist on request. Trial registered in the Iranian Registry of Clinical Trials (http://www.irct.ir/searchresult.php?id=1828&number=1)

Risk of bias

Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Unclear risk	Quote: "After taking written informed consent, the patients were randomized to 1 of the following 3 groups" Comment: No information on how the allocation sequence was generated was reported
Allocation concealment (selection bias)	Unclear risk	Quote: "After taking written informed consent, the patients were randomized to 1 of the following 3 groups" Comment: No information on how the allocation sequence was concealed was reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Quote: "Evaluations of SPADI score were done by an observer blind to treatment allocation." Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some components of the SPADI
Blinding of outcome assessment (detection bias) Objective outcomes	High risk	Comment: Trialists confirmed via personal communication that the assessor of range of motion was not blind to treatment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "Eight patients in physiotherapy group, 7 in combination therapy group and 3 in injection group did not continue, so statistical analysis was done on 69 remaining patients." Quote: "About 36 patients have been reevaluated in 24 weeks (Table-III). However we cannot consider this stage of study because of a high number of missed patients, but we can see a more subjective improvement during 6 months in physiotherapy group." Comment: Trialists did not report the reasons for participants not continuing (and did not provide this information when requested), so it is unclear whether the reasons were balanced between groups and related to the treatment received
Selective reporting (reporting bias)	Low risk	Comment: Outcome data was fully reported for all outcomes specified in the trial registry entry
Other bias	Low risk	Comment: No other sources of bias identified

Pajareya 2004

Methods	**Design:** Parallel group, two-arm single-blind randomised **Interventions:** Physical therapy (continuous short wave diathermy, mobilisation and passive glenohumeral joint stretching exercises) plus ibuprofen or ibuprofen alone **Sample size calculation:** 60 participants per group were estimated to be needed based upon detecting a difference in success rate (measured by improvement in a global pain and disability index) of 25% at the 5% level of statistical significance with 80% power **Analysis:** Per-protocol analysis (reported that intention-to-treat analysis was used to test statistical significance, but outcome data presented in tables was reported as based on the number of participants completing assessments at each week) **Source of funding:** Department of Research Promotion, Faculty of Medicine, Siriraj Hospital, Mahidol University and partially supported by Thailand Research Fund (non-industry)
Participants	**Number of participants:** 122 (61 per group) **Baseline characteristics:** Baseline characteristics reported for the participants who completed the week 3 assessment (N=119) *Physical therapy plus ibuprofen group:* Mean (SD) age = 56.3 (10.6) years; Male:Female = 14:45 Duration of symptoms: No. participants with duration <6 weeks (N=6), between 6-11 weeks (N=20), and 12 or more weeks (N=33) *Ibuprofen alone group:* Mean (SD) age = 57.7 (10) years; Male:Female = 24:36 Duration of symptoms: No. participants with duration <6 weeks (N=13), between 6-11 weeks (N=20), and 12 or more weeks (N=27) **Inclusion criteria:** 1. Had shoulder pain and limitation of a passive range of shoulder motion in all directions that interfered with their activities of daily living **Exclusion criteria:** 1. Secondary adhesive capsulitis 2. Intrinsic causes of shoulder problems such as a history of fracture, or dislocation or extrinsic causes such as neuromuscular disorders (stroke, parkinsonism), generalised arthritis, bilateral involvement, contraindication for NSAIDs 3. Bleeding tendencies

Interventions	Both groups received ibuprofen 400 mg three times daily for three weeks, and general advice (an information sheet containing advice on protection of the shoulder from vigorous activities such as pushing and pulling, and encouragement to use their arms in a normal fashion for reaching and other activities of daily life) **Physical therapy plus ibuprofen (N=61)** *Components of intervention :* - Electrotherapy: Continuous short wave diathermy - Manual therapy: Mobilisation. If, during the passive movements the patients felt pain before the therapist reached the end of the range, exercise was not attempted - Supervised exercise: Passive glenohumeral joint stretching exercises up to the participant's tolerance, based on Cyriax - Home exercise: Pulley exercises (actively assisted exercises for five minutes) and active non-assisted exercises using a towel and wall (five minutes after applying a hot pack for 20 minutes) *Dosage :* - Electrotherapy: 20 minutes - Manual therapy: Not reported - Supervised exercise: Not reported - Home exercise: 10 minutes *Frequency of administration :* - Electrotherapy: Three times a week for three weeks (9 sessions) - Manual therapy: Three times a week for three weeks (9 sessions) - Supervised exercise: Three times a week for three weeks (9 sessions) - Home exercise: Four days a week for three weeks (on the days they did not receive the hospital-based physical therapy program) *Provider :* Physical therapist **Ibuprofen (N=61)** See above

Outcomes	All outcomes assessed at the end of three weeks treatment (except for "success", which was also assessed at six, 12 and 24 weeks) **Primary outcome:** 1. "Success", measured by participants rating themselves as having disappearance of shoulder complaints or some pain/limitation which does not interfere with everyday life (on a global pain and disability index with a 5-point Likert scale with response options "disappearance of shoulder complaints", "some pain or limitation but which does not interfere with everyday life", "minimal inconvenience to everyday life", "moderate inconvenience", and "marked inconvenience") **Secondary outcomes:** 2. Shoulder pain and disability index (SPADI) (0-100 scale where a higher score indicates worse pain and/or disability) 3. Passive range of motion (abduction, external rotation, internal rotation quantified by measuring the distance between thumb and tip of C7 spine in hand behind back position) using a goniometer 4. Adverse events recorded for the physical therapy group by asking "Do you have pain that persisted more than 2 hours after treatment or more disability the next morning or not?", and by asking all patients, "Have the trial drugs and/or treatment program upset you in any way?" and examining the patient for any signs of echymosis or burn during range of motion evaluation
Notes	Adverse events due to ibuprofen were not reported separately per group: "During the 3-week period, the patients in the study group reported a total of 10 episodes of pain that persisted more than 2 hours after treatment from 4 subjects.There were no other complications recorded. Regarding NSAIDs, 15 subjects (12.6%) had gastrointestinal side effects; the number of those who had severe dyspepsia and had to stop NSAIDs was 6 (4.2%). There were 2 reports of severe oedema and 1 case with a severe headache, which rapidly subsided after the drug was discontinued" (pg 477 of trial publication). Unpublished data regarding study design (required for risk of bias assessment) provided by trialist on request.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The patients who gave informed written consent were randomly allocated to a 3-week treatment protocol by simple randomisation using a random numbers table and allocation concealed within an opaque envelope." Comment: An adequate method was used to generate the allocation sequence

Allocation concealment (selection bias)	Low risk	Quote: "The patients who gave informed written consent were randomly allocated to a 3-week treatment protocol by simple randomisation using a random numbers table and allocation concealed within an opaque envelope." Personal communication: "I prepared opaque envelopes before hand. Within each envelope, I put the letter "I" or "C". The series of "I" and "C" came from the random number table. I didn't remember any part of the series" Comment: An adequate method was used to conceal the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported a global pain and disability index and the SPADI
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "Moreover, at each follow-up, an investigator, blinded to treatment modality asked all patients "Have the trial drugs and/or treatment program upset you in any way?" and examined the patient for any signs of echymosis or burn during range of motion evaluation." Personal communication: "The range of motion assessor was blinded. I had told all of the participants that "Please don't tell the assessor about the treatment you have"" Comment: Assessors of adverse events and range of motion were probably blind to treatment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "At the end of the 3rd week, 2 subjects dropped out from the study; 1 from the control group and 1 from the study group. The total number of cases included in the analysis was 59 in the control and 60 in the study group. By the end of the 24th week, a total of 12 cases (10.1%) had withdrawn from the study (Fig. 1). All of them lost to follow-up for unknown reasons and the investigators could not contact them." Quote: "The results were analysed by intention to treat analysis even though the treatments actually received were modified from the protocol, because it was found that the reasons for modifying the treatment were strongly related to the results of allocated interventions." Comment: It is unclear whether reasons for losses to follow-up were related to the interventions received
Selective reporting (reporting bias)	Unclear risk	Quote: Outcome data was fully reported for all outcomes specified in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the results

Other bias	Low risk	Quote: "About three-quarters of the subjects of both groups received NSAIDs as prescribed. The reasons why some patients received fewer NSAIDs than the others was due to gastrointestinal discomfort, forgetting to take them or a misunderstanding about the schedule. In the study group, 7 cases (11.7%) received fewer than 6 sessions of hospital-based PT, 5 cases (8.3%) performed the home programme exercises fewer than 6 sessions. Two cases from the control group reported that they had additional treatment; 1 had Chinese herbal medicine and 1 received analgesics from a private clinic. No patient in the control group had hospital-based PT or home exercise therapy for their shoulder." Quote: "The deviation from the protocol in the present study might not reverse the results. On the contrary, the differences of the outcomes at the end of the study should be elicited more easily if there was no protocol deviation. Because the patients in the study group received fewer treatments than the schedule determined (six cases had fewer than 6 sessions of hospital-based PT and 6 cases performed home exercise fewer than 6 sessions), while the subjects in the control group received more treatment than the schedule (one case had Chinese herbal medicine and 1 case had analgesics from a private clinic)." Comment: Protocol violations are unlikely to have influenced the results

Rigato 2002

Methods	**Design:** Parallel group, three-arm, single-blind randomised controlled trial (Italy) **Interventions:** Low-frequency (100 Hz) pulsed electromagnetic field therapy (PEMF) or Therapeutic Application of a Musically Modulated Electromagnetic Field (TAMMEF) or simulated (placebo) electromagnetic field therapy **Sample size calculation:** Not reported **Analysis:** Intention-to-treat analysis **Source of funding:** Not reported
Participants	**Number of participants:** 49 (18, 17, and 14 in each respective group) **Baseline characteristics:** Age and duration of symptoms not reported. Sex by group was not reported Male:Female = 20:29 **Inclusion criteria:** 1. Unilateral non-calcified shoulder periarthritis **Exclusion criteria:** Not reported

Interventions	**Low-frequency (100 Hz) pulsed electromagnetic field (N=17)** *Components of intervention:* Low-frequency (100 Hz) electromagnetic field therapy was delivered by applying magnets to the shoulder *Dosage:* 30 minutes *Frequency of administration:* Daily for 15 days (15 sessions) *Provider:* Physicist **Therapeutic Application of a Musically Modulated Electromagnetic Field (TAMMEF) (N=18)*** *Components of intervention:* TAMMEF was delivered by applying magnets to the shoulder. The electromagnetic field parameters (frequency, intensity, waveform) were modified in time, randomly varying within the respective ranges, so that all the possible codes can occur during a single application *Dosage:* 30 minutes *Frequency of administration:* Daily for 15 days (15 sessions) *Provider:* Physicist **Simulated (placebo) electromagnetic field (N=14)** *Components of intervention:* A simulated (placebo) electromagnetic field was delivered by applying magnets to the shoulder *Dosage:* 30 minutes *Frequency of administration:* Daily for 15 days (15 sessions) *Provider:* Physicist
Outcomes	Outcomes assessed at day 7, day 15 (end of treatment) and day 45 (i.e. 30 days post-treatment cessation). No primary outcome was reported by the trialists. 1. Pain using a visual analogue scale rated from 0=absence of pain to 10=maximum intensity 2. Articular functionality by executing semeiological manoeuvres to define the functionality of single regions affected, expressed as 0=absence of functional limitation, 1=slight limitation, 2=moderate limitation, and 3=serious limitation 3. Local or systemic side effects

Notes	*This intervention is not a standard type of pulsed electromagnetic field therapy that can be applied by physical therapists, so no data for this group was included in the review This RCT included participants with shoulder periarthritis or cervical spondylosis. Pain and articular functionality outcome data was reported separately per cervical spondylosis and shoulder periarthritis participants in the two active intervention groups at the end of 15 days treatment, but not at 30 days follow-up, and was not reported separately at any time point for the placebo group. Unpublished data was requested but was unable to be provided by the trialist as he no longer had access to the data (had changed place of work).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The patients were randomly divided into three groups" Comment: No information on how the allocation sequence was generated was reported
Allocation concealment (selection bias)	Unclear risk	Comment: No information on how the allocation sequence was concealed was reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Specifically, they knew that they would be subjected to an experimental treatment based on low-frequency electromagnetic fields; they also knew of the therapeutic objectives and the previously obtained results. However, for obvious experimental reasons, they were not informed about the difference between the two treatments and the consequent division into groups." Comment: Participants (but probably not personnel) were probably blind to treatment
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported pain

Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Comment: No information on whether articular functionality was assessed by blinded outcome assessors was reported
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "All the patients of groups A and B completed the therapeutic cycle, without appreciable local or systemic side-effects that might have required suspension of the treatment." Quote: "After the first week of treatment, application of the simulated magnetic field had to be suspended in 20 group C patients (40%) because of its ineffectiveness. The remaining 30 patients (60%) completed the cycle according to the procedure described above." Comment: There were no dropouts in the two active intervention groups and 40% dropout in the placebo group which was related to the treatment received (this 40% comprises participants with cervical spondylosis or shoulder periarthritis; the number of shoulder periarthritis participants who were randomised to and who dropped out of this group was not reported)
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data was reported separately per cervical spondylosis and shoulder periarthritis participants in the two active intervention groups at the end of 15 days treatment, but not at 30 days follow-up, and was not reported separately at any time point for the placebo group. However, it is not clear whether data were incompletely reported based on the statistical significance or magnitude of the results. Also, without a trial protocol, it is unclear whether other outcomes were assessed but not reported based on the results
Other bias	Low risk	Comment: No other sources of bias identified

Ryans 2005

Methods	**Design:** Parallel group, four-arm, single blind randomised controlled trial (United Kingdom) **Interventions:** Physiotherapy (interferential current, proprioceptive neuromuscular facilitation, Maitland mobilizations and active exercise) plus glucocorticoid injection or glucocorticoid injection alone or physiotherapy plus placebo injection or placebo injection alone **Sample size calculation:** 20 participants per group were estimated to be needed based upon detecting a difference of 1.04 points on a 5-point pain scale (SD=1.6) at 4 weeks at the 5% level of statistical significance with 82% power **Analysis:** Per protocol analysis **Source of funding:** Arthritis Research Campaign (non-industry)
Participants	**Number of participants:** 80 (20 per group) **Baseline characteristics:**

Physiotherapy plus glucocorticoid injection group:

Mean (SD) age = 56.3 (6.4) years; Male:Female = 11:9

Mean (SD) duration of symptoms: 14.2 (4.4) weeks

Glucocorticoid injection alone group:

Mean (SD) age = 52.3 (9.3) years; Male:Female = 6:13

Mean (SD) duration of symptoms: 12.2 (5.3) weeks

Physiotherapy plus placebo injection group:

Mean (SD) age = 52.6 (7.7) years; Male:Female = 6:14

Mean (SD) duration of symptoms: 14.4 (4.4) weeks

Placebo injection alone group:

Mean (SD) age = 55.2 (9.4) years; Male:Female = 9:10

Mean (SD) duration of symptoms: 14.9 (3.7) weeks

Inclusion criteria:

1. Aged 18 years or older

2. A painful shoulder, in the fifth cervical (C5) dermatome distribution, of more than four weeks and less than six months duration

3. Limitation of active and passive range of movement greater than 25% in abduction and external rotation compared with the other shoulder

Exclusion criteria:

1. Pain was less than four weeks duration

2. Symptoms of more than six months duration

3. Had a previous intra-articular injection or prior physiotherapy for this episode of shoulder pain

4. Presence of restriction of active and passive range of movement in external rotation only or glenohumeral abduction only

5. Had evidence of glenohumeral osteoarthritis on plain X-ray

6. Had clinical evidence of a complete rotator cuff tear (i.e. positive drop-off sign or weakness of the rotator cuff muscles)

7. Had clinical evidence of significant cervical spine disease, history of significant trauma to the shoulder or a history of inflammatory joint disease or of a cerebrovascular accident affecting the study shoulder

	8. Had bilateral adhesive capsulitis 9. Had a contraindication to triamcinolone injection
Interventions	All participants were provided with 50x500mg paracetamol tablets with suggestions to take one or two tablets 4- to 6-hourly as required for pain, taking no more than a maximum of eight tablets daily. All participants were also instructed by a physiotherapist in an identical home exercise programme using a video and home exercise instruction sheet **Physiotherapy plus glucocorticoid injection (N=20)** *Components of physiotherapy intervention :* - Electrotherapy: Standardised interferential current - Manual therapy: Maitland mobilizations which were progressed as the condition improved, and proprioceptive neuromuscular facilitation - Supervised exercise: Active exercise therapy with gym equipment *Dosage :* Not reported *Frequency of administration :* Twice a week for four weeks (eight sessions) *Provider :* Physiotherapist *Components of glucocorticoid injection :* Injections of triamcinolone 20mg (1 ml) and normal saline 2 ml plus physiotherapy for four weeks. Injections were given (without imaging guidance) by a combined approach to the shoulder: half the solution (1.5 ml) was injected by an anterior approach and half (1.5 ml) by a lateral approach **Glucocorticoid injection alone (N=20)** The same injection method as described above was delivered **Physiotherapy plus placebo injection (N=20)** The same injection and physiotherapy method as described above was delivered, except that normal saline 3 ml was injected into the shoulder **Placebo injection alone (N=20)** The same injection method as described above was delivered, except that normal saline 3 ml was injected into the shoulder

Outcomes	Outcomes assessed at 6 and 16 weeks post-randomisation **Primary outcome:** 1. Croft Shoulder Disability Questionnaire (0-22 score range, where a score of 0 indicates no disability and a score of 5 and over represents significant disability) **Secondary outcomes:** 1. General health status using the SF-36 (assessed at 16 weeks post-randomisation only) 2. Passive and active range of motion in forward flexion, abduction, external rotation, internal rotation using a goniometer 3. Daytime pain at rest using a 100mm visual analogue scale 4. Global function using a 100mm visual analogue scale
Notes	*Outcome data fully reported only for these outcomes. No outcome data reported for other outcomes. Unpublished data regarding study design (required for risk of bias assessment) provided by trialist on request. Trial registered in ISRCTN but outcomes not provided at time of registration (http://www.controlled-trials.com/ISRCTN25152388).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Subjects were randomly allocated in permuted blocks of four using random number tables to one of four treatments. The randomization process took place in the hospital pharmacy department. Allocations were placed in sealed envelopes which were opened by the physiotherapist teaching the home exercise programme" Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Low risk	Comment: See quote above. An adequate method was used to conceal the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Injections were provided in opaque syringes, and the investigator measuring outcomes (IR) was not present at the time of randomization or injection and was blinded to all study interventions. Both patients and the physiotherapist were blinded to the nature of the injection. Clearly, it was impossible to blind subjects regarding physiotherapy but subjects were asked not to reveal if they were having physiotherapy treatment." Comment: Participants and personnel were blind to the injection component of the intervention, but not the physiotherapy component. Participants may have had different expectations about the benefits of each intervention

Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Participants self-reported pain, general health status and function, and were not blind to whether they had received physiotherapy or not. Participants may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "Injections were provided in opaque syringes, and the investigator measuring outcomes (IR) was not present at the time of randomization or injection and was blinded to all study interventions. Both patients and the physiotherapist were blinded to the nature of the injection. Clearly, it was impossible to blind subjects regarding physiotherapy but subjects were asked not to reveal if they were having physiotherapy treatment." Comment: Assessors of objective outcomes were blind to treatment.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Eighty subjects were recruited and randomly assigned to four groups. One subject was randomized twice and another failed to attend for intervention after randomization; 78 subjects were therefore available for analysis. Twenty subjects were enrolled in Group A (steroid injection and physiotherapy), 19 in Group B (steroid injection and no physiotherapy), 20 in Group C (placebo injection and physiotherapy) and 19 in Group D (placebo injection and no physiotherapy). Six subjects did not return for all follow-up visits: three in Group A, one in Group B, one in Group C and one in Group D. Fifteen subjects withdrew from the study due to failure of the study treatment. Six patients withdrew from Group B, three from Group C and six from Group D" Quote: "We also looked to see if there were significant differences in numbers dropping out in each group due to failure of treatment. Significantly more patients dropped out in Group D (placebo injection and no physiotherapy) and in Group B (steroid injection and no physiotherapy (Pearson chi-square = 8.72, P=0.033). No subjects dropped out of Group A (steroid injection and physiotherapy)." Comment: The was differential drop-out across the groups and the reasons appear to be related to the treatments received
Selective reporting (reporting bias)	High risk	Quote: "Secondary outcome measures were...range of movement as measured by passive external rotation. External rotation was chosen as the indicator range of movement as restriction in this range has been described as the most severely restricted plane of movement in shoulder capsulitis" Quote: "Analysis of improvement in the range of movement in abduction and internal rotation (thumb–C7 distance) revealed no significant association with either steroid injection or physiotherapy." Comment: Trialists reported measuring passive and active range of motion (forward flexion, abduction, external rotation, internal rotation) using a goniometer. However, outcome data was only reported for passive external rotation. The decision not to report outcome data for the other measures of range of motion appears to be related to the statistical significance of the results
Other bias	Low risk	Comment: No other sources of bias identified

Stergioulas 2008

Methods	**Design:** Parallel group, two-arm, triple-blind randomised controlled trial (Greece) **Interventions:** Low-level laser therapy (LLLT) plus home exercises or placebo laser therapy plus home exercises **Sample size calculation:** Not reported **Analysis:** Per protocol analysis **Source of funding:** Not reported

Participants	**Number of participants:** 74 (37 per group) **Baseline characteristics:** *Low-level laser therapy plus exercises group:* Mean (SD) age = 55.51 (5.84) years; Male:Female = 19:12 Mean (SD) duration of symptoms: 26.5 (12.8) weeks *Placebo laser therapy plus exercises group:* Mean (SD) age = 56.83 (6.82) years; Male:Female = 21:11 Mean (SD) duration of symptoms: 27.1 (13.6) weeks **Inclusion criteria:** 1. Painful and limited passive glenohumeral mobility 2. More restricted lateral rotation (<8°) relative to abduction and medial rotation 3. No clear signs (e.g. painful arc, positive resistance testing, or loss of power) that the shoulder pain was caused by another condition **Exclusion criteria:** 1. Insulin-dependent diabetes mellitus 2. Bilateral symptoms 3. Systemic inflammatory joint disease (such as rheumatoid arthritis or polymyalgia rheumatica) 4. Treatment with corticosteroid injections or physiotherapy during the preceding six months 5. Serious infection 6. Uncontrolled hypertension 7. Peptic ulceration for which oral steroids are contraindicated 8. Surgery, dislocation, or fracture(s) of the shoulder 9. Calcification about the shoulder joint 10. Pregnancy 11. A complete rotator cuff tear

Interventions	All patients were instructed to execute pendulum and pain-free active exercises at home **Low-level laser therapy (N=37)** *Components of intervention:* Low-level laser therapy with a 810-nm Galium-Aluminum-Arsenide (Ga-Al-As) laser with a continuous output of 60 mW applied to eight of the most painful points on the capsule of the glenohumeral joint (as indicated by the participant and checked with an algesiometer) for 30 seconds each, for a total dose of 1.8 J per point and 14.4 J per session *Dosage:* 4 minutes *Frequency of administration:* Two sessions per week from week 1-4 and one session per week from week 5-8 (12 sessions) *Provider:* Physical therapist **Placebo laser therapy (N=37)** Participants received the same interventions as described above, except that placebo laser therapy was provided
Outcomes	Outcomes assessed at the end of four and eight weeks treatment, and at eight weeks follow-up (16 weeks post-randomisation). No primary outcome was reported by the trialists 1. Overall, night, and activity-related pain using a 100mm visual analogue scale, with end points marked "no pain" at one end and "worst pain" at the other 2. Shoulder pain and disability index (SPADI) (0-100 scale where a higher score indicates worse pain and/or disability) 3. Croft shoulder disability questionnaire, which includes 22 items which participants answer each as "yes" or 'no", and the number of positive responses is summed to give a score ranging from 0-22 with higher scores indicating more severe disability 4. Disability of the Arm, Shoulder, and Hand (DASH) questionnaire, for which subjects gave their answers to each of 30 items. The DASH score is expressed as a percentage 5. Heath Assessment Questionnaire (HAQ), which is a 19-item, arthritis-specific functional assessment measure. Patients were asked to rate two or three items each in eight areas of daily life. Each item on the HAQ is scored on a scale from 0 (no disability) to 3 (greatest disability) 6. Active range of motion in flexion, abduction, and external rotation using an inclinometer 7. Adverse events
Notes	Unpublished numerical outcome data and information regarding study design (required for risk of bias assessment) provided by trialist on request.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "An assistant at the center randomized subjects into one of two groups by asking them to select one of 74 identical opaque sealed envelopes. The envelopes contained a study number and a group number: 1 (placebo) or 2 (laser). The group number corresponded to the settings on a switch on the laser unit" Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Low risk	Quote: "An assistant at the center randomized subjects into one of two groups by asking them to select one of 74 identical opaque sealed envelopes. The envelopes contained a study number and a group number: 1 (placebo) or 2 (laser). The group number corresponded to the settings on a switch on the laser unit" Comment: An adequate method was used to conceal the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Neither the assistant of the center, the treating physiotherapists, nor the patients had any knowledge of which group was receiving the active laser treatment." Comment: Participants and personnel were blind to treatment
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Quote: "Neither the assistant of the center, the treating physiotherapists, nor the patients had any knowledge of which group was receiving the active laser treatment." Comment: Blinded participants self-reported pain and function
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "A physical therapist at the center, who was unaware of the treatment type being received by each patient, performed the clinical assessments at baseline and at weeks 4, 8, and 16." Comment: Blinded outcome assessors measured range of motion
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Eleven patients (six from the experimental group and five from the control group) left the study to seek another treatment method because they still had symptoms after six treatments. The study was completed with 63 patients." Comment: The number of dropouts (and reasons for this) were similar between the groups and are unlikely to have biased the results

Selective reporting (reporting bias)	Low risk	Comment: Numerical outcome data was fully reported for overall pain, night pain, and activity-related pain. Data for all other outcomes was reported in Figures as means with unlabelled error bars and an indication of whether differences between groups were statistically significant (P<0.05) or not. However, complete numerical data for these partially reported outcomes was provided by the trialist on request
Other bias	Low risk	Comment: No other sources of bias identified

Taverna 1990

Methods	**Design:** Parallel group, two-arm double-blind randomised controlled trial (Italy) **Interventions:** Low-level laser therapy (LLLT) or placebo laser therapy **Sample size calculation:** Not reported **Analysis:** Intention-to-treat analysis **Source of funding:** Not reported
Participants	**Number of participants:** 40 (20 per group) **Baseline characteristics:** Age, sex and duration of symptoms not reported **Inclusion criteria:** 1. Diagnosed with scapulohumeral periarthritis **Exclusion criteria:** Not reported
Interventions	**Laser therapy (N=20)** *Components of intervention:* Low-level laser therapy (1000Hz, 24mW). Trialists irradiated painful points (where the pain occurs spontaneously and with a ratio more or less closely with the damaged structures), the points of greater access (points which may also not evoke a painful response, or even pressure, but where the emitted beam can penetrate better into the tissues and effectively reach treatment areas) and to a lesser extent the trigger points (points that, when excited, trigger pain in a target area that never corresponds to the trigger point) *Dosage:* 15 to 20 minutes *Frequency of administration:* Daily for six days *Provider:* Orthopaedic physician **Placebo laser therapy (N=20)** Participants received the same interventions as described above, except that placebo laser therapy was provided

Outcomes	Outcomes assessed at the end of six days treatment. No primary outcome was reported by the trialists 1. Patient-reported improvement in pain and function, rated as "excellent result" = improvement of 80% or more; "good result" = improvement between 60% to 80%; "reasonable result" = improvement between 40% to 60%; or "insufficient result" = improvement less than 40% 2. Adverse events
Notes	Article is written in Italian. MP used Google Translate to translate into English. Quality of translation was good. There were 40 additional participants in this RCT who had cervical osteoarthritis (their data has not be included in this table).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "For each type of pathology we divided the patients, using the table of random numbers, into two groups: treated and untreated with IR laser..." (Google Translate translation of Italian article) Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	Comment: No information on how the allocation sequence was concealed was reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "... and all were subjected to the same number of sessions and the same application diagrams with the apparatus of laser emission both cases "in function", with the same sounds (acoustic marks bearer of power is on) and bright light (pointing), a subgroup was actually treated while the other was used as a control being turned OFF prior to the application through the laser diode removed from the handpiece" (Google Translate translation of Italian article) Comment: Participants, but not personnel, were blind to treatment
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported pain and function

Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "The evaluation was conducted before treatment and at the end of the same, and the results were evaluated by one of A. not aware of the subgroup to which the patient belonged (treated or placebo)" (Google Translate translation of Italian article) Comment: Assessors of adverse events were probably blind to treatment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: No dropouts, losses to follow-up or exclusions were reported, and outcome data was reported as being based on the number of randomised participants
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data was fully reported for all outcomes specified in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the results
Other bias	Low risk	Comment: No other sources of bias identified

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Arslan 2001	Ineligible intervention: randomised controlled trial of glucocorticoid injection versus physical therapy plus non-steroidal anti-inflammatory drug. Not able to separate out the effect of physical therapy. Included in Cochrane Review of corticosteroid injection for shoulder disorders
Buchbinder 2007	Ineligible intervention: placebo ultrasound was provided to one group (and compared to other physical therapies)
Celik 2010	Ineligible intervention: TENS was provided to both groups (along with a physical therapy)
Fang 2006	Ineligible intervention: trial compared transcutaneous electrical point stimulation to electroacupuncture, each applied to various acupuncture points (which would not be able to be delivered by a manual therapist/physical therapist/physiotherapist)
Grossi 1986	Seventy-three patients with either lateral epicondylitis or adhesive capsulitis (numbers of each individual diagnosis not given). Not possible to separate lateral epicondylitis and adhesive capsulitis data
Johnson 2007	Ineligible intervention: therapeutic ultrasound was provided to all groups (along with a physical therapy)

Study	Reason for exclusion
Koh 2013	Ineligible intervention: TENS provided to all groups (with or without bee venom acupuncture)
Ma 2013	Ineligible intervention: therapeutic ultrasound and interferential current provided to all groups (with or without cryotherapy)
Morgan 1996	Ineligible intervention: RCT of the use of TENS to control pain during a painful intervention for shoulder disorder, not an intervention for the disorder
Nellutla 2009	Ineligible intervention: therapeutic ultrasound was provided to all groups (with or without a co-intervention)
Sharad 2011	Ineligible intervention: therapeutic ultrasound was provided to all groups (with or without a co-intervention)
Sirajuddin 2010	Ineligible intervention: therapeutic ultrasound was provided to all groups (with or without a co-intervention)
Vecchini 1984	Adhesive capsulitis data not presented separately. Twelve of the 24 subjects in the study had adhesive capsulitis, while the remaining 12 had lateral epicondylitis of the elbow
Wen 2009	Ineligible intervention: interferential current was provided to all groups (with or without a co-intervention)
Yang 2012	Ineligible intervention: therapeutic ultrasound was provided to all groups (with or without a co-intervention)
Zhu 2004	Ineligible intervention: trial compared exercises plus Chinese medicine iontophoresis to pain block therapy. A manual therapist/physical therapist/physiotherapist would be unable to deliver the Chinese medicine components

Characteristics of studies awaiting assessment [ordered by study ID]

Alicicco 2000

Methods	Currently only available as a conference abstract
Participants	Not yet assessed
Interventions	Not yet assessed
Outcomes	Not yet assessed
Notes	

Characteristics of ongoing studies [ordered by study ID]

ACTRN12611000680965

Trial name or title	The rehabilitation of glenohumeral Range of Motion in Patients with Frozen Shoulder: A Comparison Between Conventional Therapy, Placebo and 'SCENAR' Electrical Stimulation Therapy.
Methods	Parallel group, two-arm double-blind randomised controlled trial (Australia)
Participants	**Inclusion criteria:** Patients must present with frozen shoulder **Exclusion criteria:** Pregnancy, Pacemakers, Tumours, Any cognitive impairment, intellectual disability or mental illness that affects their ability to understand written and verbal instructions Age minimum: 18 years Age maximum: 65 years Gender: Both males and females
Interventions	**Self Controlled Energy Neurological Adaptive Device (SCENAR) electrical stimulation therapy** 1 X 30 minute treatment sessions on the shoulder joint per week for 12 weeks. SCENAR is administered in a setting similar to massage therapy, with the patient sitting or lying on a massage table. The device is then placed on the patients skin and moved around the area of the injury. During this the patient may feel a slight tingling sensation **SCENAR Placebo stimulation therapy** 1 X 30 minute treatment sessions on the shoulder joint per week for 12 weeks. This treatment will be exactly the same as SCENAR therapy, excpet that the patient will not feel a slight tingling sensation, this is a custom made placebo device that turns on but does not emit any electrical signal. The patients be assured that some people are more sensitive than others and may or may not feel anything during treatment
Outcomes	**Primary outcomes:** Shoulder range of motion The Constant Shoulder Score and the Shoulder Assessment Form will be used **Secondary outcomes:** To measure changes in pain and quality of life during recovery using, SF-36 PIQ (Pain Impact Questionnaire)-6
Starting date	1st June 2011
Contact information	Name: Dr Dale Lovell Address: University of the Sunshine Coast, Sippy Downs Drive, Sippy Downs, QLD, 4556, Australia Email: dlovell@usc.edu.au
Notes	ACTRN12611000680965

Data and analyses

Open in table viewer

Comparison 1. Electrotherapy modality plus manual therapy or exercise (or both) versus manual therapy or exercise (or both)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Overall pain Show forest plot	3		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 1.1

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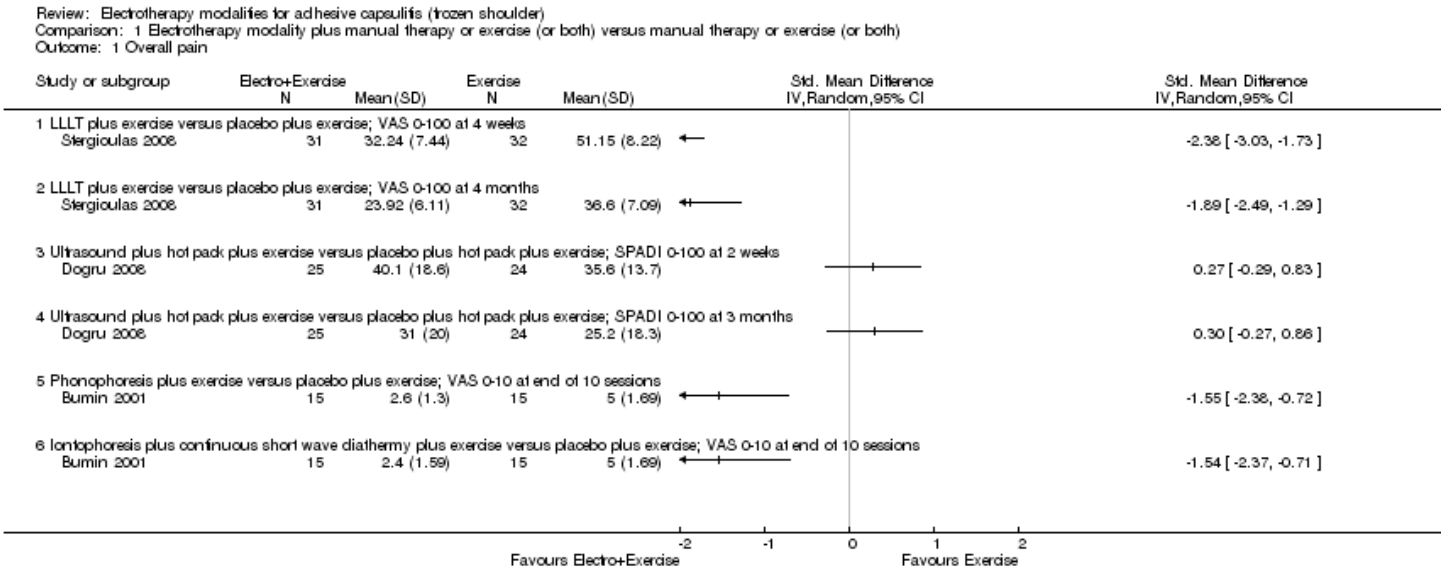

Comparison 1 Electrotherapy modality plus manual therapy or exercise (or both) versus manual therapy or exercise (or both), Outcome 1 Overall pain.

1.1 LLLT plus exercise versus placebo plus exercise; VAS 0-100 at 4 weeks	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 LLLT plus exercise versus placebo plus exercise; VAS 0-100 at 4 months	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Ultrasound plus hot pack plus exercise versus placebo plus hot pack plus exercise; SPADI 0-100 at 2 weeks	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 Ultrasound plus hot pack plus exercise versus placebo plus hot pack plus exercise; SPADI 0-100 at 3 months	1	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.5 Phonophoresis plus exercise versus placebo plus exercise; VAS 0-10 at end of 10 sessions	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.6 Iontophoresis plus continuous short wave diathermy plus exercise versus placebo plus exercise; VAS 0-10 at end of 10 sessions	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Function Show forest plot	4		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 1.2

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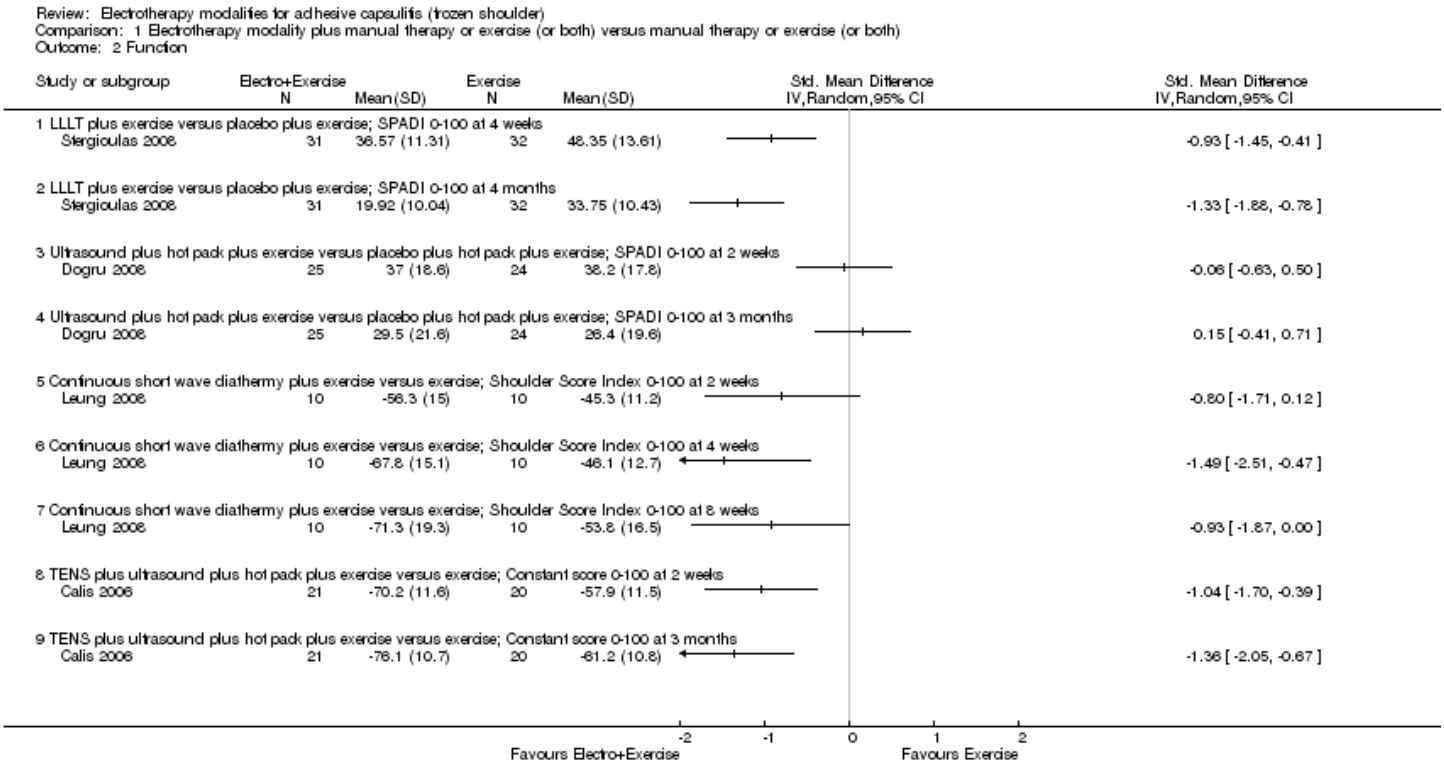

Comparison 1 Electrotherapy modality plus manual therapy or exercise (or both) versus manual therapy or exercise (or both), Outcome 2 Function.

2.1 LLLT plus exercise versus placebo plus exercise; SPADI 0-100 at 4 weeks	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.2 LLLT plus exercise versus placebo plus exercise; SPADI 0-100 at 4 months	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 Ultrasound plus hot pack plus exercise versus placebo plus hot pack plus exercise; SPADI 0-100 at 2 weeks	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.4 Ultrasound plus hot pack plus exercise versus placebo plus hot pack plus exercise; SPADI 0-100 at 3 months	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.5 Continuous short wave diathermy plus exercise versus exercise; Shoulder Score Index 0-100 at 2 weeks	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.6 Continuous short wave diathermy plus exercise versus exercise; Shoulder Score Index 0-100 at 4 weeks	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.7 Continuous short wave diathermy plus exercise versus exercise; Shoulder Score Index 0-100 at 8 weeks	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.8 TENS plus ultrasound plus hot pack plus exercise versus exercise; Constant score 0-100 at 2 weeks	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.9 TENS plus ultrasound plus hot pack plus exercise versus exercise; Constant score 0-100 at 3 months	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Information

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Contributions of authors

MJP was responsible for writing the review, performing the searches, selecting trials, performing risk of bias assessment, data extraction, analysing the data and interpreting the results of the updated review.

SG was responsible for performing the searches, selecting trials and performing the data extraction and quality assessment for the initial review, defining the review comparisons and outcomes of interest of the initial and updated review, analysing and interpreting the results, and contributing to writing both the initial and updated review.

SK was responsible for performing risk of bias assessment, data extraction and contributing to writing the manuscript for the updated review.

RJ was responsible for performing risk of bias assessment, data extraction and contributing to writing the manuscript for the updated review.

BM was responsible for selecting trials and contributing to writing the manuscript for the updated review.

RB was responsible for performing the data extraction and quality assessment for the initial review, defining the review comparisons and outcomes of interest of both the initial and updated review, analysing and interpreting the results, and contributing to writing both the initial and updated review.

Sources of support

Internal sources

- Australasian Cochrane Centre, School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia.
- Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia.

External sources

- No sources of support supplied

Declarations of interest

RB is Joint Co-ordinating Editor and RJ is Managing Editor of the Cochrane Musculoskeletal Group. To avoid bias, they excluded themselves from the editorial and publication process for this review.

SG is a practicing physiotherapist in part-time private physiotherapy practice (self employed) and as such receives remuneration for the delivery of physiotherapy interventions.

BM is a practicing physiotherapist in private physiotherapy practice and as such receives remuneration for the delivery of physiotherapy interventions.

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History

Review first published: Issue 10, 2014

Date	Event	Description
1 May 2008	Amended	Converted to RM5. CMSG ID C067-R
24 February 2003	Amended	This review is based on the original review of 'Interventions for shoulder pain'. Please see published notes for further details.
24 February 2003	New citation required and conclusions have changed	Substantive amendment

Version history

Title	Stage	Authors	Version	Publication Date
Electrotherapy modalities for adhesive capsulitis (frozen shoulder)	Review	Matthew J Page, Sally Green, Sharon Kramer, Renea V Johnston, Brodwen McBain, Rachelle Buchbinder	https://doi.org/10.1002/14651858.CD011324	1 October 2014

Differences between protocol and review

The original review outcomes were pain, range of motion (active and passive), function or disability and quality of life, strength, return to work, participant perception of overall effect, global preference, physician preference and adverse events. The outcomes reported in this review have been modified from the original review to make them as consistent as possible with other Cochrane reviews on shoulder disorders and other chronic pain conditions. To improve the succinctness of the review, we only included one measurement instrument per outcome and one time point per outcome category. We assessed study risk of bias using The Cochrane Collaboration's 'Risk of bias' tool in this update of the review. We have included a 'summary of findings' table and an ORBIT outcome matrix.

Notes

The original review, 'Physiotherapy interventions for shoulder pain' was split into four reviews upon updating: 'Manual therapy and exercise for adhesive capsulitis (frozen shoulder)', 'Electrotherapy modalities for adhesive capsulitis (frozen shoulder)', 'Manual therapy and exercise for rotator cuff disorders'. and 'Electrotherapy modalities for rotator cuff disorders'. The review has also been broadened by including all randomised and quasi-randomised clinical trials regardless of whether outcome assessment was blinded.

Appendices

Appendix 1. Search strategies

Search strategy for CENTRAL:

1. MeSH descriptor: [Shoulder Pain] explode all trees
2. MeSH descriptor: [Shoulder Impingement Syndrome] explode all trees
3. MeSH descriptor: [Rotator Cuff] explode all trees
4. MeSH descriptor: [Bursitis] explode all trees
5. ((shoulder* in All Text or rotator* in All Text) and (bursitis in All Text or frozen in All Text or impinge* in All Text or tendonitis in All Text or tendonitis in All Text or tendinopathy in All Text or pain* in All Text))
6. "rotator cuff" in All Text
7. "adhesive capsulitis" in All Text
8. #1 or #2 or #3 or #4 or #5 or #6 or #7
9. MeSH descriptor: [Rehabilitation] explode all trees
10. MeSH descriptor: [Physical Therapy Modalities] explode all trees
11. MeSH descriptor: [Exercise Movement Techniques] explode all trees
12. MeSH descriptor: [Ultrasonography, Interventional] explode all trees
13. rehabilitat* in All Text or physiotherapy* in All Text or "physical therap*" in All Text or "manual therap*" in All Text or exercis* in All Text

14. (ultrasound in All Text or ultrasonograph* in All Text or tns in All Text or tens in All Text or shockwave in All Text or electrotherap* in All Text or mobili* in All Text)
15. #9 or #10 or #11 or #12 or #13 or #14
16. #8 and #15

Search strategy for MEDLINE:

1. shoulder pain/
2. shoulder impingement syndrome/
3. rotator cuff/
4. exp bursitis/
5. ((shoulder$ or rotator cuff) adj5 (bursitis or frozen or impinge$ or tendinitis or tendonitis or tendinopathy or pain$)).mp.
6. rotator cuff.mp.
7. adhesive capsulitis.mp.
8. or/1-7
9. exp rehabilitation/
10. exp physical therapy techniques/
11. exp musculoskeletal manipulations/
12. exp exercise movement techniques/
13. exp ultrasonography, interventional/
14. (rehabilitat$ or physiotherap$ or physical therap$ or manual therap$ or exercis$ or ultrasound or ultrasonograph$ or TNS or TENS or shockwave or electrotherap$ or mobili$). mp.
15. or/9-14
16. clinical trial.pt
17. random$.mp.
18. ((single or double) adj (blind$ or mask$)).mp.
19. placebo$.mp.
20. or/16-19
21. 8 and 15 and 20

Search strategy for EMBASE:

1. 'shoulder pain'/exp
2. 'shoulder impingement syndrome'/exp
3. 'rotator cuff'/exp
4. 'bursitis'/exp
5. ((shoulder* OR rotator*) AND ('bursitis'/de OR frozen OR impinge* OR 'tendonitis'/de OR 'tendinitis'/de OR 'tendinopathy'/de OR pain*))
6. 'rotator cuff'
7. 'adhesive capsulitis'
8. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
9. 'rehabilitation'/exp
10. 'physiotherapy'/exp
11. 'kinesiotherapy'/exp
12. 'endoscopic echography'/exp
13. rehabilitat* OR physiotherapy* OR 'physical therapy' OR 'manual therapy' OR kinesiotherap* OR exercis*
14. 'ultrasound'/de OR ultrasonograph* OR 'transcutaneous nerve stimulation' OR 'transcutaneous electrical nerve stimulation' OR shockwave OR electrotherap* OR mobili*
15. #9 OR #10 OR #11 OR #12 OR #13 OR #14
16. 'randomized controlled trial'/exp
17. #8 AND #15 AND #16

Search strategy for CINAHL Plus:

- S1 MH "shoulder pain"
- S2 MH "shoulder impingement syndrome"
- S3 MH "rotator cuff"
- S4 MH bursitis+
- S5 TX (shoulder* N5 bursitis) or TX(shoulder* N5 frozen) or TX(shoulder* N5 impinge*) or TX(shoulder* N5 tend?nitis) or TX(shoulder* N5 tendinopathy) or TX(shoulder* N5 pain*)

- S6 TX (rotator cuff N5 bursitis) or TX(rotator cuff N5 frozen) or TX(rotator cuff N5 impinge*) or TX(rotator cuff N5 tend?nitis) or TX(rotator cuff N5 tendinopathy) or TX(rotator cuff N5 pain*)
- S7 TX rotator cuff
- S8 TX adhesive capsulitis
- S9 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8
- S10 MH Rehabilitation+
- S11 MH physical therapy+
- S12 MH Manual Therapy+
- S13 MH Therapeutic Exercise+
- S14 MHUltrasonography+
- S15 TX rehabilitat* or physiotherapy* or physical therap* or manual therap* or exercise* or ultrasound or ultrasonograph* or TNS or TENS or shockwave or electrotherapy* or mobili*
- S16 S10 or S11 or S12 or S13 or S14 or S15
- S17 PT clinical trial
- S18 TX random*
- S19 TX(single blind*) or TX(single mask*)
- S20 TX(double blind*) or TX(double mask*)
- S21 placebo*
- S22 S17 or S18 or S19 or S20 or S21
- S23 S9 and S16 and S22

Cochrane Library

Cochrane Database of Systematic Reviews

Electrotherapy modalities for rotator cuff disease (Review)

Page MJ, Green S, Mrocki MA, Surace SJ, Deitch J, McBain B, Lyttle N, Buchbinder R

Page MJ, Green S, Mrocki MA, Surace SJ, Deitch J, McBain B, Lyttle N, Buchbinder R.
Electrotherapy modalities for rotator cuff disease.
Cochrane Database of Systematic Reviews 2016, Issue 6. Art. No.: CD012225.
DOI: 10.1002/14651858.CD012225.

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[Intervention Review]

Electrotherapy modalities for rotator cuff disease

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ABSTRACT

Background

Management of rotator cuff disease may include use of electrotherapy modalities (also known as electrophysical agents), which aim to reduce pain and improve function via an increase in energy (electrical, sound, light, or thermal) into the body. Examples include therapeutic ultrasound, low-level laser therapy (LLLT), transcutaneous electrical nerve stimulation (TENS), and pulsed electromagnetic field therapy (PEMF). These modalities are usually delivered as components of a physical therapy intervention. This review is one of a series of reviews that form an update of the Cochrane review, 'Physiotherapy interventions for shoulder pain'.

Objectives

To synthesise available evidence regarding the benefits and harms of electrotherapy modalities for the treatment of people with rotator cuff disease.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL; 2015, Issue 3), Ovid MEDLINE (January 1966 to March 2015), Ovid EMBASE (January 1980 to March 2015), CINAHL Plus (EBSCOhost, January 1937 to March 2015), ClinicalTrials.gov and the WHO ICTRP clinical trials registries up to March 2015, unrestricted by language, and reviewed the reference lists of review articles and retrieved trials, to identify potentially relevant trials.

Selection criteria

We included randomised controlled trials (RCTs) and quasi-randomised trials, including adults with rotator cuff disease (e.g. subacromial impingement syndrome, rotator cuff tendinitis, calcific tendinitis), and comparing any electrotherapy modality with placebo, no intervention, a different electrotherapy modality or any other intervention (e.g. glucocorticoid injection). Trials investigating whether electrotherapy modalities were more effective than placebo or no treatment, or were an effective addition to another physical therapy intervention (e.g. manual therapy or exercise) were the main comparisons of interest. Main outcomes of interest were overall pain, function, pain on motion, patient-reported global assessment of treatment success, quality of life and the number of participants experiencing adverse events.

Data collection and analysis

Two review authors independently selected trials for inclusion, extracted the data, performed a risk of bias assessment and assessed the quality of the body of evidence for the main outcomes using the GRADE approach.

Main results

We included 47 trials (2388 participants). Most trials (n = 43) included participants with rotator cuff disease without calcification (four trials included people with calcific tendinitis). Sixteen (34%) trials investigated the effect of an electrotherapy modality delivered in isolation. Only 23% were rated at low risk of allocation bias, and 49% were rated at low risk of both performance and detection bias (for self-reported outcomes). The trials were heterogeneous in terms of population, intervention and comparator, so none of the data could be combined in a meta-analysis.

In one trial (61 participants; low quality evidence), pulsed therapeutic ultrasound (three to five times a week for six weeks) was compared with placebo (inactive ultrasound therapy) for calcific tendinitis. At six weeks, the mean reduction in overall pain with placebo was -6.3 points on a 52-point scale, and -14.9 points with ultrasound (MD -8.60 points, 95% CI -13.48 to -3.72 points; absolute risk difference 17%, 7% to 26% more). Mean improvement in function with placebo was 3.7 points on a 100-point scale, and 17.8 points with ultrasound (mean difference (MD) 14.10 points, 95% confidence interval (CI) 5.39 to 22.81 points; absolute risk difference 14%, 5% to 23% more). Ninety-one per cent (29/32) of participants reported treatment success with ultrasound compared with 52% (15/29) of participants receiving placebo (risk ratio (RR) 1.75, 95% CI 1.21 to 2.53; absolute risk difference 39%, 18% to 60% more). Mean improvement in quality of life with placebo was 0.40 points on a 10-point scale, and 2.60 points with ultrasound (MD 2.20 points, 95% CI 0.91 points to 3.49 points; absolute risk difference 22%, 9% to 35% more). Between-group differences were not important at nine months. No participant reported adverse events.

Therapeutic ultrasound produced no clinically important additional benefits when combined with other physical therapy interventions (eight clinically heterogeneous trials, low quality evidence). We are uncertain whether there are differences in patient-important outcomes between ultrasound and other active interventions (manual therapy, acupuncture, glucocorticoid injection, glucocorticoid injection plus oral tolmetin sodium, or exercise) because the quality of evidence is very low. Two placebo-controlled trials reported results favouring LLLT up to three weeks (low quality evidence), however combining LLLT with other physical therapy interventions produced few additional benefits (10 clinically heterogeneous trials, low quality evidence). We are uncertain whether transcutaneous electrical nerve stimulation (TENS) is more or less effective than glucocorticoid injection with respect to pain, function, global treatment success and active range of motion because of the very low quality evidence from a single trial. In other single, small trials, no clinically important benefits of pulsed electromagnetic field therapy (PEMF), microcurrent electrical stimulation (MENS), acetic acid iontophoresis and microwave diathermy were observed (low or very low quality evidence).

No adverse events of therapeutic ultrasound, LLLT, TENS or microwave diathermy were reported by any participants. Adverse events were not measured in any trials investigating the effects of PEMF, MENS or acetic acid iontophoresis.

Authors' conclusions

Based on low quality evidence, therapeutic ultrasound may have short-term benefits over placebo in people with calcific tendinitis, and LLLT may have short-term benefits over placebo in people with rotator cuff disease. Further high quality placebo-controlled trials are needed to confirm these results. In contrast, based on low quality evidence, PEMF may not provide clinically relevant benefits over placebo, and therapeutic ultrasound, LLLT and PEMF may not provide additional benefits when combined with other physical therapy interventions. We are uncertain whether TENS is superior to placebo, and whether any electrotherapy modality provides benefits over other active interventions (e.g. glucocorticoid injection) because of the very low quality of the evidence. Practitioners should communicate the uncertainty of these effects and consider other approaches or combinations of treatment. Further trials of electrotherapy modalities for rotator cuff disease should be based upon a strong rationale and consideration of whether or not they would alter the conclusions of this review.

PLAIN LANGUAGE SUMMARY

Electrotherapy modalities for rotator cuff disease

Background

Rotator cuff disease is the most common cause of shoulder pain. People with rotator cuff disease often describe their pain as being worse at night and exacerbated by movement in specific directions, including overhead activity. It is often associated with loss of function and some people describe weakness.

Electrotherapy modalities (also known as electrophysical agents) are types of physical therapy that aim to reduce pain and improve function via an increase in energy (electrical, sound, light, or thermal) into the body. Examples include therapeutic ultrasound, low-level laser therapy (LLLT), transcutaneous electrical nerve stimulation (TENS), and pulsed electromagnetic field therapy (PEMF). Electrotherapy modalities are delivered by various clinicians, including physiotherapists, chiropractors and osteopaths. In practice, people with rotator cuff disease seldom receive a single electrotherapy modality in isolation from other components of physical therapy treatment (for example manual therapy or exercise, or both).

Study characteristics

This summary of an updated Cochrane review presents what we know from research about the benefits and harms of electrotherapy modalities in people with rotator cuff disease. After searching for all relevant studies published up to March 2015, we included 47 trials (2388 participants). Among the included participants, 67% were women, the average age was 53 years, and the average duration of the condition was eight months. Electrotherapy was delivered for three weeks on average.

Key results

Pulsed therapeutic ultrasound versus placebo (inactive ultrasound) for six weeks in people with calcific tendinitis (based on one trial)

Overall pain (lower scores mean greater pain reduction)

People who had ultrasound had greater pain reduction than people who had placebo. Reduction in pain was 8.60 points more (ranging from 3.72 to 13.48 points more) at six weeks (17% absolute improvement). On a scale of 0 to 52 points, people who had ultrasound rated their reduction in pain score as -14.9 points, and people who had placebo rated their reduction in pain score as -6.3 points.

Function (higher scores mean more improvement in function)

People who had ultrasound improved more than people who had placebo. Improvement in function was 14.10 points more (ranging from 5.39 to 22.81 points more) at six weeks (14% absolute improvement). On a scale of 0 to 100 points, people who had ultrasound rated their change in function as 17.8 points, and people who had placebo rated their change in function as 3.7 points.

Treatment success

Thirty-nine more people out of 100 rated their treatment as successful with ultrasound compared with placebo; 39% absolute improvement (ranging from 18% to 60% more improvement). Ninety-one out of 100 people reported treatment success with ultrasound and 52 out of 100 people reported treatment success with placebo.

Side effects

No participant receiving ultrasound or placebo reported side effects.

Quality of the evidence

Low-quality evidence suggests that therapeutic ultrasound may improve overall pain, function, global treatment success and quality of life more than placebo at short-term (six weeks) in people with calcific tendinitis, that LLLT may improve overall pain and function more than placebo at short-term (up to three weeks), that therapeutic ultrasound and LLLT may produce no clinically important additional benefits in pain and function when combined with other physical therapy interventions alone, and that PEMF may produce no clinically important benefits in pain and function when compared with placebo. Further high quality research is likely to change our confidence in the effect estimates.

We are uncertain whether TENS improves pain and function more than placebo, whether therapeutic ultrasound improves pain and function more than other active interventions (manual therapy, acupuncture, glucocorticoid injection, glucocorticoid injection plus oral tolmetin sodium, or exercise), or whether LLLT improves pain and function more than oral nonsteroidal anti-inflammatory drugs (NSAID) and glucocorticoid injection, because of the very low quality of the evidence.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Therapeutic ultrasound compared to placebo for rotator cuff disease

Patient or population: Rotator cuff disease (diagnostic label: calcific tendinitis)
Settings: Outpatient clinics and private practices, Austria
Intervention: Pulsed therapeutic ultrasound (0.89 MHz frequency, 2.5 W/cm^2 intensity for 15 minutes, 3-5 times a week for 6 weeks)
Comparison: Placebo (inactive ultrasound, 3-5 times a week for 6 weeks)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo	Therapeutic ultrasound				
Overall pain Assessed: Binder's pain scale Scale from: 0-52 Follow-up: 6 weeks	The mean change in overall pain in the control group was **-6.3**[1]	The mean change in overall pain in the intervention group was **8.6 lower** (13.48 lower to 3.72 lower)	-	61 (1 RCT)	⊕⊕◯◯ **LOW**[2,3]	Lower score denotes greater reduction in pain. Absolute risk difference 17% (7% to 26% more); relative percentage change 42% (18% to 65% more) NNTB 4 (2 to 10)
Function Assessed with Constant-Murley total score Scale from 0-100 Follow-up: 6 weeks	The mean change in function in the control group was **3.7**[1]	The mean change in function in the intervention group was **14.1 higher** (5.39 higher to 22.81 higher)	-	61 (1 RCT)	⊕⊕◯◯ **LOW**[2,3]	Higher score denotes greater improvement in function. Absolute risk difference 14% (5% to 23% more); relative percentage change 20% (8% to 32% more) NNTB 3 (2 to 7)
Pain on motion	See comment	See comment	-	-	-	Not measured

Global assessment of treatment success Follow up: 6 weeks	**Study population**		**RR 1.75** (1.21 to 2.53)	61 (1 RCT)	⊕⊕◯◯ **LOW**[2,3]	Absolute risk difference 39% (18% to 60% more); relative percentage change 75% (21% to 153% more) NNTB 3 (2 to 6)
	517 per 1000[4]	**905 per 1000** (626 to 1000)				
Quality of life Assessed with Visual analogue scale Scale from: 0-10 Follow-up: 6 weeks	The mean change in quality of life in the control group was **0.4**[1]	The mean change in quality of life in the intervention group was **2.2 higher** (0.91 higher to 3.49 higher)	-	61 (1 RCT)	⊕⊕◯◯ **LOW**[2,3]	Higher score denotes greater improvement in quality of life. Absolute risk difference 22% (9% to 35% more); relative percentage change 33% (14% to 53% more)
Adverse events Follow-up: 9 months	**Study population**		Not estimable	60 (1 RCT)	⊕⊕◯◯ **LOW**[2,3]	No participant reported any adverse events
	0 per 1000[4]	**0 per 1000** (0 to 0)				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Mean score in placebo group in Ebenbichler 1999 used as assumed control group risk.
[2]Downgraded (-1) for indirectness. Pulsed ultrasound was delivered to participants with calcific tendinitis, so results may not generalise to people receiving continuous ultrasound, or to other patient subgroups.
[3]Downgraded (-1) for imprecision. Sample size was small, with wide 95% CI including effect estimates that are clinically important and unimportant.
[4]Risk in placebo group in Ebenbichler 1999 used as assumed risk.

BACKGROUND

Description of the condition

This review is one in a series of reviews aiming to determine the evidence for efficacy of common interventions for shoulder pain. This series of reviews forms the update of an earlier Cochrane review of physical therapy for shoulder disorders (Green 2003). Since our original review, many new clinical trials studying a diverse range of interventions have been performed. To improve usability of the review, we have subdivided the reviews by type of shoulder disorder as people within different diagnostic groupings may respond variably to different interventions. This review focuses on electrotherapy modalities for rotator cuff disease. A separate review of manual therapy and exercise for rotator cuff disease is under review (Page 2016), and reviews of manual therapy and exercise for adhesive capsulitis (frozen shoulder) (Page 2014a) and electrotherapy modalities for adhesive capsulitis (Page 2014b) were published in 2014.

Shoulder pain is common, with a point prevalence ranging from 7% to 26% in the general population (Luime 2004). Although not life-threatening, it impacts on the performance of tasks essential to daily living, such as dressing, personal hygiene, eating and work, and often results in substantial utilisation of health care resources (Largacha 2006; Mroz 2014; Van der Heijden 1999a; Virta 2012). The most common cause of shoulder pain in primary care is disorders of the rotator cuff (Linsell 2006; Ostor 2005), which comprises the supraspinatus, infraspinatus, subscapularis and teres minor muscles. These muscles facilitate both movement and dynamic stabilisation of the shoulder joint.

Numerous diagnostic labels have been used in the literature to describe disorders of the rotator cuff, for example subacromial impingement syndrome, rotator cuff tendinopathy or tendinitis, partial or full rotator cuff tear, calcific tendinitis and subacromial bursitis, but the terms are not standardised (Schellingerhout 2008). The term 'rotator cuff disease' was proposed as an umbrella term to classify disorders of the rotator cuff, regardless of the cause of disorder (e.g. degeneration or acute injury) and specific anatomical location (Buchbinder 1996; Whittle 2015). Calcific tendinitis is an uncommon form of rotator cuff disease usually applied to people who present with rapid onset of severe shoulder pain, and who have calcium deposits visible in the rotator cuff tendons on imaging. However, the exact pathophysiologic relevance of calcium deposits in the rotator cuff tendons is unclear and while calcium deposition may be seen in as many as 6.8% of people with shoulder pain, in asymptomatic shoulders the prevalence estimates for calcium deposition range from 2% to 20% (Titchener 2014). Rotator cuff disease has been found to increase in prevalence with age (Yamamoto 2010) and in those participating in occupational or sporting activities that require repetitive overhead use of the arms (e.g. swimming, tennis) (Edmonds 2014; Walker 2012). People with rotator cuff disease often describe pain in the upper outer arm exacerbated by certain movements (e.g. overhead activity); the pain is often worse at night and when lying on the affected side. Some people also describe weakness and loss of function. However, there are few data regarding the diagnostic accuracy of individual symptoms in rotator cuff disease without tears (Whittle 2015).

In addition to history-taking and clinical evaluation, the use of physical examination manoeuvres has been recommended for the diagnosis of rotator cuff disease. However there is a wide array of tests and a lack of consensus on the best test or series of tests to use, and varying descriptions of how to execute these tests (Hanchard 2013). Systematic reviews of diagnostic test accuracy studies have found that a positive painful arc test result (pain occurs between 60° and 120° during active abduction of the affected arm) is the most accurate finding for detecting rotator cuff disease, whereas the presence of a positive lag test (external or internal rotation) result was most accurate for diagnosis of a full-thickness rotator cuff tear (Hanchard 2013; Hermans 2013).

Description of the intervention

Electrotherapy modalities (also known as electrophysical agents) are types of physical therapy that aim to reduce pain and improve function via an increase in energy (electrical, sound, light, or thermal) into the body (Watson 2008a; Watson 2010). There are several electrotherapy modalities used in clinical practice, including therapeutic ultrasound, low-level laser therapy (LLLT), transcutaneous electrical nerve stimulation (TENS) and pulsed electromagnetic field therapy (PEMF). The delivery of particular electrotherapy modalities in physical therapy practice has varied over time. Between 1990 and 2010, therapeutic ultrasound delivery increased in several countries, LLLT was used at a consistent rate, and TENS administration increased in the UK but declined in Australia (Shah 2012). People seeking treatment for musculoskeletal conditions seldom receive a single electrotherapy modality in isolation. Other physical therapy interventions such as manual therapy and exercise are commonly delivered as co-interventions (Gebremariam 2014). A brief description of the electrotherapy modalities investigated in this review, and their presumed mechanisms of action, are outlined as follows.

Therapeutic ultrasound delivers energy to deep tissue sites through ultrasonic waves (often at frequencies of 1 or 3 MHz and intensities between 0.1 watts/cm^2 and 3 watts/cm^2) using a crystal sound head. Treatment can be delivered in two forms, continuous (non-stop ultrasonic waves) and pulsed (intermittent ultrasonic waves) (Allen 2006; Watson 2008b). The purpose of treatment is to increase tissue temperature and induce non-thermal physiological changes (such as cell permeability and cell growth), which are believed to promote soft tissue healing and muscle relaxation (O'Brien 2007; Watson 2008b).

Low-level laser therapy (LLLT) generates a beam of light with a particular wavelength which has the potential to deliver light

energy to tissue depths below the dermis (Basford 1989; Bjordal 2010; Peplow 2010). Studies suggest that LLLT contributes to pain relief by reducing pro-inflammatory cytokines and increasing anti-inflammatory growth factors and cytokines (Bjordal 2006; Peplow 2010; Sakurai 2000). The effects of LLLT are considered to be dependent on dosage, wavelength, site and duration of treatment, and researchers have suggested that some previous trials of LLLT with inconclusive findings may have delivered dosages that are below that expected to achieve a biological response (Bjordal 2006; Bjordal 2010).

Transcutaneous electrical nerve stimulation (TENS) delivers electrical stimulation via electrodes placed over the intact skin surface near the source of pain to activate underlying nerves (Jones 2009; Sluka 2003). Several types of TENS applications exist; the most common are conventional TENS (high frequency and low intensity, which is sufficient to produce a comfortable tingling sensation) and acupuncture-like TENS (low frequency and high intensity, which is sufficient to elicit muscle twitching) (Johnson 2008). The development of TENS was based on the Gate Control Theory of Pain (Melzack 1965), which suggests that there is a 'gating' mechanism in the dorsal horn of the spinal cord that regulates the amount of incoming painful stimuli via small diameter afferent nerve fibres, and that stimulation of large diameter afferent nerve fibres using other stimuli (such as TENS) can "close the gate" and reduce the perception of pain (Walsh 2009). Evidence from animal studies suggests that TENS reduces ongoing nociceptive cell activity and inhibits pain facilitatory pathways (DeSantana 2008; Jones 2009).

Pulsed electromagnetic field therapy (PEMF) involves the delivery of pulsing (that is 'on-off') low-frequency magnetic fields through the body, which is believed to provide temporary pain relief by influencing tissue generation and cell proliferation (Gordon 2007; Markov 2007).

Continuous short wave diathermy involves delivering a constant stream of short wave (wavelength 3 to 30 m, frequency 10 to 100 MHz) electromagnetic radiation to produce deep heating within tissues (Allen 2006; Shields 2001). The treatment is designed to produce heat at deeper tissue levels than superficial agents (such as a hot pack). The deep tissue heating is believed to induce an increase in metabolic activity, blood flow, collagen extensibility and nerve conduction, which are thought to encourage healing and relieve pain (Allen 2006; Shields 2001).

Interferential current involves crossing two medium frequency currents (most commonly 4000 Hz), which reportedly generates a low-frequency 'beating' (amplitude-modulated) effect at between 0 and 150 Hz in the deep tissues (Beatti 2010). These beat frequencies are believed to decrease pain, increase circulation and block nerve conduction.

Two electrotherapy modalities are designed to facilitate delivery of topical medication through the skin (that is transdermal delivery). Phonophoresis is administered using a therapeutic ultrasound device (Machet 2002; Watson 2008b), and iontophoresis is administered using a low-intensity electrical current (Batheja 2006; Roustit 2014). The therapeutic ultrasound device used in phonophoresis is believed to enhance the absorption of the topically applied medication (Machet 2002). The iontophoretic device is believed to induce electromigration and electro-osmosis, which are thought to facilitate the movement of positively and negatively charged drugs into the skin (Roustit 2014).

Microcurrent electrical stimulation (MENS) is a novel modality that is claimed to be capable of providing beneficial effects through delivering monophasic or biphasic pulsed microamperage currents with intensities between 1 and 999 uA across the skin (Atya 2012).

In our companion review of electrotherapy modalities for adhesive capsulitis (Page 2014b), we found that LLLT was more effective than placebo in the short-term, but there was no high quality evidence to support the use of therapeutic ultrasound, TENS, PEMF, continuous short wave diathermy, interferential current, or Iodex iontophoresis for this condition. It is unclear what effect these modalities have on people with rotator cuff disease.

Why it is important to do this review

The previous version of this review (Green 2003) included 10 trials investigating the efficacy of electrotherapy modalities for rotator cuff disease (Berry 1980; Binder 1984; Downing 1986; Ebenbichler 1999; England 1989; Nykänen 1995; Perron 1997; Saunders 1995; Shehab 2000; Vecchio 1993), and concluded that there was little overall evidence to guide treatment. Many new trials have been published since the 2003 review (as summarised in recent systematic reviews, e.g. Alexander 2010; Gebremariam 2014; Kromer 2009; Nyberg 2010). To best inform current practice, an up-to-date review which incorporates data from the most recently available trials is needed.

OBJECTIVES

To synthesise available evidence regarding the benefits and harms of electrotherapy modalities for the treatment of people with rotator cuff disease.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) of any design (e.g. parallel, cross-over, factorial) and controlled clinical trials using a quasi-randomised method of allocation, such as by alternation or date of birth. We included trials if they reported the methods used to generate the allocation sequence, or if they included a statement such as "random allocation was used". Given that some of these latter, poorly-reported trials may have used a quasi-randomised method of allocation, we considered it reasonable to include quasi-randomised trials that were clearly identified as such. Reports of trials were eligible regardless of the language, date of publication, or publication status.

Types of participants

We included trials that recruited adults (> 16 years of age) with rotator cuff disease as defined by the study authors (e.g. using terminology such as subacromial impingement syndrome, rotator cuff tendinitis or tendinopathy, supraspinatus, infraspinatus or subscapularis tendinitis, calcific tendinitis, subacromial bursitis, or rotator cuff tears), for any duration. We also included trials with participants with non-specific shoulder pain provided that the inclusion/exclusion criteria were compatible with a diagnosis of rotator cuff disease. If trials included participants with either rotator cuff disease or adhesive capsulitis, we attempted to retrieve the data for rotator cuff disease participants from the trialists. If unsuccessful, we included the trial only if > 75% of participants had rotator cuff disease. We excluded trials that included any participants with a history of significant trauma or systemic inflammatory conditions such as rheumatoid arthritis, osteoarthritis, hemiplegic shoulders, or pain in the shoulder region as part of a complex myofascial neck/shoulder/arm pain condition.

Types of interventions

We included RCTs comparing any electrotherapy modality to placebo, no treatment, a different electrotherapy modality, or any other intervention. We included RCTs where an electrotherapy modality was used as an adjunct to another treatment only if the comparison provided information on the additional effect of the electrotherapy modality. Electrotherapy modalities included therapeutic ultrasound, laser therapy, transcutaneous electrical nerve stimulation, pulsed electromagnetic field therapy, bipolar interferential current, electromyographic biofeedback, phonophoresis, iontophoresis, and short wave diathermy. Physical therapy interventions such as exercise, mobilisation, massage and manipulation were excluded and are included in a separate Cochrane review.

Types of outcome measures

We did not consider outcomes as part of the eligibility criteria.

Main outcomes

- Overall pain (mean or mean change measured by visual analogue scale (VAS), numerical or categorical rating scale).
- Function. Where trialists reported outcome data for more than one function scale, we extracted data on the scale that was highest on the following pre-defined list:
    - Shoulder Pain and Disability Index (SPADI);
    - Croft Shoulder Disability Questionnaire;
    - Constant-Murley Score;
    - any other shoulder-specific function scale.
- Pain on motion measured by VAS, numerical or categorical rating scale.
- Global assessment of treatment success as defined by the trialists (e.g. proportion of participants with significant overall improvement).
- Quality of life as measured by generic measures (such as components of the Short Form-36 (SF-36)) or disease-specific tools.
- Number of participants experiencing any adverse events.

Other outcomes

- Night pain measured by VAS, numerical or categorical rating scale.
- Pain with resisted movement measured by VAS, numerical or categorical rating scale.
- Range of motion (ROM) (e.g. flexion, abduction, external rotation and internal rotation (measured in degrees or other e.g. hand-behind-back distance in centimetres)). Where trialists reported outcome data for both active and passive ROM measures, we extracted the data on active ROM only. We prioritised active ROM because it requires the patient to initiate shoulder movement, and so is a closer proxy to what patients can actually do than passive ROM.
- Strength.
- Work disability.
- Surgery (e.g. surgical decompression, rotator cuff repair).

We extracted efficacy outcome measures (e.g. overall pain, function) at the following time points:

- up to three weeks;
- longer than three and up to six weeks (this was the main time point);
- longer than six weeks and up to six months, and;
- longer than six months.

If data were available in a trial at multiple time points within each of the above periods (e.g. at four, five, and six weeks), we only extracted data at the latest possible time point of each period. We extracted adverse events reported at all time points.

We collated the main results of the review into 'Summary of findings' (SoF) tables which provide key information concerning the quality of evidence and the magnitude and precision of the effect

of the interventions. We included the main outcomes (see above) in the SoF tables, and presented results at, or nearest, the main time point (six weeks).

Search methods for identification of studies

Electronic searches

We searched the Cochrane Central Register of Controlled Trials (CENTRAL; *The Cochrane Library* 2015, Issue 3), Ovid MEDLINE (January 1966 to March 2015), Ovid EMBASE (January 1980 to March 2015), and CINAHL Plus (EBSCOhost, January 1937 to March 2015). The complete search strategies are presented in Appendix 1. Note that the search terms used included clinical terms relevant to adhesive capsulitis and manual therapy and exercise interventions, as the current review and Cochrane reviews of manual therapy and exercise for rotator cuff disease, manual therapy and exercise for adhesive capsulitis, and electrotherapy modalities for adhesive capsulitis were conducted simultaneously.

Searching other resources

We searched for ongoing trials and protocols of published trials in the clinical trials registry that is maintained by the US National Institute of Health (http://clinicaltrials.gov) and the Clinical Trial Registry at the International Clinical Trials Registry Platform of the World Health Organization (http://www.who.int/ictrp/en/). We also reviewed the reference lists of the included trials and any relevant review articles retrieved from the electronic searches, to identify any other potentially relevant trials.

Data collection and analysis

Selection of studies

Two review authors (MJP and BM) independently selected trials for possible inclusion against a predetermined checklist of inclusion criteria (see Criteria for considering studies for this review). We screened titles and abstracts and initially categorised studies into the following groups.

- Possibly relevant - trials that met the inclusion criteria and trials from which it was not possible to determine whether they met the criteria either from their title or abstract.
- Excluded - those clearly not meeting the inclusion criteria.

If a title or abstract suggested that the trial was eligible for inclusion, or we could not tell, we obtained a full-text version of the article and two review authors (MJP and BM) independently assessed it to determine whether it met the inclusion criteria. The review authors resolved discrepancies through discussion or adjudication by a third author (SG or RB).

Data extraction and management

Two review authors (MJP and either MM, BM, SS, JD, or NL) independently extracted data using a standard data extraction form developed for this review. The authors resolved any discrepancies through discussion or adjudication by a third author (SG or RB), until consensus was reached. We pilot tested the data extraction form and modified it accordingly before use. In addition to items for assessing risk of bias and numerical outcome data, we also recorded the following characteristics.

- Trial characteristics, including type (e.g. parallel or cross-over), country, source of funding, and trial registration status (with registration number recorded if available).
- Participant characteristics, including age, sex, duration of symptoms, and inclusion/exclusion criteria.
- Intervention characteristics, including type of manual therapy or exercise, duration of treatment, use of co-interventions.
- Outcomes reported, including the measurement instrument used and timing of outcome assessment.

One author (MJP) compiled all comparisons and entered outcome data into Review Manager (RevMan) 5.3 (RevMan 2014).
For a particular systematic review outcome there may be a multiplicity of results available in the trial reports (e.g. multiple scales, time points and analyses). To prevent selective inclusion of data based on the results (Page 2013), we used the following pre-defined decision rules to select data from trials.

- Where trialists reported analysis of covariance- (ANCOVA) adjusted mean differences along with final values or change from baseline values for the same continuous outcome, we extracted ANCOVA-adjusted mean differences.
- Where trialists reported final values and change from baseline values for the same continuous outcomes, we extracted final values (change from baseline values can be less efficient than final values because measurement of the outcome twice can increase measurement error for outcomes that fluctuate or are difficult to measure precisely (Higgins 2011a)).
- Where trialists reported data analysed based on the intention-to-treat (ITT) sample and another sample (e.g. per-protocol, as-treated), we extracted ITT-analysed data.
- For cross-over RCTs, we extracted data from the first period only.

Where trials did not include a measure of overall pain but included one or more other measures of pain, for the purpose of combining data for the primary analysis of overall pain, we combined overall pain with other types of pain in the following hierarchy: unspecified pain; pain with activity; or daytime pain.

Assessment of risk of bias in included studies

Two review authors (MJP and either MM, BM, SS, JD, or NL) independently assessed the risk of bias in included trials using

The Cochrane tool for assessing risk of bias, as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011b). We assessed the following domains:

- random sequence generation;
- allocation concealment;
- blinding of participants and personnel;
- blinding of outcome assessment (assessed separately for self-reported and objectively assessed outcomes);
- incomplete outcome data;
- selective reporting;
- other sources of bias (for example, baseline imbalance)

Each item was rated as being at 'Low risk', 'Unclear risk' or 'High risk' of bias. We classified the overall risk of bias as low if all domains were at low risk of bias, as high if at least one domain was at high risk of bias, or as unclear if at least one domain was at unclear risk of bias and no domain was at high risk. We assessed the selective reporting domain for all trials, and documented it in the risk of bias tables, but did not consider it in the overall risk of bias judgement if the only types of selective reporting identified were non- or partial reporting of outcomes. Non- or partial reporting of outcomes biases the results of meta-analyses that cannot include the relevant data, not the results of trials, and is therefore considered under the Assessment of reporting biases section (Kirkham 2010). We resolved any discrepancies through discussion or adjudication by a third author (SG or RB).

Measures of treatment effect

We used the Cochrane statistical software, RevMan 5.3 (RevMan 2014), to perform data analysis. We expressed dichotomous outcomes as risk ratios (RRs) with 95% confidence intervals (CIs) and continuous outcomes as mean differences (MDs) with 95% CIs if different trials used the same measurement instrument to measure the same outcome. Alternatively, we analysed continuous outcomes using the standardised mean difference (SMD) when trials measured the same outcome but employed different measurement instruments. To enhance interpretability of dichotomous outcomes, we calculated risk differences and number needed to treat for a beneficial outcome (NNTB) or the number needed to treat for a harmful outcome (NNTH).

Unit of analysis issues

The unit of analysis was the participant for all trials except three (Ebenbichler 1999; Pan 2003; San Segundo 2008), which included participants with bilateral shoulder pain. For these trials, we included the number of shoulders as the denominator in all analyses because the number of participants was not clear. However, only a few participants in both trials had bilateral shoulder pain, so using shoulders as the unit of analysis is likely to have had little impact on the width of the 95% confidence intervals.

Dealing with missing data

When required, we contacted trialists via email (twice, separated by three weeks) to retrieve missing information about trial design, outcome data, or attrition rates such as drop-outs, losses to follow-up and post-randomisation exclusions in the included trials. For continuous outcomes with no standard deviation (SD) reported, we calculated SDs from standard errors (SEs), 95% CIs or P values. If no measures of variation were reported and SDs could not be calculated, we planned to impute SDs from other trials in the same meta-analysis, using the median of the other SDs available (Ebrahim 2013). Where data were imputed or calculated (e.g. SDs calculated from SEs, 95% CIs or P-values, or imputed from graphs or from SDs in other trials) we reported this in the tables of Characteristics of included studies.

Assessment of heterogeneity

We assessed clinical heterogeneity by determining whether the characteristics of participants, interventions, outcome measures and timing of outcome measurement were similar across trials. We assessed statistical heterogeneity using the Chi^2 statistic and the I^2 statistic (Higgins 2002). We interpreted the I^2 statistic using the following as an approximate guide:

- 0% to 40% may not be important heterogeneity;
- 30% to 60% may represent moderate heterogeneity;
- 50% to 90% may represent substantial heterogeneity;
- 75% to 100% may represent considerable heterogeneity

(Deeks 2011).

Assessment of reporting biases

To assess small study effects, we planned to generate funnel plots for meta-analyses including at least 10 trials of varying size. If asymmetry in the funnel plot was detected, we planned to review the characteristics of the trials to assess whether the asymmetry was likely due to publication bias or other factors such as methodological or clinical heterogeneity of the trials (Sterne 2011). To assess outcome reporting bias (non- or partial reporting of a pre-specified outcome, which prevents the inclusion of data in a meta-analysis), we compared the outcomes specified in trial protocols with the outcomes reported in the corresponding trial publications; if trial protocols were unavailable, we compared the outcomes reported in the methods and results sections of the trial publications (Dwan 2011; Kirkham 2010).

Data synthesis

For this review update, we identified a large number of trials, which investigated a diverse range of interventions. To define the most clinically important questions to be answered in the review, after data extraction was completed, one review author (MJP) sent the list of all possible trial comparisons to both of the original primary authors of this review (SG and RB). After reviewing the

list of possible trial comparisons, both of these review authors discussed and drafted a list of clinically important review questions and categorised each trial comparison under the most appropriate review question. This process was conducted iteratively until all trial comparisons were allocated to a single review question, and was conducted without knowledge of the results of any outcomes. They defined the following review questions.

- Are electrotherapy modalities more effective than placebo or no treatment?
- Do electrotherapy modalities provide additional benefit when added to other physical therapy interventions (e.g. manual therapy or exercise (or both))?
- Are electrotherapy modalities more effective than other active interventions (e.g. glucocorticoid injection, oral NSAID)?
- Is one type of electrotherapy modality more effective than another?

As electrotherapy modalities are seldom used in isolation, we considered the first two questions to be the most relevant for clinical practice.

We planned to pool results of trials with similar characteristics (participants, interventions, outcome measures and timing of outcome measurement) to provide estimates of benefit and harm. Provided trials were homogeneous with respect to other parameters, we planned to pool together trials irrespective of the diagnostic label used in individual trials (e.g. subacromial impingement, rotator cuff tendinitis, supraspinatus tendinitis, impingement) except for calcific tendinitis, which we planned to pool separately. We planned to synthesise effect estimates using a random-effects meta-analysis model based on the assumption that clinical and methodological heterogeneity was likely to exist and to have an impact on the results. Where we could not pool data, we presented effect estimates and 95% CIs of each trial in tables and summarised the results in text.

Subgroup analysis and investigation of heterogeneity

We did not undertake any subgroup analyses.

Sensitivity analysis

We planned to perform sensitivity analyses to investigate the robustness of the treatment effect (of main outcomes) to allocation concealment and participant blinding, by removing the trials that reported inadequate or unclear allocation concealment and lack of participant blinding from the meta-analysis to see if this changed the overall treatment effect.

Summary of findings tables

We presented the results of the most important comparisons of the review in 'Summary of findings' tables, which summarise the quality of evidence, the magnitude of effect of the interventions examined and the sum of available data on outcomes, as recommended by Cochrane (Schünemann 2011a). The 'Summary of findings' tables include an overall grading of the evidence related to each of the main outcomes, using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation Working Group) approach (Schünemann 2011b).

In the Comments column of the 'Summary of findings' table, we have reported the absolute per cent difference, the relative per cent change from baseline and the NNTB (the NNTB is provided only when the outcome shows a statistically significant difference).

For dichotomous outcomes (global assessment of treatment success, adverse events), we calculated the absolute risk difference using the risk difference statistic in RevMan (RevMan 2014), and expressed the result as a percentage; we calculated the relative per cent change as the risk ratio - 1 and expressed it as a percentage.

For continuous outcomes (overall pain, function, pain on motion, quality of life), we calculated the absolute risk difference as the improvement in the intervention group minus the improvement in the control group, expressed in the original units (i.e. mean difference from RevMan divided by units in the original scale), and expressed it as a percentage. The relative per cent change we calculated as the absolute change (or mean difference) divided by the baseline mean of the control group, expressed as a percentage.

In addition to the absolute and relative magnitude of effect provided in the 'Summary of findings' table, for dichotomous outcomes we calculated the NNTB or NNTH from the control group event rate and the risk ratio using the Visual Rx NNT calculator (Cates 2004). For continuous outcomes of function and overall pain, we calculated the NNTB using Wells calculator software, which is available at Cochrane Musculoskeletal editorial office (http://musculoskeletal.cochrane.org). We assumed a minimal clinically important difference (MCID) of 1.5 points on a 10-point scale (or 15 points on a 100-point scale) for pain (Hawker 2011), and 10 points on a 100-point scale for function or disability (for example SPADI, Constant-Murley, Disabilities of the Arm, Shoulder and Hand (DASH)) for input into the calculator (Angst 2011; Roy 2009; Roy 2010).

RESULTS

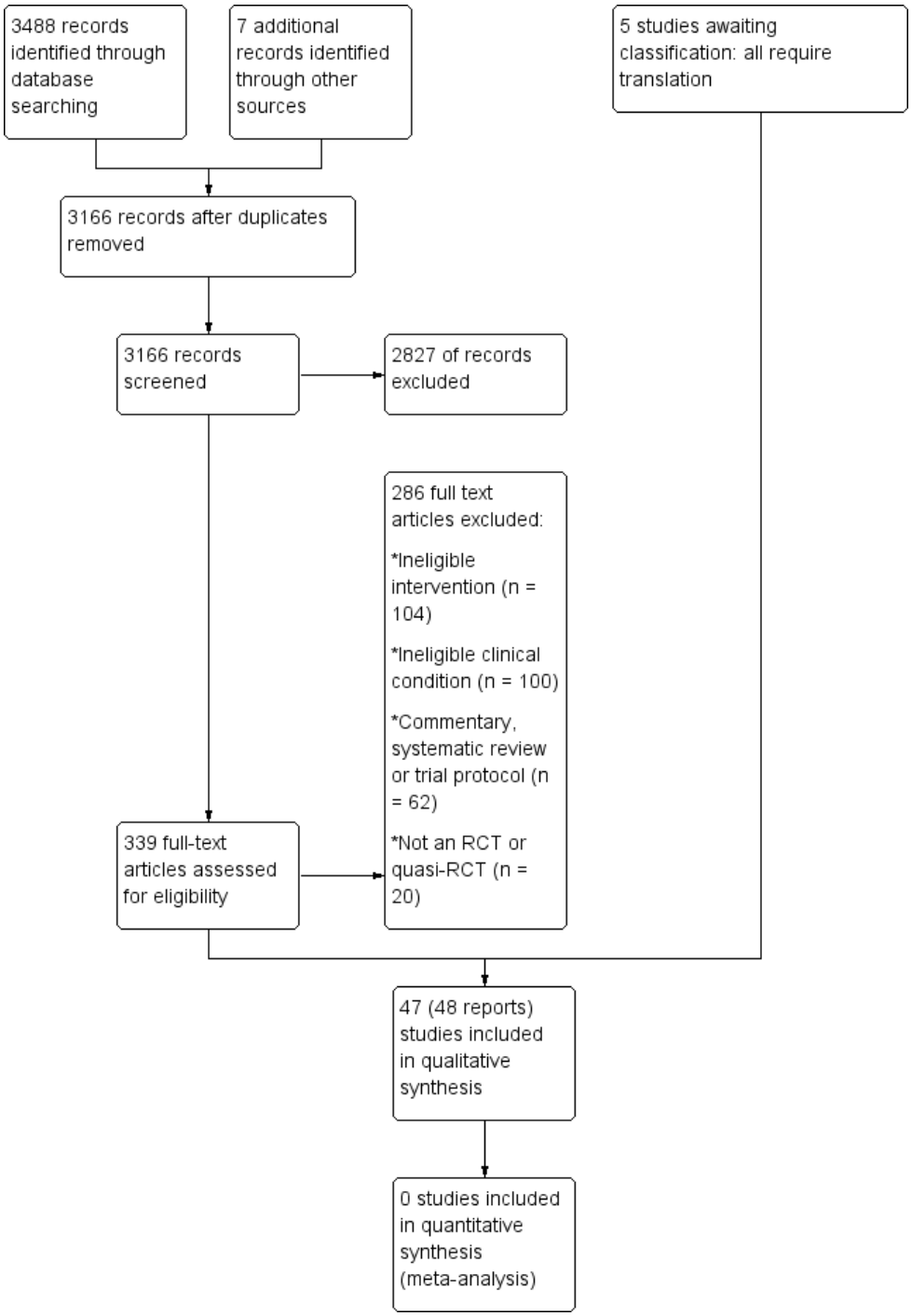
Description of studies

Results of the search

The search conducted up to March 2015 resulted in 3488 records across the four databases. Seven additional records were identified from screening reference lists of previously published systematic reviews and included trials. After removal of duplicates, 3166 unique

records remained. Of these, 339 were retrieved for full-text screening based on the title and abstract. We included 47 trials in the review (Abrisham 2011; Aktas 2007; Akyol 2012; Al Dajah 2014; Atya 2012; Bal 2009; Bansal 2011; Baskurt 2006; Berry 1980; Binder 1984; Bingöl 2005; Calis 2011; Celik 2009; Chard 1988; Clews 1987; Dogan 2010; Downing 1986; Ebenbichler 1999; England 1989; Eslamian 2012; Eyigor 2010; Galace de Freitas 2014; Giombini 2006; Grymel-Kulesza 2007; Johansson 2005; Kelle 2014; Kocyigit 2012; Korkmaz 2010; Kurtai Gursel 2004; Leduc 2003; Montes-Molina 2012a; Montes-Molina 2012b; Nykänen 1995; Otadi 2012; Ozgen 2012; Pan 2003; Perron 1997; Polimeni 2003; Rabini 2012; San Segundo 2008; Santamato 2009; Saunders 1995; Shehab 2000; Vecchio 1993; Yavuz 2014; Yeldan 2009; Yildirim 2013). Five additional trials, all of which require translation, are awaiting classification (Dal Conte 1990; Gudmundsen 1987; Güler 2009; Jiménez-García 2008; Knorre 1990; see table of Characteristics of studies awaiting classification). A flow diagram of the study selection process is presented in Figure 1.

Figure 1. Study flow diagram



Included studies

A full description of all included trials is provided in the Characteristics of included studies tables.

Design

All trials except one were described as RCTs (Kelle 2014 was a quasi-RCT), and all used a parallel-group design. Thirty-nine trials included two intervention arms (Abrisham 2011; Aktas 2007; Akyol 2012; Al Dajah 2014; Atya 2012; Bal 2009; Bansal 2011; Binder 1984; Bingöl 2005; Celik 2009; Chard 1988; Dogan 2010; Downing 1986; Ebenbichler 1999; Eslamian 2012; Eyigor 2010; Galace de Freitas 2014; Grymel-Kulesza 2007; Johansson 2005; Kocyigit 2012; Korkmaz 2010; Kurtai Gursel 2004; Leduc 2003; Montes-Molina 2012a; Montes-Molina 2012b; Nykänen 1995; Otadi 2012; Ozgen 2012; Pan 2003; Perron 1997; Rabini 2012; San Segundo 2008; Santamato 2009; Saunders 1995; Shehab 2000; Vecchio 1993; Yavuz 2014; Yeldan 2009; Yildirim 2013), six included three arms (Baskurt 2006; Calis 2011; Clews 1987; England 1989; Giombini 2006; Kelle 2014), one included four arms (Polimeni 2003) and one included five arms (Berry 1980).

Participants

A total of 2388 participants were included in the 47 trials, and the number of participants per trial ranged from 18 to 200. The median of the mean age of participants was 53 (interquartile range (IQR) 49 to 55) years, and the median of the mean duration of symptoms was 8 (IQR 6 to 13) months. Women comprised 67% of the total sample. Diagnostic labels used by trialists included subacromial impingement syndrome (n = 16: Aktas 2007; Akyol 2012; Al Dajah 2014; Atya 2012; Bal 2009; Baskurt 2006; Calis 2011; Celik 2009; Dogan 2010; Galace de Freitas 2014; Johansson 2005; Kelle 2014; Kocyigit 2012; Yavuz 2014; Yeldan 2009; Yildirim 2013), rotator cuff tendinitis (n = 10: Abrisham 2011; Berry 1980; Binder 1984; Chard 1988; Clews 1987; Eslamian 2012; Eyigor 2010; Otadi 2012; Rabini 2012; Vecchio 1993), supraspinatus tendinitis (n = 10: Bansal 2011; Downing 1986; England 1989; Giombini 2006; Korkmaz 2010; Nykänen 1995; Ozgen 2012; Polimeni 2003; Saunders 1995; Shehab 2000), calcific tendinitis (n = 4: Ebenbichler 1999; Leduc 2003; Pan 2003; Perron 1997), or a mixture of labels (i.e. some participants with impingement, others with tendinitis) (n = 5: Grymel-Kulesza 2007; Kurtai Gursel 2004; Montes-Molina 2012a; Montes-Molina 2012b; San Segundo 2008). However, there were inconsistencies in the diagnostic criteria for (or definitions of) each of the conditions (see Characteristics of included studies tables).

One trial (Bingöl 2005) included participants with non-specific shoulder pain that was compatible with a diagnosis of rotator cuff disease. One trial (Montes-Molina 2012a) included participants with rotator cuff disease or adhesive capsulitis, but participants with the latter condition comprised only 5% of the sample. Trials were conducted in Turkey (n = 17), United Kingdom (n = 6), Italy (n = 4), Iran and Spain (n = 3 each), Canada (n = 2), Australia, Austria, Brazil, Egypt, Finland, India, Kuwait, Poland, Saudi Arabia, Sweden, Taiwan, and USA (n = 1 each).

Interventions and Comparisons

A detailed description of the interventions delivered in each trial is presented in the Characteristics of included studies tables, and a summary of the intervention components across trials is presented in Table 1. The trials evaluated physical therapy interventions comprising therapeutic ultrasound (n = 21 trials: Al Dajah 2014; Bansal 2011; Berry 1980; Calis 2011; Celik 2009; Clews 1987; Downing 1986; Ebenbichler 1999; Giombini 2006; Grymel-Kulesza 2007; Johansson 2005; Kurtai Gursel 2004; Nykänen 1995; Ozgen 2012; Perron 1997; Polimeni 2003; San Segundo 2008; Santamato 2009; Shehab 2000; Yavuz 2014; Yildirim 2013), LLLT (n = 14 trials: Abrisham 2011; Bal 2009; Bingöl 2005; Calis 2011; Dogan 2010; England 1989; Eslamian 2012; Kelle 2014; Montes-Molina 2012a; Otadi 2012; Saunders 1995; Vecchio 1993; Yavuz 2014; Yeldan 2009), TENS (n = 8 trials: Baskurt 2006; Eyigor 2010; Grymel-Kulesza 2007; Kocyigit 2012; Korkmaz 2010; Ozgen 2012; Pan 2003; Shehab 2000), PEMF (n = 4 trials; Aktas 2007; Binder 1984; Chard 1988; Galace de Freitas 2014), microwave diathermy (n = 2 trials: Akyol 2012; Rabini 2012), acetic acid iontophoresis (n = 2 trials: Leduc 2003; Perron 1997), high intensity laser therapy (Santamato 2009), light therapy (Montes-Molina 2012b) and microcurrent electrical stimulation (MENS) (Atya 2012). Sixteen (34%) trials investigated the effect of an electrotherapy modality delivered in isolation (Al Dajah 2014; Atya 2012; Berry 1980; Binder 1984; Chard 1988; Ebenbichler 1999; England 1989; Giombini 2006; Kocyigit 2012; Montes-Molina 2012a; Montes-Molina 2012b; Pan 2003; Rabini 2012; Santamato 2009; Saunders 1995; Shehab 2000). The median duration of interventions was three weeks (range 1 to 8) with a median of five treatment sessions delivered per week (range 1 to 10) and a median of 10 treatment sessions provided in total across the treatment period (range 1 to 56). The dosage (e.g. frequency, intensity) of interventions varied, and several trial reports did not include important components such as the duration of each treatment session (Table 1).

Comparators were also diverse, including placebo (Atya 2012; Berry 1980; Binder 1984; Ebenbichler 1999; England 1989; Galace de Freitas 2014; Kocyigit 2012; Saunders 1995), no intervention (Perron 1997), manual therapy (Al Dajah 2014; Bansal 2011; Clews 1987), exercise (Giombini 2006), glucocorticoid injection (Berry 1980; Eyigor 2010; Kelle 2014; Rabini 2012), acupuncture (Berry 1980; Johansson 2005), oral NSAID (England 1989), extracorporeal shock wave treatment (Pan 2003), sodium hyaluronate injection (Ozgen 2012), hot pack (Baskurt 2006) and

cryotherapy (Grymel-Kulesza 2007).

Twenty-two trials investigated whether there is benefit in adding an electrotherapy modality to another physical therapy intervention (Abrisham 2011; Aktas 2007; Akyol 2012; Bal 2009; Baskurt 2006; Bingöl 2005; Calis 2011; Celik 2009; Clews 1987; Dogan 2010; Downing 1986; Eslamian 2012; Galace de Freitas 2014; Kelle 2014; Kurtai Gursel 2004; Leduc 2003; Nykänen 1995; Otadi 2012; Polimeni 2003; San Segundo 2008; Vecchio 1993; Yeldan 2009).

Twelve trials compared one type of electrotherapy modality with another (Binder 1984; Calis 2011; Chard 1988; Giombini 2006; Korkmaz 2010; Montes-Molina 2012a; Montes-Molina 2012b; Polimeni 2003; Santamato 2009; Shehab 2000; Yavuz 2014; Yildirim 2013).

Outcomes

The outcomes measured in each trial are summarised in Table 2. Of the main outcomes, most trials included a measure of overall pain (n = 40) and function (n = 33), but fewer trials included measures of pain on motion (n = 15), global assessment of treatment success (n = 10), quality of life (n = 5) or adverse events (n = 19). Overall pain was most commonly measured using a zero to 10 or zero to 100 VAS, although several different descriptors for the maximum score on the scale (e.g. "worst imaginable pain", "severe pain", "intolerable pain") were noted. Function was most commonly measured using the Constant-Murley Score (n = 15) or SPADI (n = 7). Of the other outcomes, most trials included measures of range of motion (n = 26), but fewer included measures of night pain (n = 16), pain with resisted movement (n = 5), strength (n = 10), work disability (n = 1) or surgery (n = 1).

Excluded studies

We excluded 286 full-text articles. Many of these had been retrieved for possible inclusion in one of the other three reviews in this series (i.e. investigated effects of manual therapy and exercise for rotator cuff disease or adhesive capsulitis, or electrotherapy modalities for adhesive capsulitis). The reasons for exclusion were that the intervention was ineligible (n = 104), the clinical condition was ineligible (n = 100), the article was a commentary, systematic review or trial protocol (n = 62), or the study was not an RCT or quasi-RCT (n = 20). We have listed in the table of Characteristics of excluded studies seven studies which required full-text screening by a third author (the full list of 286 excluded studies is available on request).

Risk of bias in included studies

A summary of the risk of bias in included trials is presented in Figure 2 and Figure 3.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

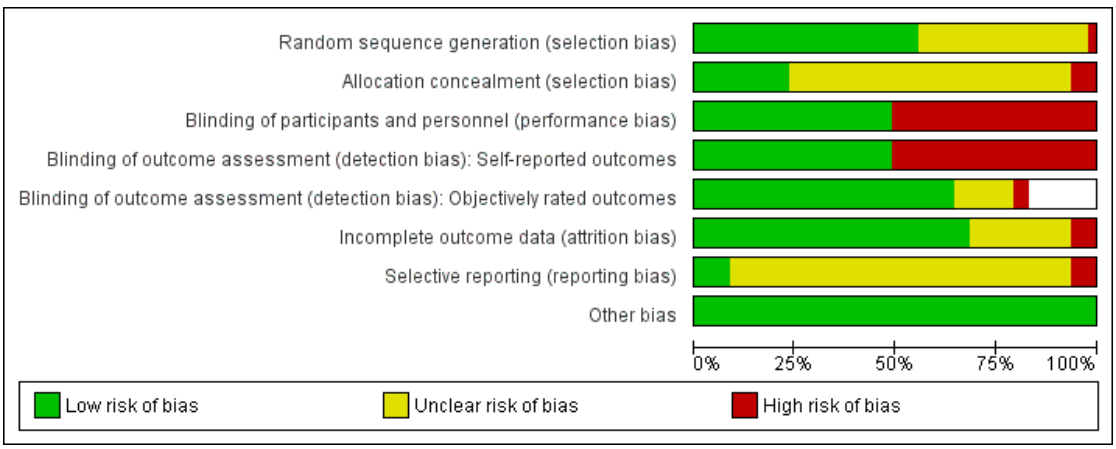
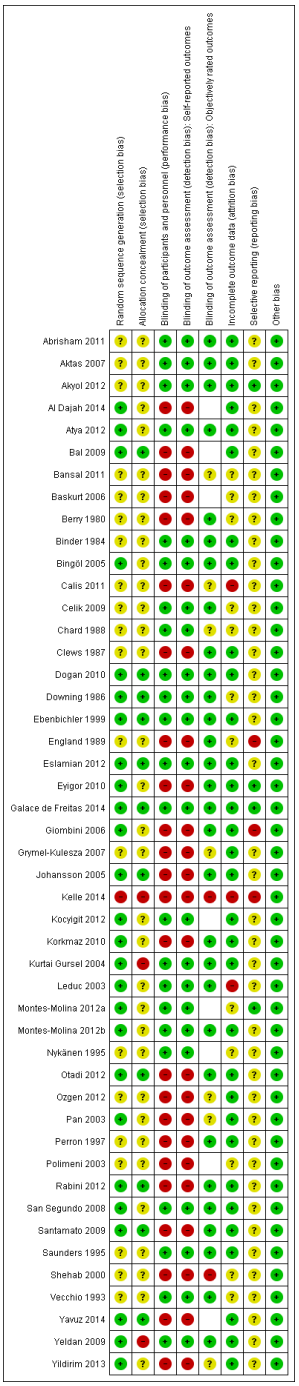


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

The method used to generate and conceal the allocation sequence was reported in 26 (55%) and 11 (23%) trials, respectively. Only 11 (23%) trials used appropriate methods to both generate and conceal the allocation sequence, and so were rated at low risk of allocation bias. We rated three (6%) trials at high risk of allocation bias because the allocator was aware of the randomisation scheme. In 20 (43%) trials the method of sequence generation was not reported and in 33 (70%) trials the method of allocation concealment was not reported. The risk of allocation bias in these trials was therefore unclear.

Blinding

We rated 23 (49%) trials at low risk of performance bias because participants were successfully blinded. We rated the remaining 24 (51%) trials at high risk of performance bias. Participants in these trial were not blinded, and their beliefs about the intervention they received may have influenced them to deviate from the interventions as planned.

Self-reported outcomes were measured in all trials. We rated 23 (49%) trials at low risk of detection bias because it was clear that participants were blinded, and the remaining 24 (51%) trials at high risk of detection bias for self-reported outcomes because participants were not blinded. Of 39 trials with outcome measures that were objectively rated (e.g. range of motion, strength), blinding of outcome assessors was reported in 30 (77%) trials and thus we rated these trials at low risk of detection bias for objective outcomes. In two (5%) trials there was no blinding of assessors of objective outcomes, so the risk of detection bias for objective outcomes was high. In seven (18%) trials it was unclear whether such blinding was done, so the risk of detection bias for objective outcomes was unclear.

Incomplete outcome data

Thirty-two (68%) trials either had no dropouts, losses to follow-up or exclusions, or had a small amount of attrition that was deemed unlikely to bias the results. In three (6%) trials there was differential dropout across groups, with reasons that appeared to be related to the treatments received, and thus we rated these trials at high risk of attrition bias. In the remaining 12 (26%) trials the quantity of or reasons for incomplete outcome data were not reported so the risk of attrition bias was unclear.

Selective reporting

We rated four (9%) trials at low risk of selective reporting bias because all outcomes specified in the trial registry entry or trial protocol were fully reported in the trial publication, or all outcomes of importance for rotator cuff disease were reported. We rated three (6%) trials at high risk of selective reporting bias because some of the outcomes that were reported in the trial registry entry or protocol were not reported at all in the results section. We rated the remaining 40 (85%) trials at unclear risk of selective reporting bias for one of two reasons. Firstly, outcome data were completely reported for all outcomes specified in the methods section of the publication, but none of these trials was registered in a trials registry or had an available trial protocol, so it was unclear whether other outcomes were measured but not reported based on the results; or secondly, outcome data were incompletely reported (e.g. reporting means without measures of variation), but it was unclear whether data were incompletely reported based on the nature of the results or because of poor reporting in general (many trials were published before the introduction of reporting guidelines).

Other potential sources of bias

All trials were rated as being free from other potential sources of bias.

Effects of interventions

See: **Summary of findings for the main comparison** Therapeutic ultrasound compared to placebo for rotator cuff disease

Summary data and effect estimates (with 95% CIs) for all trials are presented in the Additional tables section. If an outcome is not referred to within a sub-section or table, then no data for that outcome was available in the trial(s).

Therapeutic ultrasound

Is therapeutic ultrasound more effective than placebo or no treatment?

In two trials (85 participants), one at high (Berry 1980) and one at low (Ebenbichler 1999) risk of bias overall, therapeutic ultrasound was compared with placebo (i.e. application of an inactive ultrasound device) (Table 3). Ebenbichler 1999 restricted inclusion to patients with calcific tendinitis therefore data were not pooled.

Details of the ultrasound were as follows: 0.89 MHz frequency, 2.5 W/cm^2 intensity for 15 minutes, three to five times a week for six weeks in Ebenbichler 1999; in Berry 1980, frequency and intensity were not reported, but duration was twice a week for four

weeks. The only outcomes measured in both trials were overall pain and global treatment success.

Berry 1980 found no statistically significant differences between ultrasound for four weeks and placebo in overall pain (mean 41.2 versus 22 on a 100-point scale, MD 19.20, 95% CI -7.08 to 45.48, 24 participants), global treatment success (50% (6/12) versus 75% (9/12), RR 0.67, 95% CI 0.35 to 1.28, 24 participants) or shoulder abduction (mean 95.6 versus 120.8 degrees, MD -25.20, 95% CI -52.23 to 1.83, 24 participants) at four weeks, but the 95% CIs were very wide. The trialists did not report measuring adverse events. We downgraded by one point for high risk of performance bias in this trial (there were additional treatment arms other than ultrasound and placebo, which may have led participants to have different expectations about the treatment they were receiving), and one point for imprecision, and so consider this evidence to be low quality.

Ebenbichler 1999 found clinically important differences favouring therapeutic ultrasound over placebo at six weeks in terms of overall pain (mean change -14.9 versus -6.3 on a 52-point scale, MD -8.60, 95% CI -13.48 to -3.72, 61 participants), function (mean change 17.8 versus 3.7 on a 100-point scale, MD 14.10, 95% CI 5.39 to 22.81, 61 participants), global treatment success (91% (29/32) versus 52% (15/29), RR 1.75, 95% CI 1.21 to 2.53, 61 participants) and quality of life (mean change 2.6 versus 0.4 on a 10-point scale, MD 2.20, 95% CI 0.91 to 3.49, 61 participants). Between-group differences were not important at nine months for overall pain (mean change -13.7 versus -11.3 on a 52-point scale, MD -2.40, 95% CI -9.09 to 4.29, 56 participants), function (mean change 15.7 versus 12.4 on a 100-point scale, MD 3.30, 95% CI -6.69 to 13.29, 56 participants), global treatment success (77% (24/31) versus 56% (14/25), RR 1.38, 95% CI 0.93 to 2.05, 56 participants) and quality of life (mean change 2.4 versus 1.9 on a 10-point scale, MD 0.50, 95% CI -1.05 to 2.05, 56 participants). Night pain was measured, but no data were reported. No participant reported adverse events (see Summary of findings for the main comparison). We downgraded by one point for imprecision and one point for indirectness, as pulsed ultrasound was delivered to participants with calcific tendinitis, so results may not generalise to participants receiving continuous ultrasound, or to other participant subgroups. We therefore consider this evidence to be low quality.

Does therapeutic ultrasound provide additional benefits over other physical therapy interventions (e.g. manual therapy or exercise (or both)) alone?

Eight trials (277 participants) examined whether there is benefit in adding therapeutic ultrasound to another physical therapy intervention (e.g. manual therapy, exercise, TENS, interferential current, ice or multi-modal physical therapy) (Calis 2011; Celik 2009; Clews 1987; Downing 1986; Kurtai Gursel 2004; Nykänen 1995; Polimeni 2003; San Segundo 2008) (Table 4). The overall risk of bias was high in four trials (Calis 2011; Clews 1987; Kurtai Gursel 2004; Polimeni 2003) and unclear in four trials (Celik 2009; Downing 1986; Nykänen 1995; San Segundo 2008). Due to the variation in comparators, we did not perform any meta-analyses of the data.

Apart from one unblinded trial which found less overall pain at three weeks in the 'add-on' group (Calis 2011), therapeutic ultrasound did not confer additional clinically important benefits compared with other physical therapy interventions alone in the remaining five trials that measured overall pain (Celik 2009; Downing 1986; Kurtai Gursel 2004; Nykänen 1995; San Segundo 2008), seven trials that measured function (Calis 2011; Celik 2009; Downing 1986; Kurtai Gursel 2004; Nykänen 1995; Polimeni 2003; San Segundo 2008) two trials that measured pain on motion (Calis 2011; Kurtai Gursel 2004), one trial that measured global treatment success (Downing 1986), two trials that measured night pain (Calis 2011; San Segundo 2008), four trials that measured range of motion (Calis 2011; Celik 2009; Downing 1986; Kurtai Gursel 2004), or one trial that measured strength (Clews 1987).

None of the trials reported measuring adverse events.

We downgraded the evidence in these eight trials by one point for high or unclear risk of bias overall, and one point for imprecision, and so consider it to be low quality.

Is therapeutic ultrasound more effective than other active interventions (for example, glucocorticoid injection, oral non-steroidal anti-inflammatory drug (NSAID))?

Trials compared therapeutic ultrasound with:

- manual therapy (3 trials, 82 participants: Al Dajah 2014; Bansal 2011; Clews 1987);
- glucocorticoid injection (1 trial, 24 participants: Berry 1980);
- glucocorticoid injection plus oral tolmetin sodium (1 trial, 24 participants: Berry 1980);
- supervised and home pendular movement and stretching exercises (1 trial, 23 participants: Giombini 2006);
- and acupuncture (2 trials, 109 participants: Berry 1980; Johansson 2005)

See Table 5. The overall risk of bias was high in all trials due to the lack of participant blinding.

There were no clinically important differences in overall pain (i.e. > 1.5 on a 10-point scale (Hawker 2011)) between therapeutic ultrasound and:

- one session of soft tissue mobilisation and proprioceptive neuromuscular facilitation immediately post-treatment (mean 5.23 versus 3.8 on a 10-point scale, MD 1.43, 95% CI 0.89 to 1.97, 30 participants, Al Dajah 2014);
- deep friction massage daily for 10 days, at 10 days (mean 2.1 versus 1.4 on a 10-point scale, MD 0.7, 95% CI not estimable, 40 participants, Bansal 2011);

- massage daily for three days, at three days (mean 3.2 versus 2.8 on a 10-point scale, MD 0.40, 95% CI -0.96 to 1.76, 12 participants, Clews 1987);
- a single glucocorticoid injection, at 4 weeks (mean 41.2 versus 26.6 on a 100-point scale, MD 14.60, 95% CI -9.71 to 38.91, 24 participants, Berry 1980);
- a single glucocorticoid injection plus oral tolmetin sodium daily for four weeks, at four weeks (mean 41.2 versus 29.2 on a 100-point scale, MD 12.00, 95% CI -12.86 to 36.86, 24 participants, Berry 1980);
- supervised and home pendular movement and stretching exercises weekly for four weeks, at four weeks (mean 5.8 versus 5.3 on a 10-point scale, MD 0.50, 95% CI -0.17 to 1.17, 23 participants, Giombini 2006), and;
- acupuncture weekly for four weeks, at four weeks (mean 41.2 versus 34.1 on a 100-point scale, MD 7.10, 95% CI -18.70 to 32.90, 24 participants, Berry 1980).

Function was measured in only two trials, and was similar between groups receiving therapeutic ultrasound and:
- supervised and home pendular movement and stretching exercises at four weeks (mean 60 versus 61.2 on a 100-point scale, MD -1.20, 95% CI -4.31 to 1.91, 23 participants, Giombini 2006) and 10 weeks (mean 61.75 versus 63.27 on a 100-point scale, MD -1.52, 95% CI -5.57 to 2.53, 23 participants, Giombini 2006), and;
- acupuncture at six weeks (mean 76 versus 79 on a 100-point scale, MD -3.00, 95% CI -7.29 to 1.29, 85 participants, Johansson 2005) and 12 months (mean 85 versus 88 on a 100-point scale, MD -3.00, 95% CI -8.75 to 2.75, 85 participants, Johansson 2005).

Adverse events were reported as having been measured in only two of the six trials (Giombini 2006; Johansson 2005) and none were reported by any participant. No important between-group differences in global treatment success (Berry 1980; Giombini 2006), range of motion (Al Dajah 2014; Bansal 2011; Berry 1980) or strength (Clews 1987) were found.
We downgraded the evidence in these trials by two points for high risk of performance and detection bias, and one point for imprecision, and thus consider it to be very low quality.

Low-level laser therapy (LLLT)

Is LLLT more effective than placebo or no treatment?

In two trials (44 participants), both at unclear risk of bias overall, LLLT was compared with placebo (i.e. application of an inactive laser) (England 1989; Saunders 1995) (Table 6). The dosage of LLLT differed slightly between the trials; in England 1989, LLLT consisted of 904 nm wavelength, 10 W power, 4000 Hz frequency, intensity not reported, for five minutes, three times a week for two weeks, while in Saunders 1995, LLLT consisted of 820 nm wavelength, 40 mW power, 5000 Hz frequency, 30 J/cm^2 intensity, for three minutes, three times a week for three weeks. Different outcomes were measured in each trial so no meta-analyses were possible.
There were favourable effects of LLLT in both trials with respect to overall pain (median difference 2.5 on a 10-point scale, 95% CI 2.01 to 3.00, 20 participants), function (median difference 1.5 on a 10-point scale, 95% CI -0.01 to 3.99, 20 participants), active shoulder abduction (median difference 20 degrees, 95% CI 10.00 to 40.00, 20 participants), flexion (median difference 15 degrees, 95% CI 5.00 to 29.00, 20 participants) and extension (median difference 6 degrees, 95% CI 0.00 to 20.00, 20 participants) at two weeks, and pain relief (83% (10/12) versus 42% (5/12), RR 2.00, 95% CI 0.98 to 4.09, 24 participants) and strength (MD 46.46, 95% CI 18.69 to 74.23; force (N); 24 participants) at three weeks.
Neither trial reported measuring adverse events.
We considered the evidence from these two trials to be low quality after downgrading by one point for unclear risk of allocation bias, and one point for imprecision.

Does LLLT provide additional benefits over other physical therapy interventions alone?

Ten trials (520 participants) examined whether there is benefit in adding LLLT to another physical therapy intervention (Abrisham 2011; Bal 2009; Bingöl 2005; Calis 2011; Dogan 2010; Eslamian 2012; Kelle 2014; Otadi 2012; Vecchio 1993; Yeldan 2009) (Table 7). The control group received exercise in all trials except for Eslamian 2012, which added LLLT to therapeutic ultrasound plus TENS plus exercise, and Otadi 2012, which added LLLT to therapeutic ultrasound plus exercise. The overall risk of bias was low in two trials (Dogan 2010; Eslamian 2012), unclear in three trials (Abrisham 2011; Bingöl 2005; Vecchio 1993) and high in five trials (Bal 2009; Calis 2011; Kelle 2014; Otadi 2012; Yeldan 2009). The use of different measurement instruments and mixture of final values and change from baseline values across the trials prevented meta-analysis of data.
Of the nine trials that measured overall pain, only one (Eslamian 2012) found that LLLT conferred clinically important benefits when added to therapeutic ultrasound and exercise (at six weeks). Of the eight trials that measured function, only two (Eslamian 2012; Otadi 2012) found that LLLT conferred additional clinically important benefits over other physical therapy interventions alone (at four to six weeks).
Adverse events were reported as having been measured in seven of the 10 trials (Abrisham 2011; Bal 2009; Bingöl 2005; Dogan 2010; Kelle 2014; Vecchio 1993; Yeldan 2009), and none were reported by any participant.
Clinically important differences favouring the 'LLLT add-on' group were found in two of the four trials measuring pain on mo-

tion, and one of the four trials measuring night pain. However these positive results were only found in trials at high overall risk of bias. LLLT did not confer clinically important benefits over the other physical therapy intervention in the one trial that measured global treatment success (Bal 2009), any of the seven trials that measured range of motion (Abrisham 2011; Bingöl 2005; Calis 2011; Dogan 2010; Eslamian 2012; Vecchio 1993; Yeldan 2009), or the single trial that measured strength (Yeldan 2009).

We considered the evidence from these nine trials to be low quality after downgrading by one point for high or unclear risk of bias overall in most trials, and by one point for imprecision in all trials.

Is LLLT more effective than other active interventions?

One trial (20 participants), at high risk of bias overall (England 1989), reported favourable effects of LLLT (three times a week for two weeks) over NSAID (naproxen sodium 550 mg twice daily for two weeks) with respect to overall pain (median difference 2 on a 10-point scale, 95% CI 1.00 to 3.50, 20 participants), active shoulder abduction (median difference 20 degrees, 95% CI 10.00 to 40.00, 20 participants), flexion (median difference 14.99 degrees, 95% CI 5.00 to 30.00, 20 participants) and extension (median difference 10 degrees, 95% CI 0.00 to 20.00, 20 participants) at two weeks (Table 8). However, function was reported as not significantly different between groups. The evidence was downgraded by two points for high risk of performance and detection bias, and one point for imprecision, and so is considered to be very low quality.

One trial (90 participants), at high risk of bias overall (Kelle 2014) reported no clinically important differences between LLLT (three times a week for three weeks) plus home exercises and glucocorticoid injection (administered twice, with second injection delivered 10 days after the first) plus home exercises with respect to rest pain at three weeks (mean 11.1 versus 10.0 on a 100-point scale, MD 1.10, 95% CI -3.63 to 5.83, 90 participants) and six months (mean 11.5 versus 8.9 on a 100-point scale, MD 2.60, 95% CI -2.45 to 7.65, 90 participants), function at three weeks (mean 25.9 versus 27.4 on a 33-point scale, MD -1.50, 95% CI -3.30 to 0.30, 90 participants) and six months (mean 26.1 versus 26.8 on a 33-point scale, MD -0.70, 95% CI -2.97 to 1.57, 90 participants), or pain on motion at three weeks (mean 32.6 versus 23.6 on a 100-point scale, MD 9.00, 95% CI 2.13 to 15.87, 90 participants) and six months (mean 25.5 versus 22.1 on a 100-point scale, MD 3.40, 95% CI -4.38 to 11.18, 90 participants).

No participant in the Kelle 2014 trial reported adverse events, while England 1989 did not report measuring adverse events.

We downgraded by two points for high risk of performance and detection bias, and one point for imprecision, and so consider this evidence to be very low quality.

Transcutaneous electrical nerve stimulation (TENS)

Is TENS more effective than placebo or no treatment?

Only one trial (20 participants), at unclear risk of bias overall, compared TENS to placebo (i.e. application of an inactive TENS machine) (Kocyigit 2012). The trial was conducted as part of an investigation of the effect of shoulder pain on regions of the brain believed to play a role in pain perception (as measured using functional magnetic resonance imaging). The only outcome of interest to our review, overall pain, was lower in the TENS group immediately after one treatment session, but 95% CIs could not be estimated (intervention group mean (range) 34.8 (12 to 68); control group mean (range) 64.5 (38 to 95); 100-point scale; 20 participants). The trialists did not report measuring adverse events. The evidence was downgraded by one point for unclear risk of allocation bias, one point for imprecision and one point for indirectness, and so is considered to be very low quality.

Does TENS provide additional benefits over other physical therapy interventions alone?

One trial (62 participants), at high risk of bias overall (Baskurt 2006), found that one session of TENS plus hot pack resulted in less overall pain than hot pack alone, but the difference was not clinically important (mean 4.67 versus 5.38 on a 10-point scale, MD -0.71, 95% CI -1.41 to -0.01, 62 participants; Table 9). The trialists did not report measuring adverse events. We downgraded by two points for high risk of performance and detection bias, and one point for imprecision, and so consider this evidence to be very low quality.

Is TENS more effective than other active interventions?

Trials have compared TENS with hot pack (one trial, 61 participants: Baskurt 2006), glucocorticoid injection (one trial, 40 participants: Eyigor 2010) and extracorporeal shockwave treatment (one trial, 62 participants: Pan 2003) (Table 10). Pan 2003 restricted inclusion to patients with calcific tendinitis. The overall risk of bias was high in all trials due to lack of participant blinding. Baskurt 2006 found that both one session of TENS and application of a hot pack had similar effects on overall pain (mean 5.36 versus 5.38 on a 10-point scale, MD -0.02, 95% CI -0.72 to 0.68, 61 participants). The trialists did not report measuring adverse events. We downgraded the evidence in this trial by two points for high risk of performance and detection bias, and one point for imprecision, and so consider it to be very low quality.

In Eyigor 2010, clinically important differences favouring a single glucocorticoid injection plus home exercises over TENS plus home exercises (five times a week for three weeks) were found for function at one week (mean 67.6 versus 37.9 on a 100-point scale, MD 29.70, 95% CI 17.59 to 41.81, 40 participants), four weeks (mean 42.5 versus 22.1 on a 100-point scale, MD 20.40, 95% CI 10.91 to 29.89, 40 participants), and 12 weeks (mean 28.5 versus 13.7 on a 100-point scale, MD 14.80, 95% CI 7.03 to 22.57,

40 participants), global treatment success at one week (20% (4/20) versus 70% (14/20), RR 0.29, 95% CI 0.11 to 0.72, 40 participants), and night pain at one week (mean 4.2 versus 2.1 on a 10-point scale, MD 2.10, 95% CI 0.92 to 3.28, 40 participants). Further, statistically significant differences favouring glucocorticoid injection were found for rest pain, pain on motion, night pain at four and 12 weeks, and active shoulder abduction at one, four and 12 weeks, but none of these differences were considered clinically important. Also, nearly all other measures of active range of motion and all measures of quality of life were not significantly different between groups. No participant reported adverse events. We downgraded by two points for high risk of performance and detection bias, and one point for imprecision, and so consider this evidence to be very low quality.

In Pan 2003, clinically important differences favouring extracorporeal shockwave treatment (two sessions delivered over a four-week period) over TENS (three times a week for four weeks) were found for overall pain at four weeks (mean change -1.1 versus -3 on a 10-point scale, MD 1.90, 95% CI 0.82 to 2.98, 62 participants) and 12 weeks (mean change -1.74 versus -4.08 on a 10-point scale, MD 2.34, 95% CI 1.15 to 3.53, 62 participants), and function at four weeks (mean change 9.59 versus 24.21 on a 100-point scale, MD -14.62, 95% CI -20.45 to -8.79, 62 participants) and 12 weeks (mean change 11.86 versus 28.31 on a 100-point scale, MD -16.45, 95% CI -23.04 to -9.86, 62 participants). However, improvement in strength was no different between groups (at four weeks 52% (15/29) versus 64% (21/33), RR 0.81, 95% CI 0.53 to 1.26; at 12 weeks 62% (18/29) versus 70% (23/33), RR 0.89, 95% CI 0.62 to 1.28, 62 participants). None of the participants receiving TENS reported adverse events, whereas 16% (5/32) of participants receiving shockwave treatment reported soreness in the upper arm after treatment (RR 0.11, 95% CI 0.01 to 1.85, 59 participants). This evidence was considered to be very low quality due to the high risk of performance and detection bias (downgraded by two points) and imprecision (downgraded by one point).

Pulsed electromagnetic field (PEMF)

Is PEMF more effective than placebo or no treatment?

PEMF was compared to placebo (application of an inactive PEMF machine) in two trials (75 participants), one at low (Galace de Freitas 2014) and one at unclear risk of bias overall (Binder 1984) (Table 11). The dosage and frequency of administration varied substantially between the trials (five to nine hours every day for eight weeks in Binder 1984; 30 minute sessions, three times a week for three weeks in Galace de Freitas 2014).

Incomplete reporting prevented calculation of 95% CIs in Binder 1984, although effect estimates favouring PEMF were noted with respect to overall pain and range of motion at two and four weeks. Galace de Freitas 2014 found no clinically important differences between groups in overall pain (mean 4.8 versus 6 on a 10-point scale, MD -1.20, 95% CI -2.51 to 0.11, 46 participants), function (mean 40.7 versus 35.6 on a 100-point scale, MD 5.10, 95% CI -1.95 to 12.15, 46 participants), and strength measures at three weeks. Neither trial reported measuring adverse events. We downgraded by one point for unclear risk of allocation bias in one trial (Binder 1984), and one point for imprecision in both trials, and so consider this evidence to be low quality.

Does PEMF provide additional benefits when added to other physical therapy interventions alone?

Two trials (86 participants) examined whether there is benefit in adding PEMF to an exercise programme (Aktas 2007; Galace de Freitas 2014) (Table 12). The overall risk of bias was unclear in one trial (Aktas 2007) and low in the other (Galace de Freitas 2014). Pooling was not possible because of the different timing of outcome assessment (three weeks in Aktas 2007, three months in Galace de Freitas 2014).

No clinically important difference between groups was found in overall pain at three weeks (mean 0.9 versus 0.85 on a 10-point scale, MD 0.05, 95% CI -0.91 to 1.01, 40 participants) and three months (mean 2.7 versus 3.4 on a 10-point scale, MD -0.70, 95% CI -2.46 to 1.06, 46 participants), function at three weeks (mean 72.65 versus 72 on a 100-point scale, MD 0.65, 95% CI -9.02 to 10.32, 40 participants) and three months (mean 52.7 versus 50.4 on a 100-point scale, MD 2.30, 95% CI -4.55 to 9.15, 46 participants), pain on motion (mean 2.7 versus 2.75 on a 10-point scale, MD -0.05, 95% CI -1.52 to 1.42, 40 participants), night pain (mean 0.8 versus 2.25 on a 10-point scale, MD -1.45, 95% CI -3.04 to 0.14, 40 participants) and active range of motion (mean 35.9 versus 36.7 on a 40-point scale, MD -0.80, 95% CI -4.12 to 2.52, 40 participants) at three weeks, and strength measures at three weeks and three months.

Neither trial reported measuring adverse events.

The evidence in these trials was downgraded by one point for unclear risk of allocation bias in one trial, and one point for imprecision, and so is considered to be low quality.

Is PEMF more effective than other active interventions?

We did not find any trials comparing PEMF with another active intervention.

Other electrotherapy modalities: microcurrent electrical stimulation (MENS), microwave diathermy, acetic acid iontophoresis, and multiple modalities

Are other electrotherapy modalities more effective than placebo or no treatment?

One trial (40 participants), at unclear risk of bias overall, compared MENS with placebo (Atya 2012) (Table 13). Participants receiving MENS (three times a week for six weeks) had statistically significantly less overall pain (mean 6 versus 6.8 on a 10-point scale, MD -0.80, 95% CI -1.47 to -0.13, 40 participants) and better function (mean 60.65 versus 67.6 on a 100-point scale, MD -6.95, 95% CI -11.49 to -2.41, 40 participants) at six weeks than participants receiving placebo. However we did not consider these differences to be clinically important. The trialists did not report measuring adverse events. We downgraded by one point for unclear risk of allocation bias, and one point for imprecision, and so consider this evidence to be low quality.

One trial (21 participants), at high risk of bias overall, compared multi-modal electrotherapy (acetic acid iontophoresis plus therapeutic ultrasound) with no treatment in participants with calcific tendinitis (Perron 1997) (Table 14). The trialists found no difference between groups in pain on motion (mean 1.38 versus 1.59 on a five-point scale, MD -0.21, 95% CI -0.95 to 0.53, 21 participants) or passive shoulder abduction (mean 113.18 versus 93.75 degrees, MD 19.43, 95% CI -8.75 to 47.61, 21 participants). The trialists did not report measuring adverse events. The evidence was downgraded to very low quality (downgraded by two points for high risk of performance and detection bias and by one point for imprecision).

Do other electrotherapy modalities provide additional benefits over other physical therapy interventions alone?

Two trials (67 participants) examined whether there is benefit in adding an electrotherapy modality to an exercise programme plus hot pack (Akyol 2012; Leduc 2003). Akyol 2012, which was at unclear risk of bias overall, examined the additional effects of microwave diathermy (Table 15), whereas Leduc 2003, which was also at high risk of bias overall, examined the additional effects of acetic acid iontophoresis in participants with calcific tendinitis (Table 16).

Microwave diathermy (five times a week for three weeks) did not provide clinically important benefits over exercise plus hot pack in terms of overall pain at three weeks (mean change -2.65 versus -2.95 on a 10-point scale, MD 0.30, 95% CI -1.18 to 1.78, 40 participants) and seven weeks (mean change -2.8 versus 2.8 on a 10-point scale, MD 0, 95% CI -1.76 to 1.76, 40 participants), function at three weeks (mean change -48.2 versus -48.85 on a 100-point scale, MD 0.65, 95% CI -1.12 to 2.42, 40 participants) and seven weeks (mean change -49.75 versus -54.2 on a 100-point scale, MD 4.45, 95% CI 2.65 to 6.25, 40 participants), pain on motion at three weeks (mean change -4.05 versus -3.45 on a 10-point scale, MD -0.60, 95% CI -2.34 to 1.14, 40 participants) and seven weeks (mean change -5.1 versus -4.1 on a 10-point scale, MD -1.00, 95% CI -2.68 to 0.68, 40 participants), or quality of life, night pain, active range of motion and strength at three weeks and seven weeks. No participant reported adverse events.

Acetic acid iontophoresis (one to two times a week for six weeks) conferred clinically important benefits over exercise plus hot pack with respect to function at six weeks (mean 23 versus 40 on a 100-point scale, MD -17.00, 95% CI -29.72 to -4.28, 27 participants), but not active range of motion. However, there was a high amount of attrition in this very small trial, which may have biased results in favour of the 'add-on' group. The trialists did not report measuring adverse events.

We downgraded the evidence from these two trials by two points for high risk of attrition bias in one trial and unclear risk of allocation bias in both trials, and one point for imprecision, and thus consider it to be very low quality.

Are other electrotherapy modalities more effective than other active interventions?

Two trials (54 participants), both at high risk of bias overall, compared therapeutic ultrasound plus TENS plus other physical therapy with either cryotherapy (CO_2 vapours at -75 degrees Celsius for three minutes) (Grymel-Kulesza 2007) or sodium hyaluronate injection (one per week for three weeks) plus other physical therapy (Ozgen 2012) (Table 17). In Grymel-Kulesza 2007, night pain at the end of two weeks' treatment was reported by 73% (11/15) of participants receiving cryotherapy but not by any participant receiving therapeutic ultrasound plus TENS (RR 0.04, 95% CI 0.00 to 0.68, 30 participants). However, there were no important differences between groups in active range of motion and strength. Ozgen 2012 only reported medians and IQRs so MDs and 95% CIs could not be calculated. There were no or very small between-group differences in median scores for rest pain, function, pain on motion, global treatment success, night pain, and active range of motion at three weeks, three months and four years. Further, no participant reported any adverse events. The evidence from these two trials was downgraded by two points for high risk of performance and detection bias, and one point for imprecision, and so is considered to be very low quality.

Rabini 2012, which included 82 participants and was at high risk of bias overall, compared microwave diathermy (three times a week for four weeks) with glucocorticoid injection (one injection every two weeks for total of three injections) (Table 18). There was no clinically important difference between groups with respect to overall pain at four weeks (mean 35.1 versus 29.6 on a 100-point scale, MD 5.50, 95% CI -2.65 to 13.65, 82 participants), 12 weeks (mean 38.4 versus 28.9 on a 100-point scale, MD 9.50, 95% CI 1.19 to 17.81, 82 participants) and 24 weeks (mean 37.6 versus 29 on a 100-point scale, MD 8.60, 95% CI -2.07 to 19.27, 82 participants), or function at four weeks (mean 90.1 versus 82.4 on a 100-point scale, MD 7.70, 95% CI 0.61 to 14.79, 82 participants), 12 weeks (mean 86.6 versus 83.2 on a 100-point scale, MD 3.40, 95% CI -1.55 to 8.35, 82 participants) and 24 weeks (mean 88.1 versus 89.9 on a 100-point scale, MD -1.80, 95% CI -9.08 to 5.48, 82 participants). No participant reported

any adverse events. We considered this evidence to be very low quality (downgraded by two points for high risk of performance and detection bias and by one point for imprecision).

Is one type of electrotherapy modality more effective than another?

In 12 trials (674 participants), one type of electrotherapy modality was compared with another.

- Therapeutic ultrasound versus LLLT (Calis 2011; Yavuz 2014)
- Therapeutic ultrasound versus microwave diathermy (Giombini 2006)
- Therapeutic ultrasound versus radar (with mobilisation and exercise in both groups) (Polimeni 2003)
- Therapeutic ultrasound versus diadynamic current (with mobilisation and exercise in both groups) (Polimeni 2003)
- Therapeutic ultrasound versus high intensity laser therapy (Santamato 2009)
- Therapeutic ultrasound versus TENS (with exercise and cold pack in both groups) (Shehab 2000)
- Therapeutic ultrasound for four minutes versus therapeutic ultrasound for eight minutes (with superficial heat plus TENS plus exercise in both groups) (Yildirim 2013)
- PEMF for six weeks versus PEMF for two weeks (Binder 1984)
- PEMF for eight weeks versus PEMF for four weeks (Binder 1984)
- PEMF for eight hours per day versus PEMF for two hours per day (Chard 1988)
- TENS versus pulsed radiofrequency treatment (with exercise in both groups) (Korkmaz 2010)
- Interferential LLLT versus continuous LLLT (Montes-Molina 2012a)
- Interferential light therapy generated by two light probes versus conventional light therapy generated by one light probe (Montes-Molina 2012b)

The overall risk of bias was unclear in four (Binder 1984; Chard 1988; Montes-Molina 2012a; Montes-Molina 2012b), and high in eight trials (Calis 2011; Giombini 2006; Korkmaz 2010; Polimeni 2003; Santamato 2009; Shehab 2000; Yavuz 2014; Yildirim 2013).

In Giombini 2006, the authors observed clinically important differences favouring microwave diathermy over therapeutic ultrasound (both delivered three times a week for four weeks) in terms of rest pain at four weeks (MD 3.40, 95% CI 2.81 to 3.99; 10-point scale, 26 participants) and 10 weeks (MD 3.95, 95% CI 3.36 to 4.54; 10-point scale, 26 participants), function at four weeks (MD -18.10, 95% CI -20.96 to -15.24; 100-point scale, 26 participants) and 10 weeks (MD -20.25, 95% CI -24.07 to -16.43; 100-point scale, 26 participants), and global treatment success (number of participants returning to sport) at 10 weeks (RR 0.39, 95% CI 0.17 to 0.89; 26 participants). No participant reported adverse events.

Santamato 2009 observed clinically important differences favouring high intensity laser therapy over therapeutic ultrasound (both delivered five times a week for two weeks) in terms of overall pain (MD -2.02, 95% CI -2.67 to -1.37; 10-point scale, 70 participants), but not function (MD 3.80, 95% CI 0.53 to 7.07; 100-point scale, 70 participants) at two weeks. The trialists did not report measuring adverse events.

Nine trials found no clinically important or statistically significant differences between groups on any outcome (Binder 1984; Calis 2011; Chard 1988; Korkmaz 2010; Montes-Molina 2012a; Montes-Molina 2012b; Polimeni 2003; Shehab 2000; Yavuz 2014). In one trial (Yildirim 2013), statistically significant differences favouring a longer duration of therapeutic ultrasound were found in overall pain, function and active range of motion at five weeks.

Adverse events were reported as having been measured in six of the 12 trials (Binder 1984; Chard 1988; Giombini 2006; Korkmaz 2010; Montes-Molina 2012a; Montes-Molina 2012b), and none were reported by any participant (see Table 19).

The results of all of the above trials should be interpreted with caution given that small, single trials evaluated each comparison. We considered the evidence from these 12 trials to be very low quality (downgraded by two points for high risk of performance and detection bias or unclear risk of allocation bias, and by one point for imprecision).

Assessment of reporting bias

Three trials either did not report or partially reported a pre-specified outcome; however, we were unable to assess the impact of this outcome reporting bias on meta-analyses since no meta-analyses were performed. We were unable to generate funnel plots to assess small study effects. Despite this, we considered the risk of publication bias to be low because nearly all of the published studies reported statistically non-significant results for most outcomes. While some unpublished studies with non-significant results may exist, their inclusion in the review is unlikely to change our conclusions.

DISCUSSION

Summary of main results

We have considered the results of 47 trials investigating the benefits and harms of various electrotherapy modalities for rotator cuff disease. The trials were heterogeneous in terms of population, intervention and comparator, so data could not be combined in a meta-analysis. The findings need to be interpreted with caution

given they are often based on a single small trial at high risk of bias overall.

Therapeutic ultrasound

Based upon low quality evidence from one small trial of people with rotator cuff disease without calcification, pulsed therapeutic ultrasound was no more effective than placebo with respect to overall pain, global treatment success or shoulder abduction at four weeks (Berry 1980). Based on low quality evidence from another small trial in people with calcific tendinitis, pulsed therapeutic ultrasound was more effective than placebo with respect to overall pain, function, global treatment success and quality of life at six weeks (Ebenbichler 1999). By nine months, groups had similar overall pain and function, likely because participants in both groups experienced natural recovery.

Based upon low quality evidence from eight trials, therapeutic ultrasound produced no clinically important additional benefits when combined with other physical therapy interventions in terms of overall pain, function, pain on motion, night pain, global treatment success, range of motion and strength (Calis 2011; Celik 2009; Clews 1987; Downing 1986; Kurtai Gursel 2004; Nykänen 1995; Polimeni 2003; San Segundo 2008). Further, there were no clinically important differences between therapeutic ultrasound and manual therapy (Al Dajah 2014; Bansal 2011; Clews 1987), glucocorticoid injection (Berry 1980), glucocorticoid injection plus oral tolmetin sodium (Berry 1980), exercise (Giombini 2006) and acupuncture (Berry 1980; Johansson 2005) with respect to overall pain, function, global treatment success, range of motion and strength; however we are uncertain about these results because the evidence is very low quality.

None of the participants in any of the three trials that measured harms reported adverse events (Ebenbichler 1999; Giombini 2006; Johansson 2005).

Low-level laser therapy (LLLT)

Based on low quality evidence from two placebo-controlled trials (England 1989; Saunders 1995), there were favourable effects of LLLT with respect to overall pain, function, active range of motion and strength up to three weeks. Based on low quality evidence, LLLT produced few additional benefits when combined with other physical therapy interventions with respect to overall pain, function, pain on motion, global treatment success, night pain, range of motion and strength (Abrisham 2011; Bal 2009; Bingöl 2005; Calis 2011; Dogan 2010; Eslamian 2012; Kelle 2014; Otadi 2012; Vecchio 1993; Yeldan 2009). Also, LLLT had favourable effects over oral NSAID in overall pain and function (England 1989), while an additional trial comparing LLLT to glucocorticoid injection observed no between-group differences (Kelle 2014); however we are uncertain about these results because the evidence is very low quality.

None of the participants in any of the seven trials that measured harms reported adverse events of LLLT (Abrisham 2011; Bal 2009; Bingöl 2005; Dogan 2010; Kelle 2014; Vecchio 1993; Yeldan 2009).

Transcutaneous electrical nerve stimulation (TENS)

Based on a small single trial, TENS was found to provide greater pain relief immediately after treatment compared with placebo (Kocyigit 2012), but this trial was conducted in a setting not reflective of clinical practice. Further, TENS was found to provide similar pain relief to a hot pack (Baskurt 2006) and no additional pain relief when added to a hot pack (Baskurt 2006). It was also less effective than glucocorticoid injection with respect to function up to 12 weeks, although there were no between-group differences observed in pain, global treatment success and active range of motion (Eyigor 2010). TENS was also less effective than extracorporeal shockwave treatment in terms of pain and function up to 12 weeks in people with calcific tendinitis (Pan 2003). However, we are uncertain about all of these results because the evidence is very low quality.

None of the participants in either of the two trials that measured harms reported adverse events of TENS (Eyigor 2010; Pan 2003).

Pulsed electromagnetic field (PEMF)

Based on low quality evidence, PEMF provided no clinically important benefits when compared with placebo (Binder 1984; Galace de Freitas 2014), or when added to exercise (Aktas 2007; Galace de Freitas 2014).

None of the trials investigating the effects of PEMF measured adverse events.

Other electrotherapy modalities

Based upon low or very low quality evidence, there were no clinically relevant between-group differences in outcome in trials comparing MENS versus placebo (Atya 2012), acetic acid iontophoresis plus therapeutic ultrasound versus no treatment (Perron 1997), microwave diathermy versus glucocorticoid injection (Rabini 2012), therapeutic ultrasound plus TENS versus cryotherapy (Grymel-Kulesza 2007) or therapeutic ultrasound plus TENS versus sodium hyaluronate injection (Ozgen 2012). Further, both microwave diathermy (Akyol 2012) and acetic acid iontophoresis (Leduc 2003) produced no additional benefits over exercise plus hot pack.

None of the participants receiving microwave diathermy reported any adverse events (Akyol 2012; Rabini 2012). None of the trials investigating the effects of MENS or acetic acid iontophoresis measured adverse events.

One type of electrotherapy modality versus another

There was very low quality evidence from 12 single trials comparing one electrotherapy modality to another (Binder 1984; Calis 2011; Chard 1988; Giombini 2006; Korkmaz 2010; Montes-Molina 2012a; Montes-Molina 2012b; Polimeni 2003; Santamato 2009; Shehab 2000; Yavuz 2014; Yildirim 2013). Only two found clinically important differences between groups: one trial favouring microwave diathermy over therapeutic ultrasound (Giombini 2006); and another trial favouring high intensity laser therapy over therapeutic ultrasound (Santamato 2009). The results of all of these trials should be interpreted with caution given that small, single trials evaluated each comparison.

Overall completeness and applicability of evidence

Participants in the included trials were mostly representative of populations most affected by rotator cuff disease. Nearly all trials enrolled a community sample of people attending routine physical therapy care. Across the trials, the median age was 53 (IQR 49 to 55) years. Thus, results are applicable to those likely to be seen in practice (Linsell 2006; Yamamoto 2010). Further, trials were conducted in 18 different countries, including a range of high- and low- to middle-income countries. However, it is difficult to determine how representative participants in the included trials were with respect to duration of symptoms, as this characteristic was not reported in 17 (36%) trials.

A comprehensive range of treatment comparisons were captured across the trials. The review was dominated by trials investigating whether electrotherapy modalities provided benefit when added to manual therapy or exercise, or whether one electrotherapy modality was more effective than another. Several placebo-controlled trials were also included (Atya 2012; Berry 1980; Binder 1984; Ebenbichler 1999; England 1989; Galace de Freitas 2014; Kocyigit 2012; Saunders 1995), and electrotherapy modalities were compared to many other active interventions (glucocorticoid injection, sodium hyaluronate injection, oral NSAID, acupuncture, extracorporeal shock wave treatment, hot pack and cryotherapy). Participants underwent treatment for a median of three weeks (interquartile range 2 to 4), so the findings may not generalise to treatment packages delivered over a longer period.

In several trial reports, the components of the electrotherapy modalities were incompletely described. For example, some trialists did not specify the frequency (e.g. Hz or MHz), intensity (e.g. W/cm^2), power (e.g. W), duration of session (e.g. five minutes) or frequency of administration (e.g. three times a week for three weeks). This poor reporting is not surprising given that many trials were published prior to the dissemination of reporting guidelines (e.g. CONSORT (Schultz 2010)). Nevertheless, incomplete intervention descriptions hinder trial replication, and limit reliable implementation of the intervention into clinical practice. We recommend that future trialists follow recommendations for reporting of intervention details, as outlined in the template for intervention description and replication (TIDieR) checklist (Hoffman 2014).

Another concerning issue is the variable choice of outcomes measured in the trials. Overall pain and function were measured in most trials (85% and 70%, respectively), but these domains should be measured in all rotator cuff disease trials given that pain and functional limitations are the most common presenting symptoms of the condition (Whittle 2015). Further, adverse events were measured in less than a half the trials (40%). The other main outcomes of the review were measured in even fewer trials: pain on motion (32%), global assessment of treatment success (21%), and quality of life (11%). Outcome measurement has improved since the first version of our review (Green 1998), where function was measured in only 26% of trials (none with a validated disability index), and none of the trials measured quality of life. However, a core domain set and core outcome measurement set for rotator cuff disease trials would likely improve measurement of patient-important outcomes in future trials, and would facilitate efforts to synthesise the evidence in future (Buchbinder 2003; Page 2015). Together with an international panel, we are currently developing these core sets according to the guidance of the Outcome Measures in Rheumatology (OMERACT) initiative, who have approved a special interest group session on shoulder pain at the OMERACT 2016 meeting, and the Core Outcome Measures in Effectiveness Trials (COMET) initiative.

Quality of the evidence

We used the GRADE approach (Schünemann 2011b) to assess the quality of all included trials. We downgraded all the trials to either low or very low quality based on three factors: firstly, the risk of allocation bias was unclear because trialists did not report whether the allocation sequence was concealed; secondly, the risk of performance and detection bias was high for self-reported outcomes because participants were not blinded; and thirdly, evidence was based on small, single trials, leading to concerns about imprecision of effect estimates. Trials with unclear allocation concealment have been found to overestimate treatment effects by 7% (ratio of odds ratios 0.93, 95% credible interval 0.87 to 0.99), and unblinded assessment of self-reported outcomes (such as pain and function) is estimated to exaggerate the treatment benefit by about 22% (ratio of odds ratios 0.78, 95% credible interval 0.65 to 0.92) (Savovic 2012). Given that 77% of trials included in our review had unclear or no allocation concealment, and 51% had unclear or non-blinded assessment of self-reported outcomes, further high quality trials may show even smaller effect estimates than those reported in this review.

Potential biases in the review process

We searched CENTRAL, MEDLINE, EMBASE and CINAHL, but not PEDro, a database of randomised trials, systematic reviews and clinical practice guidelines relevant to physiotherapy. An empirical study comparing the indexing of 400 physiotherapy trials in eight bibliographic databases found that almost all were indexed in CENTRAL (95%), PEDro (92%) MEDLINE (89%) and EMBASE (88%). Further, only one of the 400 trials was uniquely indexed in PEDro (Michaleff 2011). Therefore, we think it is very unlikely that we missed relevant trials that would change the conclusions of our review. Two review authors independently assessed the trials for inclusion in this review, extracted data and assessed the risk of bias, and a third review author adjudicated when any discrepancy arose. Review questions of interest were defined with full knowledge of the possible comparisons that could be undertaken, but no knowledge of the results of any comparisons. To prevent selective inclusion of results (Page 2013), we used pre-defined decision rules to select data from trials when multiple measurement scales, time points and analyses were reported.

A potential limitation was that we excluded one trial (Taverner 2014) which may have included participants with rotator cuff disease, but the eligibility criteria and participant characteristics were not reported in enough detail for us to determine this. Further, we excluded two trials (Ainsworth 2007; Herrera-Lasso 1993) where approximately two thirds of participants had rotator cuff disease and a third had adhesive capsulitis, but we were unable to obtain data for the rotator cuff disease subgroup. Further, we were unable to translate five trials reported in a language other than English, but will endeavour to include these trials in the next update of this review. In addition, we did not undertake a search for grey literature (e.g. proceedings of specific conferences, theses or unpublished reports). However, since the majority of the evidence we included had "negative" findings, we believe that identification and inclusion of unpublished studies with non-significant results is unlikely to have changed our conclusions.

Agreements and disagreements with other studies or reviews

Following the earlier Cochrane review of physical therapy for shoulder pain (Green 2003), there have been three systematic reviews of electrotherapy modalities and other physical therapy interventions for rotator cuff disease (Gebremariam 2014; Kromer 2009; Nyberg 2010), and one systematic review of therapeutic ultrasound for shoulder pain (Alexander 2010). All of these reviews have been narrower in scope than ours. Review authors either restricted their participant eligibility criteria according to the diagnostic label used by trialists (e.g. focusing only on subacromial impingement syndrome), or used broad participant eligibility criteria but focused on one electrotherapy modality (i.e. therapeutic ultrasound). Therefore, to our knowledge, ours is the most comprehensive review of electrotherapy modalities for rotator cuff disease. Our conclusions that there may be little or no important benefits of electrotherapy modalities for rotator cuff disease are consistent with the conclusions of all other systematic reviews.

AUTHORS' CONCLUSIONS

Implications for practice

Based on low quality evidence, therapeutic ultrasound may have short-term benefits over placebo in people with calcific tendinitis, and LLLT may have short-term benefits over placebo in people with rotator cuff disease. In contrast, based on low quality evidence, PEMF may not provide clinically relevant benefits over placebo, and therapeutic ultrasound, LLLT and PEMF may not provide additional benefits when combined with other physical therapy interventions. We are uncertain whether TENS is superior to placebo, and whether any electrotherapy modality provides benefits over other active interventions (e.g. glucocorticoid injection) because of the very low quality of the evidence. Until further evidence confirms or refutes these results, practitioners should communicate the uncertainty of effect and consider other approaches or combinations of treatment.

Implications for research

High quality placebo-controlled trials are needed to confirm the favourable effects of therapeutic ultrasound for calcific tendinitis and LLLT for rotator cuff disease observed in previous trials. Further trials of other electrotherapy modalities for rotator cuff disease should be based upon a strong rationale and consideration of whether or not they would alter the conclusions of this review. Novel multi-modal interventions combining electrotherapy modalities such as ultrasound or LLLT, with manual therapy and exercise, should be compared with a realistic placebo (e.g. use of inactive ultrasound and application of an inert gel) in high quality randomised trials. The interventions should be described in enough detail to inform interpretation of findings and allow replication. Trials should use strategies designed to minimise the potential for bias, including adequate allocation concealment and blinding of participants and outcome assessors. Development of a core set of outcomes for trials of rotator cuff disease and other shoulder disorders would facilitate our ability to synthesise the evidence in future.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Abrisham 2011

Methods	**Study design**: Parallel group RCT **Setting:** Physiotherapy clinic **Intervention**: Laser treatment (pulsed infrared laser) plus exercise therapy **Control**: Placebo laser plus exercise therapy **Source of Funding:** Not reported
Participants	**Diagnostic label used by trialists:** Rotator cuff and bicep tendinitis **Criteria for defining the shoulder condition being treated:** Subacromial syndrome (rotator cuff and bicep tendinitis) defined by: • clinical history; and • physical exam indicating rotator cuff tendinitis (Neer sign, Kennedy-Hawkins test or Jobe test); or • physical exam indicating bicep tendinitis (Speed test) **Any restriction on duration of symptoms** • None **Inclusion Criteria (not listed above)** • 18 years or older **Exclusion Criteria (not listed above):** • significant trauma or systemic inflammatory condition (rheumatoid arthritis); or • neurological or structural abnormality affecting the shoulder; or • post-operative and peri-operative shoulder pain; or • pregnancy or breast-feeding; or • anticoagulation therapy; or • diabetes mellitus; or • cardiac-type chest pain; or • cigarette smoking; or • shoulder infection; or • shoulder trauma; or • contraindications to laser therapy **Baseline characteristics** *Intervention: Low-level laser* Number randomised: 40 Number included in analyses: 40 Age: 55.2 ± 5.7 years old Sex: F/M 24/16 Duration of symptoms: not reported *Control: Placebo laser* Number randomised: 40 Number included in analyses: 40 Age: 51.2 ± 6.7 years old Sex: F/M 26/14 Duration of symptoms: not reported

Abrisham 2011 (*Continued*)

Interventions	**Intervention: Low-level laser therapy** *Description of modality used*: infrared laser radiation delivered by a Mustang-024 device at 890 nm wavelength in pulsed mode. Three points on the shoulder (anterior/coracoid, posterior/glenohumeral joint, lateral/rotator cuff tendon) were irradiated. The biceps tendon was irradiated if applicable *Dose*: 2 min over 3 areas with an energy density of 2-4 J/cm^2 • 1st-3rd sessions: power of 7 W with a wavelength of 890 nm and a frequency of 80 Hz • 4th-5th sessions: power of 9 W with a wavelength of 890 nm and a frequency of 150 Hz • 6th-8th sessions: power of 8 W with a wavelength of 890 nm and a frequency of 1500 Hz • 9th-10th sessions: power of 10 W with a wavelength of 890 nm and a frequency of 80 Hz *Frequency of administration*: 10 sessions over 2 weeks **Control: Placebo laser** *Description of modality used*: infrared laser radiation delivered by a Mustang-024 device. Three points on the shoulder (anterior/coracoid, posterior/glenohumeral joint, lateral/rotator cuff tendon) were irradiated. The biceps tendon was irradiated if applicable *Dose*: no lasers were emitted *Frequency of administration*: 10 sessions in 2 weeks **Both groups** *Description of modality used*: in the clinic - pulley and shoulder wheel exercises; at home - pendular shoulder exercises for the first 2 sessions and isometric exercises and active assisted exercises from the third session *Dose*: not reported *Frequency of administration*: 10 sessions in 2 weeks
Outcomes	Outcomes assessed at 2 weeks • Overall pain: VAS with 0 indicating "no pain" and 10 indicating "severe pain" • Active and passive flexion, abduction and external rotation measured using a goniometer • Adverse events
Notes	**Conflict of interest:** the authors reported that they had nothing to declare **Funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised in two groups by using sealed envelopes method" Comment: The method used to generate the allocation sequence was not clearly reported

Abrisham 2011 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Comment: The method used to conceal the allocation sequence was not clearly reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Patients in the second group were treated with placebo laser therapy. The same device which seemed to be working was used but no laser beams were transferred to the treated area." Comment: Patients were likely blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "Shoulder ROM was measured by a blinded physician"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All of the 80 participants completed the treatment." Comment: There were no losses to follow-up, drop-outs or post-randomisation exclusions
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes specified in the methods section. However, without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Aktas 2007

Methods	**Study design**: Parallel group RCT **Setting:** Hospital, Turkey **Intervention:** Pulsed electromagnetic field plus exercise plus cold pack **Control:** Sham pulsed electromagnetic field plus exercise plus cold pack **Source of Funding:** This study was supported by the Department of Physical Medicine and Rehabilitation, Cerrahpasa Medical Faculty, Istanbul University
Participants	**Diagnostic label used by trialists:** Subacromial impingement syndrome **Criteria for defining the shoulder condition being treated:** Diagnosis of shoulder impingement syndrome by: • positive impingement test (Neer, Hawkins-Kennedy, painful arc)

	• positive subacromial injection test **Any restriction on duration of symptoms** • None **Inclusion Criteria (not listed above)** • None **Exclusion Criteria (not listed above)** • Other concomitant shoulder pathologies such as adhesive capsulitis, calcific tendinitis, partial and full-thickness tears of the rotator cuff, osteoarthritis of the acromioclavicular joint, dislocations, acute traumatic conditions, etc. • Cervical pain or other painful conditions such as fibromyalgia • Inflammatory or systemic diseases • History of gastritis or peptic ulcer that may cause complications with NSAID use • Prior applications of any treatment modality such as physiotherapy, corticosteroid injections, and NSAID during the preceding 3 months • Malignancy • Female patients who might be pregnant • Pulmonary disorders and cardiac pace makers **Baseline characteristics** *Intervention: PEMF* Number randomised: 20 Number included in analyses: 20 Age: 48 ± 7.9 years old Sex: F/M 15/5 Duration of symptoms: 4.82 ± 3.75 *Control: Sham PEMF* Number randomised: 20 Number included in analyses: 20 Age: 53.9 ± 11.12 years old Sex: F/M 15/5 Duration of symptoms: 4.80 ± 3.47
Interventions	**Intervention: PEMF** *Description of modality used*: Magnetoterapia model MG/3P (Elettromed) *Dose*: Frequency 50 Hz with a field intensity of 30 G for 25 min per session *Method of administration*: the switch that allowed the machine to produce waves was set to 'on' and a U-shaped applicator 30 x 15 cm in size was used *Frequency of administration*: 5 sessions per week for 3 weeks **Control: Sham PEMF** *Description of modality used*: Magnetoterapia model MG/3P (Elettromed) *Dose*: none for a 25-min session *Method of administration*: the switch that allowed the machine to produce waves was set to 'off' and a U-shaped applicator 30 x 15 cm in size was used *Frequency*: 5 sessions per week for 3 weeks **Both Groups** *Description of modality used* • Exercise: Codman's pendulum exercises • Cold pack: cold pack gel *Dose* • Exercise: 5 min each time

	• Cold pack: 20 min per session *Method of administration* • Cold pack: applied to painful shoulder *Frequency* • Exercise: 5 times per day for 3 weeks • Cold pack: 5 times per day for 3 weeks *Any additional treatment during trial* • Restriction of above-head activities • 15 mg daily Meloxicam tablet
Outcomes	Outcomes assessed at 3 weeks • Function: Constant total score (0-100 with higher scores denoting better function) • Rest pain: VAS 0-10 where 0 = no pain and 10 = intolerable pain • Pain on motion: VAS 0-10 where 0 = no pain and 10 = intolerable pain • Night pain: VAS 0-10 where 0 = no pain and 10 = intolerable pain • Active range of motion (Constant sub-score 0-40, higher = better ROM) • Strength (Constant sub-score 0-25, higher = better strength)
Notes	**Conflict of interest:** not reported **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly divided into two equal groups of 23 patients in a simple systematic manner (x + 1) according to the therapeutic PEMF or sham PEMF application." Comment: There was no information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Quote: "A separate individual was provided the randomization list and informed therapist." Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Patients and physicians remained blind to the group allocation throughout the study." Quote: "One group was given PEMF; the other group was given sham PEMF. A magnetic field treatment unit was used with a concealed switch for either the presence or absence of waves when activated by the patient's attendant."

Aktas 2007 (*Continued*)

		Comment: Participants and personnel were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quotes: "Patients and physicians remained blind to the group allocation throughout the study." Comment: Assessors of objective outcomes were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Forty patients completed the study. Three patients from each group could not continue treatment program. Therefore, six patients dropped out of the study." Comment: The rate and reasons for attrition were equal between groups. Also, analysis was based on all randomised participants
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Akyol 2012

Methods	**Study design:** Parallel group RCT **Setting:** University, Turkey **Interventions:** Microwave diathermy plus superficial heat plus exercise **Control:** Sham microwave diathermy plus superficial heat plus exercise **Source of funding:** Not reported
Participants	**Diagnostic label used by trialists:** Subacromial impingement syndrome **Criteria for defining the shoulder condition being treated** • Unilateral shoulder pain consistent with subacromial impingement syndrome (SIS) for at least 3 months • Shoulder pain aggravating with overhead activity • Positive impingement tests (Neer, Hawkins-Kennedy) • Marked loss of active and passive shoulder motion or painful range of motion

	• Diagnosed by magnetic resonance imaging as a reference standard **Inclusion criteria** • Taken no treatment in another physiotherapy clinic in the last 6 months **Exclusion criteria** • History of frozen shoulder, disorders of the acromioclavicular joint, degenerative arthritis of the glenohumeral joint, calcific tendinopathy, shoulder instability, post-traumatic disorders, or shoulder surgery and/or elbow, hand, wrist and cervical spine disorders • Specific contraindication to microwave diathermy (conditions known to be sensitive to increase cell proliferation rates or skin treated in the past 6 months with radiotherapy, ischaemia, local thrombosis or defective arterial circulation, impaired cutaneous thermal sensitivity, metal implants, local infections, and indwelling electronic equipment, e.g. pumps or cardiac pacemakers) **Baseline characteristics** Total n randomised = 40 participants Total n analysed = 40 participants *Intervention: Microwave diathermy* Number randomised: 20 Number included in analyses: 20 Mean ± SD (range) age: 55.35 ± 14.50 (21-78) years Sex: F/M 15/5 Mean ± SD (range) duration of symptoms: 10.5 ± 8.59 (3-36) months *Control: Sham microwave diathermy* Number randomised: 20 Number included in analyses: 20 Mean ± SD (range) age: 51.2 ± 6.82 (42-65) years Sex: F/M 15/5 Mean ± SD (range) duration of symptoms: 14.1 ± 18.38 (3-84) months
Interventions	**Intervention: Microwave diathermy** *Components of intervention*: microwave diathermy (Curadar 409 (Enraf-Nonius, The Nederland) equipped with 2,450 MHz microwaves generator with a maximum output power of 100 W, applied for 20 min) **Control: Sham microwave diathermy** *Components of intervention*: As above but device was set to the "on" mode, dials were lit but no energy was delivered to the tissue **Both groups** Superficial heat via hot pack (20 min) plus exercise (15 min shoulder active range of motion (Codman's pendulum, wall-climbing, and shoulder wheel), 5 min stretching and 10 min strengthening exercise including rotator cuff muscles, rhomboids, levator scapulae, and serratus anterior with an elastic band). Both of the programmes were performed 5 days a week, for 3 weeks, and a total of 15 sessions as an inpatient 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
Outcomes	Outcomes assessed at the end of 3 weeks' treatment and at 1 month follow-up (i.e. 7 weeks)

	• Function using total SPADI score (higher scores indicate worse function) • Rest pain using 0-10 cm VAS (higher scores indicate more pain) • Activity pain using 0-10 cm VAS (higher scores indicate more pain) • Night pain using 0-10 cm VAS (higher scores indicate more pain) • Active range of flexion, extension, abduction, adduction, external rotation and internal rotation (in degrees) using a goniometer • Isokinetic shoulder muscle strength using an isokinetic dynamometer, for 60º/s internal rotation, 60º/s external rotation, 180º/s internal rotation, and 180º/s external rotation (maximum peak torque values in Newton-meters were calculated) • Quality of life using the SF-36 (scores range from 0 (worst) to 100 (best) with higher scores indicating better health status • Adverse events
Notes	**Conflict of interest:** none **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Forty patients were randomized (using concealed envelopes) into one of two groups". Comment: There was not enough information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: There was not enough information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "In control group, MD [microwave diathermy] device was set to the "on" mode, dials were lit but no energy was delivered to the tissue." Comment: Participants were blinded to treatment received
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "Patients were assessed three times by the same physician (YA), who was blinded with regard to the type of treatment the patients receive" Comment: Blinded assessor measured objective outcomes (e.g. ROM, strength)

Akyol 2012 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "No dropouts occurred during the trial, and all subjects in both groups completed the treatment program."
Selective reporting (reporting bias)	Low risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication. Despite the absence of a protocol, all clinically important outcomes were measured (according to the trial publication) so selective reporting bias is not suspected
Other bias	Low risk	Comment: No other sources of bias identified

Al Dajah 2014

Methods	**Study design:** Parallel group RCT **Setting:** Physiotherapy outpatient department, Saudi Arabia **Intervention:** Therapeutic ultrasound **Control:** Soft tissue mobilisation and proprioceptive neuromuscular facilitation **Source of Funding:** Not reported
Participants	**Diagnostic label used by trialists:** Shoulder impingement syndrome **Criteria for defining the shoulder condition being treated** • Positive results in the Neer impingement test • Negative results in the capsule stretch test • Visual analogue scale (VAS $\geq$ 5) • External rotation = 35° ± 5° • Overhead reach of 155 ± 10 cm **Inclusion Criteria (not listed above)** • Aged between 40 and 60 years • No use of analgesics and anti-inflammatory drugs and muscle relaxants within 24 hours before the participation in the study **Exclusion Criteria (not listed above)** • Open wounds • Infection • Acute injuries or fractures • Recent surgeries • Swelling • Rheumatoid arthritis • Reflex sympathetic syndrome • Adhesive capsulitis **Baseline characteristics** • Not reported

Interventions	**Intervention: Therapeutic ultrasound** *Components of intervention:* the arm was abducted to 45° and the forearm was rested on the pillow for support. Ultrasound therapy was given to the subscapularis muscle insertion at the shoulder region *Dose:* frequency - 3 MHz; intensity - 0.5 W/cm^2; duration: 10 min *Frequency of administration:* once **Control: Soft tissue mobilisation (STM) and proprioceptive neuromuscular facilitation (PNF)** *Components of intervention:* the subjects were positioned with the humerus abducted to 45° with elbow flexed to 90°, and the humerus was externally rotated to a midrange position, typically about 20° to 25° of external rotation. The subscapularis was palpated in the axilla to identify areas of myofascial mobility restrictions, taut bands, or trigger points. Identified restrictions were treated with STM utilising a combination of sustained manual pressure, and slow deep strokes to the subscapularis myofascia for 7 min. The STM was followed by contract-relax PNF for the subscapularis and other glenohumeral medial rotators, beginning in the same position used for the STM. The participants were instructed to perform maximal glenohumeral internal rotation against an opposing, isometric, manual resistance applied by the treating physical therapist for 7 seconds. Afterwards, the participant actively moved the humerus into full available external rotation. This position was maintained for 15 seconds. This 7-second internal rotation contraction against resistance followed by full active external rotation was repeated 5 times. Subjects were then instructed to actively move through the PNF flexion-abduction external-rotation diagonal pattern for 5 repetitions with manual facilitation *Dose:* 10 min *Frequency of administration:* once
Outcomes	Outcomes assessed immediately after one treatment session (day 1) • Overall pain: VAS (scale units not reported but assumed 0-10) • Range of motion: external rotation using a goniometer (unclear if active or passive)
Notes	**Conflicts of interest:** not reported **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "The subjects were assigned randomly into two groups by lot method" Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different ex-

Al Dajah 2014 (*Continued*)

		pectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants, who may have had different expectations about the benefits of the intervention they received, self-reported pain
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: There was no attrition because all participants were treated and assessed in a single session
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the results
Other bias	Low risk	Comment: No other sources of bias identified

Atya 2012

Methods	**Design:** Parallel group RCT **Setting:** Outpatient clinic of Faculty of Physical Therapy, Cairo University, Egypt **Interventions:** Microcurrent electrical stimulation (MENS) **Control:** Placebo microcurrent electrical stimulation **Source of funding:** Not reported
Participants	**Diagnostic label used by trialists:** Subacromial impingement syndrome **Inclusion criteria** • Symptoms for more than 3 months • Superiolateral shoulder pain more than 5 on VAS • Presence of 2 out of 4 specified objective signs and symptoms of subacromial impingement syndrome: a positive (painful) Neer impingement test, a positive (painful) Hawkins-Kennedy impingement test, painful arc with active shoulder elevation (flexion, abduction, scaption), pain or limitation with the functional movement patterns of hand-behind-back or hand-behind-head • Pain with one of the following resistance tests: external rotation, internal rotation, abduction, or flexion **Exclusion criteria** • Physician diagnosis of adhesive capsulitis • Rotator cuff tear • Calcific tendinitis confirmed by radiology • Cervical radiculopathy • History of shoulder surgery • Corticosteroid injection within the past month

	• Received physical therapy treatment for their shoulder within the past 3 months **Baseline characteristics** Total n randomised = 40 participants (40 shoulders) *Intervention: MENS* Number randomised: 19 Age: 48.8 ± 6 years (range not reported) Sex: F/M 9/10 Mean ± SD (range) duration of symptoms: 5.67 ± 3.13 months (range not reported) *Control: Placebo MENS* Number randomised: 21 Age: 9.1 ± 3.3 years (range not reported) Sex: F/M 12/9 Mean ± SD (range) duration of symptoms: 6.55 ± 2.21 months (range not reported)
Interventions	**Intervention: MENS** *Description of modality used:* HARLY physio 3000 unit. MENS is a novel electrotherapeutic modality. It is claimed to be capable of providing beneficial effects through delivering monophasic or biphasic pulsed microamperage currents with intensities between 1 and 999 uA across the skin *Components of intervention*: participants received a microcurrent stimulation with the following parameters: intensity 30-40 mA, pulse frequency 10 Hz, pulse width 50 ms, with duration 20 min/session. Current was applied via two skin surface carbon fibre electrodes containing an integral coupling gel **Control: Placebo MENS** *Description of modality used:* delivered in the same way as described above with the exception that the electrodes were not connected to the microcurrent device *Components of intervention*: each participant received 18 treatment sessions at a rate of 3 sessions per week for 6 weeks
Outcomes	Outcomes assessed at the end of 6 weeks' treatment • Function using the Dutch Shoulder Disability Questionnaire (0-100 with higher scores denoting worse function) • Pain on motion using a 10 cm VAS
Notes	**Conflicts of interest:** not reported **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomly assigned by means of a computer generated schedule, with random permuted block size of 2" Comment: An adequate method was used to generate the allocation sequence

Atya 2012 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The staff administering the treatments were not blinded." Quote: "The setting for patients enrolled into the placebo group was identical with the exception that the electrodes were not connected to the microcurrent device. As the administered microcurrent does not induce any sensations nor muscle twitching, patients were not able to distinguish between placebo or verum treatment" Comment: Participants were blinded to treatment, but personnel delivering the intervention were not (though this is unlikely to have affected the outcomes)
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "The staff administering the treatments were different from the staff administering the outcome measures: the latter were blinded to which treatment group (active or control) each patient was about to receive or had just received" Comment: Blinded assessors measured objective outcomes (proprioception accuracy)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: There were no drop-outs, losses to follow-up or exclusions
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data fully reported for all outcomes specified in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Bal 2009

Methods	**Study design**: Parallel group RCT **Setting:** Outpatient clinic, Turkey **Intervention:** Low-level laser therapy (LLLT) plus home exercise programme **Control:** Home exercise programme **Source of Funding:** Not reported
Participants	**Diagnostic label used by trialists:** Subacromial impingement syndrome **Criteria for defining the shoulder condition being treated** • Presence of shoulder pain • Positive Neer and Hawkins-Kennedy sign • Positive subacromial injection test **Any restriction on duration of symptoms:** • 6 weeks to 6 months **Inclusion Criteria (not listed above)** • Aged 18-70 **Exclusion Criteria (not listed above)** • Other shoulder pathology • A history of acute trauma • Prior treatment other than analgesics in the last 6 months • Contraindications to injections • Previous shoulder surgery **Baseline characteristics** *Intervention: LLLT plus exercise* Number randomised: 22 Number included in analyses: 20 Age: 51.7 ± 14.1 years old Sex: F/M 15/5 Duration of symptoms: not reported *Control: Exercise* Number randomised: 22 Number included in analyses: 20 Age: 53.1 ± 8.4 years old Sex: F/M 13/7 Duration of symptoms: not reported
Interventions	**Intervention: LLLT therapy** *Description of modality used*: LLLT applied over the tuberculum majus and minus, the anterior and posterior faces of the capsule and the subacromial regions. The head of the instrument was held perpendicular to the body surface without pressure. A Ga-As diode laser instrument (Roland Serie, Elettronica Pagani) was used *Dose*: 10 min sessions with each body point being treated for 120 seconds. Wavelength 904 nm, 5500 Hz frequency, 27 W maximum power output per pulse was used, with a 13.2 mW average power, 0.8 cm^2 spot size, 1.6 J of total energy was delivered per point at each session at a power density of 16.5 mW/cm^2. The cumulative energy per point for all sessions was 16 J *Frequency of administration*: 5 times per week for 2 weeks **Control: Home exercise programme** No direct comparator was used in the control group. Participants only received the same home exercise programme as intervention group

	Both groups: Home exercises *Description of modality used*: comprehensive home exercise programme comprising pendulum circumduction and passive shoulder self-stretching followed by isometrics in all planes; theraband exercises with three different therabands (low, medium, and high resistances); strengthening exercises for the muscles of scapular stabilisation; and advanced muscle- strengthening exercises with dumbbells. Progress was checked at the clinic twice weekly when the new exercises were taught. hot pack use before and cold pack use after each session was encouraged *Dose*: not reported *Frequency of administration*: over a period of 12 weeks *Any additional treatment during trial*: oral paracetamol (1500 mg/d) as needed
Outcomes	Outcomes assessed at 1 week, 2 weeks and 12 weeks • Function: SPADI total score 0-100 with a higher score indicating worse function • Night pain: 100 mm VAS ranging from no pain to most severe pain • Global assessment of treatment (rating of "excellent", "good" or "poor" on UCLA end-result score) • Adverse effects
Notes	**Conflict of interest:** "No conflicting financial interests exist." **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "The patients were randomised into two groups after initial evaluation by selecting a sealed unmarked envelope containing a letter indicating their group assignment." Comment: An adequate method was likely used to generate the allocation sequence
Allocation concealment (selection bias)	Low risk	Comment: An adequate method was likely used to conceal the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "All patients were informed about the nature of the study procedure" Comment: Given the nature of the interventions, participants were not blinded, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants, who may have had different expectations about the benefits of each intervention, self-reported all outcomes

Bal 2009 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Two patients in group 1 and two patients in group 2 were lost to follow-up" Comment: While reasons for loss to follow-up were not reported, the numbers were the same across both treatment and control group, so attrition is unlikely to have biased the results
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Bansal 2011

Methods	**Design:** Parallel group RCT **Setting:** University, India **Intervention:** Therapeutic ultrasound plus Codman's exercises **Control:** Deep friction massage plus Codman's exercises **Source of funding:** Not reported
Participants	**Diagnostic label used by trialists:** Supraspinatus tendinitis **Criteria for defining the shoulder condition being treated** Supraspinatus tendinitis defined by: • point tenderness at greater tuberosity of humerus • positive empty can test • painful resisted abduction **Inclusion Criteria (not listed above)** • None **Exclusion criteria (not listed above)** • History of trauma around shoulder • Corticosteroid injections in the past • Infective conditions • Surgery around shoulder region • Bony changes on radiological investigation **Baseline characteristics** *Intervention: Therapeutic ultrasound and Codman's exercises* Number randomised: 20 Mean (SD) age: 30.35 (5.76) years Sex: F/M 111/9 Duration of symptoms: not reported *Control: Deep friction massage and Codman's exercises*

	Number randomised: 20 Mean (SD) age: 30.90 (5.33) years Sex: F/M 8/12 Duration of symptoms: not reported
Interventions	**Intervention: Therapeutic ultrasound** *Components of intervention:* pulsed ultrasound applied to the supraspinatus tendon with the participants positioned with hand behind back *Dosage:* intensity 0.6 W/cm^2, frequency 1 MHz, pulse rate 4:1 for 6-8 min for 10 sessions over 10 days *Frequency of administration:* not explicitly reported, assumed daily for 10 days **Control - Deep friction massage** *Components of intervention:* deep friction massage to supraspinatus tendon in a transverse direction with the tip of the index finger, reinforced by middle finger. Participants were positioned half-lying with hand behind back (shoulder adduction and internal rotation) *Dosage:* 10-12 min for 10 sessions over 10 days *Frequency of administration:* not explicitly reported, assumed daily for 10 days **Both groups** All participants were instructed in Codman's exercises consisting of pendulum or swinging motion of the arm in flexion, extension, horizontal abduction, adduction and circumduction *Dosage*: not reported. *Frequency of administration*: Intensity (arc of motion) was increased as tolerated. Participants were also advised to avoid strenuous work involving the affected upper limb
Outcomes	Outcomes assessed at 5 days and 10 days • Overall pain using a VAS, ranging from 0 (no pain) to 10 (maximum pain) • Active range of shoulder abduction measured using a goniometer with the participant in a seated position
Notes	**Conflicts of interest:** not reported **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "The individuals were randomly divided into two groups" Comments: There was no information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment and may have had different expectations about the benefits of each inter-

Bansal 2011 (*Continued*)

		vention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants, who may have had different expectations about the benefits of the intervention they received, self-reported pain
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Unclear risk	Comment: No information was reported regarding the assessors of the objective outcome (active range of shoulder abduction)
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: Trialists did not report whether there were any dropouts, losses to follow-up or exclusions, or the number of participants included in each analysis
Selective reporting (reporting bias)	Unclear risk	Comment: Only mean scores (no measures of variation) were reported for all outcomes. However, it is not clear whether data were incompletely reported based on the statistical significance or magnitude of the results. Also, without a trial protocol, it is unclear whether other outcomes were assessed but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias were identified

Baskurt 2006

Methods	**Study design**: Parallel group RCT **Setting:** Orthopaedic physiotherapy unit, Turkey **Intervention 1:** Transcutaneous electrical nerve stimulation (TENS) **Intervention 2:** Hot pack **Intervention 3:** TENS plus hot pack **Source of Funding:** Not reported
Participants	**Diagnostic label used by trialists:** Shoulder impingement syndrome **Criteria for defining the shoulder condition being treated** • Stage 1 shoulder impingement syndrome **Any restriction on duration of symptoms** • None **Inclusion Criteria (not listed above)** • None **Exclusion Criteria (not listed above)** • Neuropathies • Disc pathologies • Nerve injuries in the upper extremities

	• Endocrine disorders • Pregnancy **Baseline characteristics** *Intervention 1: TENS* Number randomised: 30 Number included in analyses: 30 Age (mean and SD, or range): 57.10 ± 4.43 years Number of men and women: F/M 20/10 Duration of symptoms: not reported *Intervention 2: Hot pack* Number randomised: 31 Number included in analyses: 31 Age (mean and SD, or range): 56.54 ± 9.99 years Number of men and women: F/M 22/9 Duration of symptoms: not reported *Intervention 3: TENS plus hot pack* Number randomised: 31 Number included in analyses: 31 Age (mean and SD, or range): 57.32 ± 10.61 years Number of men and women: F/M 18/13 Duration of symptoms: not reported
Interventions	**Intervention 1: TENS** *Description of modality used*: TENS delivered to participant who was comfortably seated in a chair with back support and a pillow in the lap for arm support *Dose*: 100 Hz 0.1 ms pulse duration, symmetric biphasic wave form of tolerable intensity for 20 min *Frequency*: 1 session only *Any additional treatment during trial*: none **Intervention 2: Hot pack** *Description of modality used*: hot pack delivered to participant who was comfortably seated in a chair with back support and a pillow in the lap for arm support *Dose*: 39 degrees Celsius for 20 min *Frequency*: 1 session only *Any additional treatment during trial*: none **Intervention 3: TENS plus hot pack** *Description of modality used*: the third group was a combination of the methods previously mentioned (i.e. 20 min of TENS and 20 min of heat) *Dose*: See above *Frequency*: 1 session only *Any additional treatment during trial*: none
Outcomes	Outcome assessed immediately post treatment • Overall pain: VAS from 0 (no pain) to 10 (extreme pain)
Notes	**Conflict of interest:** not reported **Funding:** not reported
Risk of bias	

Baskurt 2006 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The patients were randomly divided into three groups." Comment: There was no information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants, who may have had different expectations about the benefits of the intervention they received, self-reported pain
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: Trialists did not report whether there were any dropouts, losses to follow-up or exclusions, or the number of participants included in each analysis
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Berry 1980

Methods	**Study design**: Parallel group RCT **Setting:** Outpatient hospital. UK **Intervention 1:** Therapeutic ultrasound **Intervention 2:** Glucocorticoid injection plus active tolmetin sodium **Intervention 3:** Glucocorticoid injection plus placebo tolmetin sodium **Intervention 4**: Acupuncture **Control**: Placebo ultrasound plus placebo tolmetin sodium **Source of Funding:** Not reported
Participants	**Diagnostic label used by trialists:** Rotator cuff lesions **Criteria for defining the shoulder condition being treated** Pain arising from the shoulder due to a rotator cuff lesion defined as: • pain on resisted movements of the shoulder, with loss of passive movement, mainly in abduction (many participants had painful arc syndrome) **Any restriction on duration of symptoms** • None **Inclusion Criteria (not listed above)** • None **Exclusion Criteria (not listed above)** • Frozen shoulder • Presence of an underlying fracture • Associate inflammatory arthritis • Known renal or hepatic disease • Haemopoietic disorder • Malignancy • Any mental disorder likely to interfere with the course or assessment of the disease process • History of severe indigestion, peptic ulceration, or any significant gastro-intestinal condition likely to affect drug absorption • Women who were pregnant or at risk of pregnancy **Baseline characteristics** *Intervention 1: Therapeutic ultrasound* Number randomised: 12 Number included in analyses: 12 Age (SD): 55.1 (12.7) years Sex: F/M 7/5 Duration of symptoms (SD): 16.3 (14.5) weeks *Intervention 2: Glucocorticoid injection/tolmetin sodium* Number randomised: 12 Number included in analyses: 12 Age (SD): 51.2 (14.6) years Sex: F/M 8/4 Duration of symptoms (SD): 28.3 (15.2) weeks *Intervention 3: Steroid injection/placebo tolmetin sodium* Number randomised: 12 Number included in analyses: 12 Age (SD): 54.1 (16.7) years Sex: F/M 6/6 Duration of symptoms (SD): 23.6 (27.9) weeks, excluding one participant with a dura-

	tion of 10 years *Intervention 4: Acupuncture* Number randomised: 12 Number included in analyses: 12 Age (SD): 52.3 (10.8) years Sex: F/M 4/8 Duration of symptoms (SD): 20.3 (16.9) weeks *Control: Placebo ultrasound plus placebo tolmetin sodium* Number randomised: 12 Number included in analyses: 12 Age (SD): 56.2 (11.2) years old Sex: F/M 6/6 Duration of symptoms (SD): 27.5 (35) weeks
Interventions	**Intervention 1: Therapeutic ultrasound** *Description of modality used*: therapeutic ultrasound delivered by a qualified physiotherapist *Dose*: 10 min (intensity and frequency not reported) *Frequency of administration*: 8 sessions over 4 weeks **Intervention 2: Glucocorticoid injection plus tolmetin sodium** *Description of modality used*: methyl prednisolone and lignocaine injection given by the same person using the anterior approach to the shoulder joint plus tolmetin sodium (1200 mg) *Dose*: injection - 40 mg methyl prednisolone with 2 mL 2% lignocaine; tolmetin sodium - 2 x 200 mg tablets 3 times a day) *Frequency of administration*: 1 injection; tolmetin sodium 2 tablets 3 times per day for 4 weeks **Intervention 3: Glucocorticoid injection plus placebo tolmetin sodium** *Description of modality used*: methyl prednisolone and lignocaine injection given by the same person using the anterior approach to the shoulder joint plus placebo tolmetin sodium *Dose*: Injection - 40 mg methyl prednisolone with 2 mL 2% lignocaine; placebo tolmetin sodium - 2 tablets 3 times a day for 4 weeks *Frequency of administration*: 1 injection; placebo tolmetin sodium 2 tablets 3 times per day **Intervention 4: Acupuncture** *Description of modality used*: classical Chinese acupuncture with moxibustion administered by a medically qualified doctor *Dose*: NA *Frequency of administration*: once per week for 4 weeks **Control: Placebo ultrasound plus placebo tolmetin sodium** *Description of modality used*: placebo ultrasound delivered by a qualified physiotherapist. The participant sat in front of the machine, which was not turned on *Dose*: none Frequency of administration: 8 sessions over 4 weeks **All groups** Paracetamol as needed, up to 8 tablets per day

Berry 1980 (*Continued*)

Outcomes	Outcomes assessed at 2 weeks and 4 weeks • Overall pain: VAS from 0-100 mm with a higher score indicating worse pain • Shoulder abduction using a goniometer (unclear if active or passive) • Global assessment of treatment success (failure defined by clinician as the need for a glucocorticoid injection) • Adverse events (only assessed in the 2 groups receiving active or placebo tolmetin sodium tablets, by asking "Has the treatment upset you in any way?")
Notes	**Conflicts of interest:** not reported **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Each group contained 12 patients who were allocated treatment according to a random code." Comment: There was no information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants, who may have had different expectations about the benefits of the intervention they received, self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "...the following indices were recorded by a blind, external observer at the start of the study and at 2 and 4 weeks" Comment: Assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: Trialists did not report whether there were any dropouts, losses to follow-up or exclusions, or the number of participants included in each analysis
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the

Berry 1980 (*Continued*)

		methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Binder 1984

Methods	**Study design:** Parallel group RCT **Setting:** Hospital, UK **Intervention:** Pulsed electromagnetic field therapy (PEMF) for 8 weeks **Control:** Placebo PEMF for 4 weeks followed by active PEMF for 4 weeks **Source of Funding:** Not reported
Participants	**Diagnostic label used by trialists:** Rotator cuff tendinitis **Criteria for defining the shoulder condition being treated** • Rotator cuff tendinitis based on the Cyriax criteria (shoulder pain being exacerbated by movement against resistance in abduction, internal rotation and/or external rotation) • Lesions were spontaneous or precipitated by minor trauma • A "painful arc" on abduction was often but not invariably present **Any restriction on duration of symptoms** • At least three months **Inclusion Criteria (not listed above)** • Participants had no more than transient benefit from previous conservative therapy • Normal erythrocyte sedimentation rates • Normal latex tests for rheumatoid factor **Exclusion Criteria (not listed above)** • Severe neck pain • Neurological changes in the upper limbs • Clinical or radiological evidence of glenohumeral, acromioclavicular or generalised arthritis • Radiological calcification of the soft tissues • Clinical diagnosis of rotator cuff rupture • Painful and restricted (frozen) shoulder **Baseline characteristics** *Intervention- PEMF for 8 weeks* Number randomised: 15 Number included in analyses: 15 Age: mean of 54.4 years old Sex: F/M 5/10 Diagnosis: • Supraspinatus tendon: 8 • Supraspinatus and infraspinatus: 5

	• Infraspinatus: 2 • Subscapularis: 0 Duration of symptoms mean (range): 9.2 (3 - 24) months *Control- Placebo PEMF for 4 weeks followed by active PEMF for 4 weeks* Number randomised: 14 Number included in analyses: 14 Age: 53.2 years old Sex: F/M 2/11 Diagnosis: • Supraspinatus tendon: 6 • Supraspinatus and infraspinatus: 5 • Infraspinatus: 1 • Subscapularis: 2 Duration of symptoms mean (range): 9.5 (3 - 24) months
Interventions	**Intervention: PEMF for 8 weeks** *Description of modality used*: a single ovoid coil (12.2 ±1.2 x 13.2 ± 0.7 cm^2) consisting of 50 turns of copper wire 1.4 mm in diameter was fitted over padding to the outer aspect of the affected shoulder so that the coils protruded from the centre of the pad. Two Velcro straps held it in place *Dose*: the pulse generators were set at 73 ± 2 Hz and a waveform varying by less than 7%. Participants were instructed to use the coil for 5-9 hours per day with each session lasting at least 1 hour *Frequency of administration*: 8 weeks *Any additional treatment during trial*: paracetamol if required **Control: Placebo PEMF for 4 weeks followed by active PEMF for 4 weeks** *Description of modality used*: Same as above *Dose*: same as above, except there was no dose during the first 4 weeks *Frequency of administration*: 8 weeks *Any additional treatment during trial*: paracetamol if required
Outcomes	Outcomes assessed at 2, 4, 6, 8, 12 and 16 weeks • Overall pain: VAS 0-10, including the sum of pain at night, movement and at rest taken to the nearest 0.5 cm on a 10-cm scale, with a higher score indicating worse pain • Pain on resisted movement (induced by resisted abduction and external and internal rotation) on 4-point scale (0 = no pain; 1 = slight pain but full power; 2 = moderate pain and reduced power; 3=severe pain with absent power against even minimum resistance) • Total active range of movement (sum of abduction, forward flexion and rotation) using a goniometer • Global assessment of treatment success: number of participants who completed the follow-up as symptomless (rather than had minor residual symptoms or severe disability • Adverse events
Notes	**Conflict of interest:** no conflict of interests reported **Funding:** Arthritis and Rheumatism Council Mean values reported graphically only, so were extracted from the graphs

Binder 1984 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients fulfilling the criteria were randomly allocated to the treatment group (A), or the control group (B)" Comment: There was no information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Neither patient not medical assessor was aware of the treatment group. At the end of 4 weeks and without breaking the code, both groups were given active coils and therapy was continued for another 4 weeks (phase II). Treatment was then stopped but patients continued to be reviewed for another 8 weeks (phase III), at the end of which the grouping was revealed to patient, medical assessor, and others involved in the study." Comment: participants were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "Neither patient nor medical assessor was aware of the treatment group" Comment: Assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: There was no loss to follow-up within the study and analysis was based on the number of randomised participants
Selective reporting (reporting bias)	Unclear risk	Comment: Data for all continuous outcomes was either partially reported (only means presented on figures). However, it is not clear whether data were incompletely reported based on the statistical significance or magnitude of the results. Also, without a trial protocol, it is unclear whether other outcomes were assessed but not reported based on the nature of the re-

Binder 1984 (*Continued*)

		sults
Other bias	Low risk	Quote: "4 patients (all group A) refused therapy after 4 weeks since symptoms had resolved. Thus 11 patients had active therapy over 8 weeks and 18 patients over only 4 weeks. However, the duration of therapy did not affect the outcome." Comment: No other sources of bias identified

Bingöl 2005

Methods	**Study design**: Parallel group RCT **Setting:** Physical therapy clinic, Turkey **Intervention:** Low-level laser therapy (LLLT) plus exercises **Control:** Placebo LLLT plus exercises **Source of Funding:** Not reported
Participants	**Diagnostic label used by trialists:** None **Criteria for defining the shoulder condition being treated** • Shoulder pain VAS score greater than or equal to 3 • With or without accompanying passive or active restriction of range of motion and noted pain aggravation with motion **Any restriction on duration of symptoms** • At least 3 months **Inclusion Criteria (not listed above)** • None **Exclusion Criteria (not listed above)** • Inflammatory arthritis • Polymyalgia rheumatica • Cervical spondylosis • History of shoulder dislocation or fracture • Previous deltoid surgery • Neurologic problems • Osteoarthritis • Rotator cuff rupture • Local or systemic steroid therapy or physiotherapy applied during the last 6 months **Baseline characteristics** *Intervention: LLLT plus exercises* Number randomised: 20 Number included in analyses: 20 Age: 63.80 ± 9.77 years old Sex: F/M 12/8 Duration of symptoms: not reported *Control: Placebo LLLT plus exercises* Number randomised: 20

Bingöl 2005 (*Continued*)

	Number included in analyses: 20 Age: 57.25 ± 10.21 years old Sex: F/M 19/1 Duration of symptoms: not reported
Interventions	**Intervention: LLLT** *Description of modality used*: laser was applied over the tuberculum majus and minus, bicipital groove, and anterior and posterior faces of the capsule, regardless of the existence of sensitivity, using a GaAs diode laser instrument (Roland Serie Elettronica Pagani) *Dose*: Wavelength 904 nm. Laser density and spot size 2.98 J/cm^2 (at peak power = 50 W, frequency = 2000 Hz, for a duration of 60 s) and 0.8 cm^2 respectively for each target point *Frequency of administration*: 10 sessions over 2 weeks **Control: Placebo LLLT** *Description of modality used*: same as above, but while laser was switched on, no laser was applied *Dose*: none *Frequency of administration*: 10 sessions over 2 weeks **Both groups** *Description of modality used*: supervised exercise programme using Codman, shoulder wheel and finger-stair components *Dose*: 15 min *Frequency*: 10 sessions over 2 weeks *Any additional treatment during trial*: paracetamol not exceeding 2000 mg/day
Outcomes	Outcomes assessed at 2 weeks • Overall pain: VAS 0 (no pain) to 10 (unbelievably severe pain) • Active and passive shoulder abduction, flexion, extension, internal rotation, external rotation and adduction using a goniometer • Adverse events
Notes	**Conflict of interest:** not reported **Funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Before the start of the study, another staff physician who was unaware of the examination results of the patients allocated the individuals into two groups of 20 each (either active laser treatment, Group I, or placebo laser [control], Group II) by drawing one card for each patient from a bag where cards numbered from 1 to 40 were placed." Comment: An adequate method was used to generate the allocation sequence

Bingöl 2005 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Comment: It is unclear if the cards drawn from the bag had "intervention" or "control" written on them (and thus it is unclear if the physician drawing the cards knew which group the presenting participant would be allocated to)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "A physiotherapist instructed and supervised the exercises and performed laser applications in Group I and placebo laser in Group II, where the instrument was switched on and the patients thought they were receiving laser treatment but no laser was applied. Thus, a double-blind study model was formed." Comment: participants were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "All evaluations before and after treatment were performed by a third staff physician who was not informed about the group of any patient." Comment: Assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All of the 12 females and eight males in Group I, and 19 females and one male in Group II completed the study" Comment: All participants completed follow-up
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Calis 2011

Methods	**Study design**: Parallel group RCT **Setting:** Outpatient physical medicine and rehabilitation unit, Turkey **Intervention 1:** Therapeutic ultrasound plus exercise plus hot pack **Intervention 2:** Laser plus exercise plus hot pack **Control:** Exercise plus hot pack **Source of Funding:** Not reported
Participants	**Diagnostic label used by trialists:** Subacromial impingement syndrome **Criteria for defining the shoulder condition being treated** • Diagnosis of subacromial impingement syndrome, stage 2 according to Zlatkin's MRI staging **Any restriction on duration of symptoms** • None **Inclusion Criteria (not listed above)** • None **Exclusion Criteria (not listed above)** • Aged under 18 or over 65 • Systemic, infectious or inflammatory rheumatic disease • Malignant disease • Decompensate heart failure • Past surgery of the shoulder or neck • Calcified tendinitis and/or bursitis • Cervical radiculopathy **Baseline characteristics** *Intervention 1: Ultrasound (plus hot pack and exercise)* Number randomised: 22 Number included in analyses: 21 Age: 50.42 ± 12.41 years Sex: F/M 14/7 Duration of symptoms (range): 3 (1-12) months *Intervention 2: Laser (plus hot pack and exercise)* Number randomised: 22 Number included in analyses: 15 Age: 46.2 ± 12.14 years Sex: F/M 10/5 Duration of symptoms: 3 (1-24) months *Control:* hot pack*plus exercise* Number randomised: 22 Number included in analyses: 16 Age: 50.34 ± 13.69 years Sex: F/M 11/5 Duration of symptoms: 3 (1-24) months
Interventions	**Intervention 1: Ultrasound** *Description of modality used*: therapeutic ultrasound applied to the shoulder using a Model Sonopuls 463 (Enraf Nonius Co.) with a 20 mm diameter probe, in a continuously circular mode *Dose*: Intensity of 1.5 W/cm^2, frequency of 3 MHz, continuously circular mode for 5 min *Frequency of administration*: daily for 15 days

	Intervention 2: Laser *Description of modality used*: A Ga As laser (Laserpet 100, Petas Co.) was used continuously in a direct contact technique with a 90 degree straight angle to the shoulder *Dose*: 904 nm wavelength. 6 mW average power, 1 J/cm^2 dosage, at 16 Hz frequency for 2 min *Frequency*: for 15 days **All groups: Exercise and hot pack** *Description of modality used*: hot pack applied to the affected shoulder, and an exercise programme (starting with passive ROM exercises and Codman's exercises, later switching to shoulder stretching and strengthening exercises. These were delivered by a physiotherapist) *Dose*: • Hot pack: 20 min • Exercise: 5 repetitions for 5 seconds for each exercise *Frequency*: • hot pack: Not reported • Exercise: Every weekday in the physical therapy unit for 15 days *Any additional treatment during trial:* paracetamol
Outcomes	Outcomes assessed at 3 weeks • Function: Constant-Murley total score from 0-100 with a higher score indicating better function • Rest pain: VAS from 0-10 with a higher score indicating worse pain • Pain on motion: VAS from 0-10 with a higher score indicating worse pain • Night pain: VAS from 0-10 with a higher score indicating worse pain • Range of motion: abduction, flexion, internal rotation, external rotation (using a goniometer, unclear if active or passive)
Notes	**Conflict of interest:** not reported **Funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "All patients included in the study were offered sealed envelopes containing treatment groups in writing and were allocated accordingly" Comment: There was no information on how the allocation sequence was generated prior to putting into envelopes
Allocation concealment (selection bias)	Unclear risk	Quote: "All patients included in the study were offered sealed envelopes containing treatment groups in writing and were allocated accordingly" Comment: There was no information on who disseminated the envelopes and

Calis 2011 (*Continued*)

		whether they were sequentially numbered, opaque and consecutively disseminated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Unclear risk	Comment: There was no information on whether the assessor of objective outcomes was blinded or not
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "In the beginning of the study groups of twenty two patients are planned. However, one from group one, seven from group two, six from group three are excluded from the study because of incompliance to the study" Comment: There was unequal attrition between groups, and analysis was based on the per-protocol sample. Excluding participants because of non-compliance to treatment is likely to have biased the results
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Celik 2009

Methods	**Study design**: Parallel group RCT **Setting:** Private clinic, Turkey **Intervention:** Therapeutic ultrasound plus TENS plus exercises **Control:** Placebo ultrasound plus TENS plus exercises **Source of Funding:** Not reported
Participants	**Diagnostic label used by trialists:** Subacromial impingement syndrome **Criteria for defining the shoulder condition being treated** • Positive Neer impingement test, Hawkin's sign or Jobe supraspinatus test with less than 30% restriction on passive movement when compared to the other side **Any restriction on duration of symptoms** • At least six months **Inclusion Criteria (not listed above)** • 40 years or older • Not engaged in sporting activities • Fully informed consent given • Absence of deformities such as mesoacromion or degenerative arthritis on radiographic examination • Absence of pathological findings on MRI except subacromial oedema **Exclusion Criteria (not listed above)** • Symptoms of less than 6 months duration • Great than 30% restriction of passive movement when compared to the opposite side • Previous shoulder surgery, subacromial injections or entered a physiotherapy and rehabilitation programme • Evidence of rotator cuff tears on MRI scans or pathological findings on radiography • Participants undergoing psychiatric therapy **Baseline characteristics** *Overall cohort of participants* Number randomised: assumed 36 (20 to active and 16 to placebo) Number included in analyses: 36 Age (mean and SD, or range): 51.4 (40-69) years old Number of men and women: F/M 29/7 Duration of symptoms: not reported
Interventions	**Intervention: Ultrasound** *Description of modality used*: pulsed ultrasound applied to an area 12 cm^2 along the supraspinatus while the affected arm was in a position of adduction, 90 degrees' internal rotation and 30 degrees' hyperextension *Dose*: Frequency 1 mHz, intensity 1 W/cm^2, for 4 min *Frequency of administration*: 15 sessions over 3 weeks **Control: Placebo ultrasound** *Description of modality used*: placebo ultrasound, where the arm was placed in the same position as active treatment *Dose*: none *Frequency of administration*: 15 sessions over 3 weeks **Both groups** *Description of modality used*: wand exercises, posterior and inferior capsule stretching

	exercises and exercises to strengthen the rotator cuff, carried out individually with a physiotherapist and at home. TENS and ice were also applied *Dose* • TENS: 20 min (no other details provided) • Ice: 15 min • Exercises: 20 times once a day under the supervision of a physiotherapist and then repeat each exercise twice another 20 times at home the same day *Frequency* • Ice: daily for 3 weeks • Exercise: daily for 3 weeks *Any additional treatment during trial*: NSAIDS
Outcomes	Outcomes assessed at 3 weeks and 6 weeks • Function: Constant score out of 100 with a higher score indicating better function • Overall pain: VAS score from 0-10 with a higher score indicating worse pain • Range of motion: forward elevation, internal rotation and external rotation (using a goniometer, unclear if active or passive)
Notes	**Conflict of interest:** not reported **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were divided randomly into two groups according to the type of ultrasound to be used." Comment: There was no information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The second group received placebo ultrasound with the arm placed in the same position." Comment: Participants were likely blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "Before treatments, at the end of the third and sixth weeks, a medical practitioner blind to the treatments used in the study assessed the results" Comment: Assessor of objective outcomes was blinded

Celik 2009 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: Trialists did not report whether there were any dropouts, losses to follow-up or exclusions, or the number of participants included in each analysis
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Chard 1988

Methods	**Study design:** Parallel group RCT **Setting:** Rheumatology research unit, United Kingdom **Intervention 1:** High dose pulsed electromagnetic field therapy (PEMF) (8 hours/day) **Intervention 2:** Low dose PEMF therapy (2 hours/day) **Source of funding:** "E.B.I Medical Systems provided the apparatus and generously provided support"
Participants	**Diagnostic label used by trialists:** Rotator cuff tendinitis **Criteria for defining the shoulder condition being treated** • Had diagnosis of rotator cuff tendinitis of at least 3 months' duration despite previous conservative treatment. Rotator cuff tendinitis was diagnosed by the method of Cyriax 1971, i.e. shoulder pain aggravated by movement against resistance. This was present with one or more of the following: abduction (supraspinatus tendinitis); external rotation (infraspinatus tendinitis); internal rotation (subscapularis tendinitis). Pain usually limited active movement, but passive range was virtually normal. Only cases occurring spontaneously or after minor trauma were included **Inclusion criteria** • Over 18 years of age **Exclusion criteria** • Severe neck pain • Abnormal upper limb neurology • Evidence of an arthropathy (generalised, glenohumeral, or acromioclavicular) • Clinical evidence of a rotator cuff rupture or frozen shoulder • Received a local steroid injection for at least 1 month before inclusion **Baseline characteristics** Total n randomised: 49 participants (49 shoulders) Total n analysed: 43 participants *Intervention 1: High dose PEMF* Number randomised: 24 Number completed: 24

Chard 1988 (*Continued*)

	Mean age: 52.8 years Sex: F/M 8/16 Mean duration of symptoms: 14.2 months *Intervention 2: Low dose PEMF* Number randomised: 25 Number completed: 19 Mean age 50.1 years Sex: F/M 10/9 Mean duration of symptoms: 14.6 months
Interventions	**Intervention: High dose coil (8 hours/day) PEMF therapy** *Components of intervention*: participants were instructed to use the treatment coil which consisted of an ovoid concave coil (8.5 ± 0.6 x 11.5 ± 1 cm^2) consisting of 120 turns of copper wire (0.8 mm diameter) covered with insulating tape. This was fitted over padding to the outer aspect of the affected shoulder with the coil protruding from the centre of the pad. An elasticated chest strap and Velcro arm strap held it in place. A bi-osteogen pulse generator was used. This was a portable unit operated by rechargeable nickel cadmium batteries. The signal was set at 72 ± 3 Hz with a pulse duration of 380 ± 10 µs. When not being used the unit was kept on charge *Dose:* continuously for an 8-hour period *Frequency of administration*: daily for 8 weeks **Control: Low dose coil (2 hours/day) PEMF therapy** *Components of intervention*: participants were instructed to use the same apparatus as described above *Dose*: continuously for an 8-hour period (but the coil switched itself off after 2 hours without indication to the participant) *Frequency of administration*: daily for 8 weeks
Outcomes	Outcomes assessed at 2, 4, 6, and 8 weeks • Overall pain (scale not reported) • Active range of motion in abduction, flexion and rotation using a goniometer • Global assessment of treatment success • Rest pain (scale not reported) • Pain on movement (scale not reported) • Night pain (scale not reported) • Pain on resisted movements of abduction, external rotation and internal rotation graded on a 4-point scale (0 = no pain; 1 = slight pain but full power; 2 = moderate pain with reduced power; 3 = severe pain with absent power against even minor resistance
Notes	**Conflicts of interest:** not reported **Funding:** E.B.I Medical Systems provided the apparatus and support

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly allocated to a 2 h treatment (Group I) or an 8 h treatment (Group II)."

Chard 1988 (*Continued*)

		Comment: There was no information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Group I received treatment with a 'live unit' and coil that switched itself off after 2 h without indication to the patient, and for group II a standard unit without any automatic switch off was used." Quote: "All patients were instructed to use the apparatus for a continuous 8 h period each day, and neither assessor nor patient was aware of the treatment group" Comment: Participants were blind to treatment whereas personnel were not (though this is unlikely to have affected the outcomes)
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Unclear risk	Comment: There was no information on whether the assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "Forty nine patients fulfilled the entry criteria and were entered into the study, 25 patients in the 2 h Group I and 24 in the 8 h Group II. Unfortunately, 6 patients in Group I failed to co-operate in using the equipment for a continuous 8 h treatment. This resulted in interrupted treatment which reset the timing device, and hence they received more than 2 h PEMF per day. Thus, these patients had to be excluded from further analysis, and so the data of the remaining 19 patients in Group I were used." Comment: There was more drop-out in the control group (all for the same reason), and it is unclear what impact this could have had on the results
Selective reporting (reporting bias)	Unclear risk	Comment: For some outcomes, outcome data were reported in Figure (as means with unlabelled error bars), whereas for other

Chard 1988 (*Continued*)

		outcomes, the trialists only indicated that there was no significant difference between groups. However, this pattern of reporting was not associated with whether results were significant or not (i.e. some non-significant findings were presented in Figure format). However, without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Clews 1987

Methods	**Study design**: Parallel group RCT **Setting:** Australian Institute of Sport, Australia **Intervention 1:** Therapeutic ultrasound plus ice **Intervention 2:** Massage plus ice **Control:** Placebo ultrasound plus ice **Source of funding:** Not reported
Participants	**Diagnostic label used by trialists:** Rotator cuff tendinitis **Criteria for defining the shoulder condition being treated** • Unilateral shoulder pain; and • localised dull pain in the antero/lateral shoulder region with no radiation of symptoms; and • tenderness to palpation at least on the long head of biceps in the bicipital groove, the insertion of the supraspinatus tendon or the musculotendinous portion of the long head of biceps; and • pain on resisted shoulder abduction, flexion or resisted supination of the forearm; and • a positive impingement sign; and • absence of cervical sign symptoms or signs pointing the problem being referred from the neck, including negative Elvey's test; and • no treatment other than ice having been instituted for the injury **Inclusion Criteria (not listed above)** • None **Exclusion Criteria (not listed above)** • None **Baseline characteristics** *Overall cohort of participants* Number randomised: 18 (6 per group) Age (mean and SD, or range): not reported Sex: not reported Duration of symptoms: not reported

Clews 1987 (*Continued*)

Interventions	**Intervention 1: Therapeutic ultrasound** *Components of intervention*: pulsed ultrasound *Dose*: 15 min at an intensity 0.8 W/cm^2 *Frequency of administration*: every day for 3 days **Intervention 2: Massage** *Components of intervention*: massage of the long head of biceps, biceps tendon, pectorals, supraspinatus and infraspinatus muscle *Dose*: 15 min *Frequency of administration*: every day for 3 days **Control 2: Sham ultrasound** *Components of intervention*: sham ultrasound *Dose*: 15 min *Frequency of administration*: every day for 3 days **All groups** *Components of intervention*: ice packs applied to the affected shoulder, and NSAIDs *Dose*: Ice for 15 min twice daily and 1 tablet of diclofenac sodium (Voltaren) taken with meals *Frequency of administration*: every day for 3 days
Outcomes	Outcomes assessed at 3 days • Overall pain: VAS scale on strength testing from 0-10 with a higher score indicating worse pain • Strength (maximal isometric force production, measured in peak force)
Notes	**Conflicts of interest:** not reported **Funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "After the diagnosis had been made and inclusion in the study was confirmed, each subject was randomly assigned to one of these three groups." Comment: There was no information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention

Clews 1987 (*Continued*)

Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "One co-author did all the testing and was not aware of the subjects' group assignment" Comment: Outcome assessor of objective outcomes was blind to treatment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: There was complete follow-up of all randomised participants in the study
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias were identified

Dogan 2010

Methods	**Study design**: Parallel group RCT **Setting:** University, Turkey **Intervention:** Low-level laser therapy (LLLT) plus exercise plus ice **Control:** Placebo LLLT plus exercise plus ice **Source of Funding:** Not reported
Participants	**Diagnostic label used by trialists:** Subacromial impingement syndrome **Criteria for defining the shoulder condition being treated** • Subacromial impingement syndrome on physical and neurological exam (no other details provided) **Any restriction on duration of symptoms** • None **Inclusion Criteria (not listed above)** • None **Exclusion Criteria (not listed above)** • Presence of acute trauma • Acromioclavicular or glenohumeral arthritis • Rotator cuff tear • Neurologic or inflammatory diseases • Referring pain due to neck pathologies and history of physical therapy • Surgery, subacromial or intra-articular injection within 6 months

	Baseline characteristics *Intervention: LLLT plus exercise program plus ice* Number randomised: 30 Number included in analyses: 30 Age mean (SD): 53.7 ± 12.6 years Sex: F/M 20/10 Duration of symptoms mean (SD): 11.66 ± 18.04 months *Control: Placebo LLLT plus exercise program plus ice* Number randomised: 22 Number included in analyses: 22 Age mean (SD): 53.45 ± 9.64 years Sex: F/M 13/9 Duration of symptoms mean (SD): 15.27 ± 25.13 months
Interventions	**Intervention: LLLT** *Description of modality used*: LLLT using a Gallium-Aluminum-Arsenide (GaAlAs, infrared laser) diode laser device (Chattanooga group) with a wave-length of 850 nm, power output of 100 mV, continuous wave and 0.07 cm^2 spot area. The laser was applied at a maximum of 5-6 painful points for 1 min at each point over subacromial region of the shoulder *Dose*: 3 J/cm^2 at each point for 1 min *Frequency of administration*: once per day, 5 times per week for 14 sessions **Control: Placebo LLLT** *Description of modality used*: Placebo laser was applied in the same way as above but the device was turned off during treatment sessions *Dose*: none *Frequency*: once per day, 5 times per week for 14 sessions **Both groups** *Description of modality used*: cold pack applied by a physiotherapy and exercise programme which included range of motion, stretching and progressive resistance exercises *Dose*: cold pack (10 min); exercise (10-15 repetitions) *Frequency*: once per day, 5 times per week for 14 sessions *Any additional treatment during trial*: none
Outcomes	Outcomes assessed at 3 weeks • Function: SPADI from 0-100 with a higher score indicating worse disability • Overall pain: VAS from 0 (no pain) to 10 (severe pain) • Range of motion: flexion, extension, abduction, adduction, internal and external rotation using a goniometer (unclear if active or passive) • Adverse events
Notes	**Conflicts of interest:** not reported **Funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Low risk	Quote: "Randomization was allocated by numbered envelopes method. Treatment program either LLLT or placebo was written in these closed envelopes and patients selected one of them and randomly assigned into two groups." Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Low risk	Comment: An adequate method was used to conceal the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Placebo laser was applied in the same way but the device was turned off during treatment sessions. Patients and physiotherapist were asked to use protective eyeglasses during therapy for safety." Quote: "Both of the physicians and patients were blinded. Only the physiotherapist was aware of the procedure." Comment: participants were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "At the beginning, sociodemographic (age, sex) and clinic (disease duration, localization of shoulder pain) characteristics of the patients were recorded. Pain severity, range of motion and functional status of all patients were evaluated before and after the treatment by different physicians. Both of the physicians and patients were blinded." Comment: Assessors of objective outcomes were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All patients were able to complete the therapy program"
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results

Dogan 2010 (*Continued*)

Other bias	Low risk	Comment: No other sources of bias identified

Downing 1986

Methods	**Study design**: Parallel group RCT **Setting:** Outpatient clinic, USA **Intervention:** Therapeutic ultrasound plus exercise plus NSAID **Control:** Sham ultrasound plus exercise plus NSAID **Source of Funding:** Not reported
Participants	**Diagnostic label used by trialists:** Supraspinatus tendinitis or subacromial bursitis **Criteria for defining the shoulder condition being treated** • Presence of pain during at least one activity (sleep, dress, work, grooming, sports) and at the end of at least one range of motion test (scapulothoracic flexion, scapulothoracic abduction, glenohumeral flexion, glenohumeral abduction, internal rotation, external rotation) • A loss of 10 degrees of more in one or more range of motion tests • Baseline glenohumeral abduction greater than 45 degrees (to eliminate those participants with established 'frozen shoulders') **Any restriction on duration of symptoms** • Longer than 1 month and less than 1 year **Inclusion Criteria (not listed above)** • None **Exclusion Criteria (not listed above)** • Complicating rheumatic disorder or direct shoulder trauma • Previous ultrasound treatments for any condition • New medical therapy (including intra-articular or intrabursal corticosteroid) in the week before entry to study **Baseline characteristics** *Intervention: Therapeutic ultrasound* Number randomised: 11 Number included in analyses: 11 Mean age: 54 years Sex: F/M 5/6 Mean duration of symptoms: 6.5 months *Control: Sham ultrasound* Number randomised: 9 Number included in analyses: 9 Mean age: 52 years Sex: F/M 7/2 Mean duration of symptoms: 6.2 months
Interventions	**Interventions: Therapeutic ultrasound** *Description of modality used*: the applicator (sound head) had a radiating surface of 10 cm ^{2} and a continuous output was used. Aquasonic gel was the coupling medium applied to the shoulder. Gel was warmed in a beaker of water on a hot plate before each application so that the gel was hot to touch but tolerable. Ultrasound covered a field size of 150

	cm^2. If the participant appeared to have localised tendinitis, ultrasound was localised to the particular area in addition to the anterior, medial and posterior aspects of the glenohumeral joint. If spasm existed in the trapezius muscle of supraspinatous muscle area, ultrasound was applied to that area for an addition 5 min *Dose*: frequency of 1 MHz. Intensity used throughout the study was determined by participant's tolerance. The maximal dosage was defined as the intensity at which the participant experienced a dull ache in the joint. An intensity 10% lower than the maximal (submaximal dosage) was used for each treatment. Mean intensity: 1.2 W/cm^2. Each treatment lasted 6 min and covered a field size of about 150 cm^2 *Frequency of administration*: 3 treatments per week for 4 weeks (total 12 sessions) **Control: Sham ultrasound** *Description of modality used*: ultrasound was administered in the same manner as the true ultrasound except the machine was disconnected to the power outlet *Dose*: mean intensity: 1.3 W/cm^2; no frequency *Frequency of administration*: 3 treatments per week for 4 weeks (total 12 sessions) **Both groups** *Description of modality used*: range of motion exercises (active, active assisted and passive) following each true or sham ultrasound treatment, home exercise, and 5 participants per group were also receiving NSAIDs *Frequency of administration*: 3 treatments per week for 4 weeks (total 12 sessions)
Outcomes	Outcomes assessed at 4 weeks • Function measured by participant's perception of interference in activities (sleeping, dressing, work, grooming, sports activities). At baseline participants stated if their condition interfered with these activities of daily living. At the final assessment, the therapist asked them whether they had improved, worsened or remained the same in performing the 5 activities • Overall pain measured by a 4-point descriptive scale (0 = asymptomatic, 1 = minimal, 2 = moderate, 3 = severe) • Global assessment of treatment success: participant's perceived overall status measured by scale (much better, better, no change, worse) • Global assessment of treatment success: participant's overall status determined by the physician and physical therapist by scale (much better, better, no change, worse) • Active and passive range of movement (scapulothoracic flexion, scapulothoracic abduction, glenohumeral flexion, glenohumeral abduction, internal rotation and external rotation) measured by goniometer
Notes	**Conflicts of interest:** not reported **Funding:** National Institutes of Health Multipurpose Arthritis Center; from the National Arthritis Foundation; and from the Arthritis Foundation, Connecticut chapter

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "We randomly assigned the patients according to a table of random numbers to receive the true or sham US." Comment: An adequate method was used

Downing 1986 (*Continued*)

		to generate the allocation sequence
Allocation concealment (selection bias)	Low risk	Quote: "We randomly assigned the patients according to a table of random numbers to receive the true or sham US. After the therapist turned the intensity of US to the submaximal dosage, she covered the controls of the machine so that neither she nor the patient were aware of whether true US was being administered. A third party kept the envelopes containing numbers that assigned the patients to the true or sham group. This person was responsible for leaving the machine connected to the electrical outlet if the patient was to receive true US or disconnecting the machine from the electrical plug if the patient was to receive sham US. " Comment: An adequate method was used to conceal the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "We heated the gel to blind the sham patients, because the coupling medium becomes warm during the administration of true US" Quote: "After the therapist turned the intensity of US to the submaximal dosage, she covered the controls of the machine so that neither she nor the patient were aware of whether true US was being administered." Quote: "As an extra precaution the therapist avoided touching the gel during and after each US application to prevent knowing, by the coolness or warmth, which treatment the patient received." Quote: "Both the patients and the therapist were inaccurate in guessing whether the sham or true US was used. Six patients (2 sham, 4 true) guessed correctly, and 3 (1 sham, 2 true) guessed incorrectly. Eleven (6 sham, 5 true) were uncertain whether they had received the US. The therapist guessed 11 patients (3 sham, 8 true) correctly and 6 (4 sham, 2 true) incorrectly. She was uncertain about 3 patients (2 sham, 1 true)" Comment: participants and personnel were blinded

Downing 1986 (*Continued*)

Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "The therapist and physician evaluated the patients independently of one another recording present and past medical history." Quote: "After the therapist turned the intensity of the US to the submaximal dosage, she covered the controls of the machine so that neither she nor the patient were aware of whether true US was being administered. " Comment: Assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: Trialists did not report whether there were any dropouts, losses to follow-up or exclusions, or the number of participants included in each analysis
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Ebenbichler 1999

Methods	**Study design**: Parallel group RCT **Setting:** Outpatient clinics and private practices, Austria **Intervention:** Pulsed therapeutic ultrasound **Control:** Sham ultrasound **Source of funding:** Not reported
Participants	**Diagnostic label used by trialists:** Calcific tendinitis of the shoulder **Criteria for defining the shoulder condition being treated** • Idiopathic calcific tendinitis type 1 (clearly circumscribed and dense appearance on radiography) or type 2 (dense or clearly circumscribed appearance) according to the classification of Gartner and Heyer. Diameter of calcification had to exceed 5.0 mm **Any restriction on duration of symptoms** • Mild to moderate pain present for more than four weeks OR restricted range of

	motion of the affected shoulder(s) **Inclusion Criteria (not listed above)** • None **Exclusion Criteria (not listed above)** • Idiopathic calcific tendinitis type 3 (translucent or cloudy appearance without clear circumscription) • Systemic diseases associated with increased risk of calcification (such as gout, hypercalcaemia of any cause and various rheumatic diseases) as indicated by pre-defined pathological findings • Previous surgery for calcifications or percutaneous needle aspiration, ultrasonography or shock-wave therapy for calcific tendinitis • Glucocorticoid injection in the shoulder within three months preceding the study • Regular use of analgesic or anti-inflammatory drugs for relief of tendinitis **Baseline characteristics** *Intervention: Pulsed ultrasound* Number randomised: 35 shoulders Number included in analyses: 32 shoulders Mean age: 49 ± 11 years Sex: not reported Median duration of symptoms: 8 weeks, IQR: 4-20 weeks *Control: Sham treatment* Number randomised: 35 shoulders Number included in analyses: 29 shoulders Mean age: 54 ± 10 years Sex: not reported Median duration of symptoms: 8 weeks, IQR: 4-19weeks
Interventions	**Intervention: Pulsed ultrasound** *Description of modality used*: ultrasound therapy used with pulsed mode (1:4) over the calcifications. The transducer was 5 cm^2 and an aquasonic gel was used as the couplant. To optimise treatment of the affected areas in the supraspinatus and infraspinatus muscles and tendons, the transducer was moved slowly in circles distal to the lateral acromion and the acromial part of the clavicle while the participant flexed his or her upper arm and internally rotated the forearm. Treatment of calcium deposits in the subscapularis muscle was performed with the participant's upper arm in an abducted and externally rotated position. The device was standardised initially, and output was monitored regularly by means of a simple underwater radiation balance. An on-off key introduced into the transducer circuit allowed normal ultrasonic output as well as mock insonation (sham treatment) *Dose*: frequency: 0.89 MHz; intensity: 2.5 W/cm^2; administered for 15 min per session *Frequency of administration*: 24 x 15 min sessions; first 15 treatments given daily 5 times per week and the remaining were given 3 times a week for 3 weeks **Control: Sham ultrasound** *Description of modality used*: ultrasound therapy used in same method as true treatment however ultrasonic generator was not turned on *Dose*: none *Frequency of administration*: 24 x 15 min sessions; first 15 treatments given daily 5 times per week and the remaining were given 3 times a week for 3 weeks *Any additional treatment during trial*: occasional pain relief - analgesic drugs (usually

Ebenbichler 1999 (*Continued*)

	tramadol); NSAIDs were not allowed
Outcomes	Outcomes assessed at 6 weeks and 9 months • Function measured by Constant score; score: 1-100, higher score indicating better function • Overall pain (pain, pain on resisted movement, pain on active abduction) measured on pain score of Binder, score: 0-52, higher score indicating worse pain • Global assessment of treatment success ("clinical improvement", no other details provided) • Rest pain at night and during the day measured by 10 cm VAS, score: 0-10, higher score indicating worse pain • Pain on motion at night and during the day measured by 10 cm VAS, score: 0-10, higher score indicating worse pain • Pain on resisted abduction in the neutral position and eternal and internal rotation of shoulder measured by 4-point scale; score: 0-3; 0 = absence of pain, 1 = slight pain but full power, 2 = moderate pain and reduced power, 3 = severe pain with no power against even minimal resistance • Quality of life measured on a 10 cm VAS, score 0-10; 0 = excellent quality of life, 10 = worst imaginable • Work disability • Require surgery • Adverse events
Notes	**Conflicts of interest:** not reported **Funding:** not reported Trialists randomised shoulders rather than participants, but did not control for the correlation between outcomes in participants with bilateral shoulder pain

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "A spreadsheet program (Lotus Symphony, Lotus) was used to generate a list of random numbers. Since patients could have calcific tendinitis in one or both shoulders, randomization was conducted according to shoulders rather than patients. Thus, a patient could receive sham treatment for one shoulder and ultrasound treatment for the other." Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Low risk	Quote: "A therapist who was not involved with treatment handed out the treatment assignments, which were in sealed, opaque envelopes." Comment: An adequate method was used

Ebenbichler 1999 (*Continued*)

		to conceal the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The patients and the therapists applying the therapy were blinded to the treatment assignments. The therapist who handed out the treatment assignments also switched the ultrasonic generator to either active or sham mode so that they therapist applying the therapy were blinded. Since the intensity of ultrasound therapy was usually below the threshold of sensitivity, patients were theoretically unable to distinguish between genuine and sham ultrasonography." Comment: Patients and personnel were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "Radiography was performed at each follow-up visit, and the results were assessed independently by two radiologists who were unaware of the patients' treatment assignments" Comment: Assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "A total of 63 consecutive patients (70 shoulders) were enrolled. Nine patients (nine shoulders, 13 percent) did not complete treatment: seven (seven shoulders; three in the ultrasound-treatment group and four in the sham-treatment group) dropped out soon after the first session, and two patients (two shoulders) in the sham-treatment group withdrew because of excessive pain. The characteristics of these patients did not differ significantly from the characteristics of those who completed the study. A total of 54 patients (61 shoulders: 32 in the ultrasound-treatment group and 29 in the sham-treatment group) completed the treatment. Of the seven patients who received bilateral treatment, five received ultrasound treatment for one shoulder and sham treatment for the other, one received bilateral ultrasound

Ebenbichler 1999 (*Continued*)

		treatment, and one received bilateral sham treatment. Of these, 50 patients (56 shoulders: 31 in the ultrasound-treatment group and 25 in the sham-treatment group) also completed the nine-month follow-up." Comment: The characteristics of the patients who did not complete the study did not differ significantly from the characteristics of those who did complete the study. Reasons for dropping out of the study were reported
Selective reporting (reporting bias)	Unclear risk	Comment: No outcome data for rest pain at night and pain on motion at night was reported, despite these outcomes being specified in the methods section. Further, "clinical improvement" was reported as an outcome in the results section but was not specified in the methods section, and it was not clear how improvement was defined. Also, without a trial protocol it is unclear if other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

England 1989

Methods	**Study design**: Parallel group RCT **Setting:** Rheumatology outpatient clinic, UK **Intervention 1:** Laser therapy **Intervention 2:** NSAID **Control:** Placebo laser therapy **Source of funding:** Not reported
Participants	**Diagnostic label used by trialists:** Supraspinatus or bicipital tendinitis **Criteria for defining the shoulder condition being treated** • Supraspinatus tendinitis (a full range of passive glenohumeral movement with pain on restricted abduction of the shoulder) or bicipital tendinitis (pain on resisted flexion of the elbow and resisted supination of the forearm in the presence of a full range of passive glenohumeral movement) **Any restriction on duration of symptoms** • At least four weeks duration **Inclusion Criteria (not listed above)** • None **Exclusion Criteria (not listed above)** • Inflammatory arthropathies

England 1989 (*Continued*)

	• Degenerative changes • Calcific periarthritis on shoulder X-rays **Baseline characteristics** *Overall cohort of participants if reported* Number of participants at enrolment: 30 Number randomised: 30 (10 in each group) Number included in analyses: not reported Age: mean: 48 years (range: 18-78 years) Sex: 15 males, 15 females Diagnosis: equal number of supraspinatus tendinitis and bicipital tendinitis Duration of symptoms: mean: 12.5 weeks (range: 5-56 weeks)
Interventions	**Intervention 1: Laser therapy** *Description of modality used*: active infrared laser therapy - gallium-arsenic semiconductor diode operating in the infrared region at 904 nm wavelength. Laser was applied to point of maximal tenderness with the shoulder abducted, slightly extended and medially rotated 90 degrees *Dose*: 4000 Hz frequency with 180 nanosecond pulses, peak power output 10 W for 5 min of 3 mW therapy *Frequency of administration*: 3 times weekly for 2 weeks **Intervention 2: Drug therapy** *Description of modality used*: naproxen sodium 550 mg twice daily for the 2-week treatment period **Control: Dummy laser therapy** *Description of modality used*: same laser used as active laser therapy however laser not turned on. A cardboard screen was used to blind the participant to light emission from the laser *Dose*: none *Frequency of administration*: 3 times weekly for 2 weeks
Outcomes	Outcomes assessed at 2 weeks • Function: VAS, score: 0-10; higher number indicating worse function • Overall pain: VAS, score: 0-10; higher number indicating higher pain intensity • Active range of motion (flexion, extension and abduction) measured by shoulder goniometry
Notes	**Conflicts of interest:** not reported **Funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly assigned to three treatment groups." Comment: There was no information on how the allocation sequence was generated

England 1989 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "A cardboard screen was used to blind the patient to light emission from the laser. Thus the patient and assessor were blind to therapy though the therapists were not for reasons of safety and practicality." Comment: Participants receiving active or placebo laser were blinded, but were not blinded in regards to laser therapy versus NSAID
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "The patient and assessor were blind to therapy". Comment: Assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: Trialists did not report whether there were any dropouts, losses to follow-up or exclusions, or the number of participants included in each analysis
Selective reporting (reporting bias)	High risk	Comment: Outcome data only fully reported for outcomes that were statistically significant. Also, without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Eslamian 2012

Methods	**Design:** Parallel group RCT **Setting:** Physical Medicine and Rehabilitation Clinic of Tabriz Shohada Hospital, Iran **Intervention:** Low-level laser therapy (LLLT) plus routine physiotherapy (therapeutic ultrasound, TENS and exercise programme) **Control:** Placebo laser plus routine physiotherapy **Source of funding:** Not reported, but stated that "The authors also certify that they have no affiliation with or financial involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in the manuscript."
Participants	**Diagnostic label used by trialists:** Rotator cuff tendinitis **Inclusion criteria** • 2 out of 5 of the following criteria: ○ painful arc syndrome ○ impingement test ○ Hawkins-Kennedy test ○ palpation sensitivity ○ supraspinatus test • Since (according to the trialists) 30% of the cases with rotator cuff tendinitis are accompanied by biceps tendinitis, participants with both symptoms were included **Exclusion criteria** • Shoulder joint pain associated with cervical radiculopathies, acromioclavicular joint (ACJ) dysfunction or frozen shoulder • History of oral corticosteroid intake or corticosteroid injection • Complete or incomplete tear of rotator cuff tendons • Systemic inflammatory diseases such as rheumatoid arthritis. **Baseline characteristics** Total n randomised = 50 participants Total n analysed = 50 participants *Intervention: LLLT* Number randomised: 25 Mean ± SD (range) age: 50.16 ± 12.10 (25-68) years Sex: F/M 10/15 Mean ± SD (range) duration of symptoms: not reported *Control: Placebo LLLT* Number randomised: 25 Sex: F/M 16/9 males Mean ± SD (range) age: 50.2 ± 11.72 (25-75) years Mean ± SD (range) duration of symptoms: not reported
Interventions	**Intervention: LLLT** *Components of intervention*: LLLT was performed by gallium-aluminum-arsenide (Ga-Al-As) infrared diode laser 476, wavelength 830 nm, average power output of 100 mW, and energy density or intensity of 4 J/cm^2. Laser irradiation was delivered in continuous-wave mode on 1-cm^2 surface area with 20-s irradiation for each point and total treatment duration of 5 min over the painful regions of shoulder up to 10 painful points *Frequency of administration*: 3 times a week with 10 sessions in total (i.e. 3-4 weeks) **Control:** Placebo**LLLT** *Components of intervention*: wearing eyeglasses and using a probe laser on the shoulder, but in off mode *Frequency of administration*: 3 times a week with 10 sessions in total (i.e. 3-4 weeks)

	Both groups *Components of intervention*: therapeutic parameters for deep-heat or ultrasound application consisted of pulse mode, 1-MHz frequency, pulse intensity: 1.5-2 W/cm^2 and duty factor: 25% for 5-min treatment duration with slowly circular movements of ultrasound probe over painful regions of shoulder. Therapeutic parameters for TENS therapy included high frequency currents of 100 Hz, low current intensity of 10-30 mA, and short pulse width or 50 μs. Treatment duration for both surface heat and TENS was approximately 20 min for each modality. Also, participants were given an exercise program that included range of motion, and stretching and strengthening exercises of shoulder abductors and flexors. Each exercise was performed once a day with 10 repetitions *Frequency of administration*: 3 times a week with 10 sessions in total (i.e. 3-4 weeks)
Outcomes	Outcomes assessed at 6 weeks (3 weeks post treatment cessation) • Function using the Croft Shoulder Disability Questionnaire (scored from 0-22, with higher scores denoting more disability) • Overall pain using a 10 cm VAS, with 0 indicating "no pain" and 10 indicating "unbearable pain" • Active and passive range of motion (abduction and external rotation) using a goniometer
Notes	**Conflicts of interest:** "The authors declare that they have no conflicts of interest." **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "All of the patients, who had inclusion criteria, were referred to physical medicine and rehabilitation clinic and assigned to two equal groups randomly. After obtaining the written consent, the patients were given closed packets including letters A and B, and in this way they were allocated into an experimental group (A: laser+ physiotherapy) and a control group (B: physiotherapy only)." Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Low risk	Comment: An adequate method was used to generate the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "All treatment regimes were administrated by an expert physical therapist. To form a double-blind study, only the physiotherapists knew the patients in the experimental and control groups. Patients were not aware of being given or not being given

Eslamian 2012 (*Continued*)

		the effective laser therapy and the examiner physician was not aware of the group's label. The sham laser was also used to induce a placebo laser effect in the control group of patients. Wearing eyeglasses and using a probe laser on the shoulder, but in off mode, was in fact the method of using the sham laser in our study. Finally, the physiotherapist announced the patient's experimental or control group label." Comment: Participants were blinded.
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "To form a double-blind study, only the physiotherapists knew the patients in the experimental and control groups." Comment: Assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: There were no drop-outs, exclusions or losses to follow-up, and outcome data were reported as based on the total number of randomised participants
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Eyigor 2010

Methods	**Study design**: Parallel group RCT **Setting:** Outpatient clinic, Turkey **Intervention:** Transcutaneous electrical nerve stimulation (TENS) plus home exercises **Control:** Glucocorticoid injection plus home exercises **Source of funding:** Not reported
Participants	**Diagnostic label used by trialists:** Rotator cuff tendinitis **Criteria for defining the shoulder condition being treated** • Rotator cuff tendinitis detected by shoulder ultrasonography

Eyigor 2010 (*Continued*)

	Any restriction on duration of symptoms • At least 3 months **Inclusion Criteria (not listed above)** • Age: 18-80 years old **Exclusion Criteria (not listed above)** • Inflammatory arthritis (rheumatoid arthritis, ankylosing spondylitis etc) • Active synovitis in the joints • History of shoulder surgery • History of nerve blocks to the shoulder • Intra-articular injection within the last 3 months • Trauma within the last 6 months • Physical therapy within the last 6 months • Rotator cuff total rupture • Very severe pain (VAS ≥ 9) • Shoulder instability • Positive drop arm test • Presence of calcific tendinitis • Advanced osteoarthritis • Referred pain in the shoulder • Neurological impairments (stroke, Parkinson's disease, paresis) • Severe cardio-vascular disease (acute myocardial infarction, congestive heart failure, uncontrolled hypertension) • Unstable chronic or terminal illness (diabetes mellitus, malignancies) • Bleeding problems • Major depression • Severe cognitive impairment • Presence of pacemaker • Severe musculoskeletal impairment **Baseline characteristics** *Intervention: TENS plus home exercises* Number randomised: 20 Number included in analyses: 20 Age: mean: 57.60 ± 9.92 years Sex: female: 14; male: 6 Duration of symptoms: mean: 8.6 ± 4.5 months *Control: Glucocorticoid injection plus home exercises* Number randomised: 20 Number included in analyses: 20 Age: mean: 60.8 ± 12.5 years old Sex: female: 15; male: 5 Duration of symptoms: mean: 8.9 ± 5.1 months
Interventions	**Intervention: TENS** *Description of modality used*: TENS on the anterior and posterior aspects of the joint *Dose*: mean frequency of 100 Hz, 15 mA amplitude, 150 µsn *Frequency of administration*: 5 times per week for 15 sessions (i.e. 3 weeks) **Control: Glucocorticoid injection** *Description of modality used*: all injections were performed by single physician specialised in the field. The injection procedure was standardised. In order to perform the surgical

	procedure under sterile conditions, the intra-articular injection procedure was performed in the operating room. Each participant was placed in a supine position, and the skin overlying the operating area was prepared and draped. Fluoroscopy was adjusted to show the shoulder joint in antero-lateral position. Acromioclavicular joint entry point was marked and local anaesthetic was applied to the skin (0.5 cc prilocaine). A 22 G spinal needle was inserted into the acromioclavicular joint. The injection was placed through the subacromial space and it was observed to penetrate into the glenohumeral joint. Entry into the joint was proved by giving 0.5 cc contrast substance. The prepared mixture was injected as 3.5 cc to glenohumeral joint, 2.5 cc to subacromial space and 1 cc to acromioclavicular joint *Dose*: the prepared mixture consisted of 0.5 cc triamcinolone (40 mg/ml) (Kenacort-A) , 3.5 cc bupivacaine (5 mg/ml) (Marcaine), 3 cc serum physiologic *Frequency of administration*: once **Both groups: Home exercises** Exercises for increasing the range of motion, strengthening exercises and finger ladder exercises were recommended. For each of the exercises, participants were provided with simple, step-by-step written instructions with illustrations *Any additional treatment during trial*: only paracetamol (maximum 4 g daily) allowed
Outcomes	Outcomes assessed at 1 week, 4 weeks and 12 weeks • Function measured by Turkish translation of Shoulder Disability Questionnaire (0-100, where the higher the score, the greater the disability) • Rest pain measured by VAS 0-10 • Pain on motion measured by VAS 0-10 • Night pain measured by VAS 0-10 • Global assessment of treatment success measured by participants and physicians on 5-point ordinal scale: 0 = ineffective, 1 = minor effects, 2 = moderately effective, 3 = good results, 4 = very good results • Active and passive range of motion (flexion, abduction, external rotation, internal rotation) measured using a goniometer • Quality of life measured by Short Form-36
Notes	**Conflicts of interest:** not reported **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomised to the two groups by using double randomisation from the random number table." Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed

Eyigor 2010 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "The assessments were performed by the same physician who was blinded to the treatment protocols." Comment: Assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: There were no losses to follow-up. All outcome data were reported as based on all randomised participants
Selective reporting (reporting bias)	Low risk	Comment: Outcome data were fully reported for all outcomes specified in the methods section. No protocol was available, but all patient-important outcomes were measured in this trial so it is unlikely that other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Galace de Freitas 2014

Methods	**Study design:** Parallel group RCT **Setting:** Outpatient rehabilitation of a public hospital, Brazil **Intervention:** Pulsed electromagnetic field (PEMF) for 3 weeks followed by exercises for 6 weeks **Control:** Placebo PEMF for 3 weeks followed by exercises for 6 weeks **Source of funding:** Not reported
Participants	**Diagnostic label used by trialists:** Shoulder impingement syndrome **Criteria for defining the shoulder condition being treated** • Medical diagnosis of grade I or II shoulder impingement syndrome based on a history of shoulder pain for at least 3 months • Received a clinical examination and ultrasonography or magnetic resonance imaging, according to Neer's criteria • Able to actively elevate their shoulders in overhead activities

	Any restriction on duration of symptoms • At least 3 months **Inclusion Criteria (not listed above)** • Both men and women **Exclusion Criteria (not listed above)** • Had a neurologic disorder • Had an injury to the cervical region, elbow, or hand • Had rheumatoid arthritis • Had a heart condition • Had previous surgery involving the upper extremities • Were pregnant • Had received intra-articular anti-inflammatory infiltrations in the past 60 days • Had other pathologic disorders of the shoulder such as hooked acromion, osteoarthritis, adhesive capsulitis, or traumatic labrum tears **Baseline characteristics** *Intervention: PEMF plus exercises* Number randomised: 26 Number included in analyses: 26 Age: mean: 50.1 ± 8.2 years old Sex: female: 16; male: 10 Duration of symptoms: mean: 22 ± 17.7 months *Control: Placebo PEMF plus exercises* Number randomised: 30 Number included in analyses: 30 Age: mean: 50.8 ± 9.6 years Sex: female: 20; male: 10 Duration of symptoms: mean: 21.2 ± 19 months
Interventions	**Intervention: PEMF** *Components of intervention*: electrodes were positioned on the anterior and posterior part of the shoulder joint with the subject positioned in lateral decubitus. The equipment used was a previously calibrated Magnetherp 330 *Dose*: device pulsed with a frequency of 50 Hz and an intensity of 20 mT or 200 G for 30 min *Frequency of administration*: 3 times a week for 3 weeks **Control: Placebo PEMF** *Components of intervention*: same equipment used and participants remained in the same position as the active group *Dose*: device kept on standby mode without any electromagnetic field being applied, for 30 min *Frequency of administration*: 3 times a week for 3 weeks **Both groups: Exercises** *Components of intervention and Dose*: after 3 weeks of active or placebo PEMF, all subjects initiated a therapeutic exercise programme, comprised of range of motion and strengthening exercises (see below) Range of motion exercises • Pendular exercise: bend forward 90 degrees at waist using table for support. Body in a circular pattern to move arm clockwise and counterclockwise, 3 sets of 1 min • Doorway pectoral stretch: bring arm out to the side with elbow bent, forearm

	contacting wall. Turn your body away from the wall until you feel a stretch, 3 sets of 30 seconds • Cross-body posterior shoulder stretching: bring arm across your body and use other hand to apply overpressure, pulling the elbow, 3 sets of 30 seconds • Shoulder external rotation cane stretch: grasp cane with affected elbow bent. Use unaffected arm to push hand back toward plinth, 3 sets of 10 repetitions Strengthening exercises • Resisted shoulder medial rotation (neutral): begin with forearm out to the side and elbow against body. Pull toward your abdomen, then slowly release. Can use towel in armpit if more comfortable, 10 sets of 10 seconds • Resisted shoulder lateral rotation: begin with hand in front of the stomach. Pull away from abdomen, then slowly release. Can use towel in armpit if more comfortable, 10 sets of 10 seconds • Resisted scapular protraction: grasp tube while lying on your back with arm flexed to 90 degrees. Punch arm up toward the ceiling while keeping arm straight. Your shoulder blade should lift off table, 3 sets of 10 repetitions • Sidelying lateral rotation: lie on uninvolved side, with involved arm at side of body and elbow bent to 90 degrees. Keeping the elbow of involved arm fixed to side, raise arm, 3 sets of 10 repetitions • Push Up: push-up plus - do a push-up (on either your hands or forearms) and then really push to bring your spine to the ceiling, 3 sets of 10 repetitions *Frequency of administration*: twice a week for 6 weeks (after the 3-week PEMF/placebo PEMF treatment period)
Outcomes	Outcomes assessed at 3 weeks, 9 weeks and 3 months • Function: Constant-Murley total score (0-100) with higher scores denoting better function • Function: UCLA total score (30 points) with higher scores denoting better function • Overall pain: VAS 0-10 where 0 = no pain and 10 = worst imaginable pain (during the last week) • Strength: external rotation, internal rotation and elevation using a handheld dynamometer. Strength values were measured in kg and were normalised by body mass (kg) using the following formula: (Strength/Body mass) x 100
Notes	**Conflicts of interest:** "No commercial party having a direct financial interest in the results of the research supporting this article has conferred or will confer a benefit on the authors or on any organization with which the authors are associated." **Funding:** not reported Trial registered in ClinicalTrials.gov (NCT01452204) Participants did not receive the exercise component until the end of 3 weeks of PEMF or placebo PEMF, so there are two comparisons in this trial: • PEMF for 3 weeks versus placebo PEMF for 3 weeks • PEMF plus exercise for 9 weeks versus placebo PEMF plus exercise for 9 weeks

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Random sequence generation (selection bias)	Low risk	Quote: "The assignment of subjects to the 2 groups was performed randomly using opaque, sealed envelopes, each containing the name of 1 of the groups (active PEMF or placebo PEMF). The envelopes were selected by an individual not involved in the study." Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Low risk	Quote: "The assignment of subjects to the 2 groups was performed randomly using opaque, sealed envelopes, each containing the name of 1 of the groups (active PEMF or placebo PEMF). The envelopes were selected by an individual not involved in the study." Comment: An adequate method was used to conceal the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "A single therapist (T.Y.F.) was responsible for setting up the equipment (active or placebo) before treatment in order to maintain the randomized, double-blind design. This therapist did not remain beside the patient during the session to avoid influencing the results. Two therapists (F.B.M., S.G.R.) were trained in delivering the exercise protocols used for the study and provided all treatment. These 2 therapists and all patients were blinded in relation to active PEMF or placebo PEMF treatment. " Comment: Participants and personnel were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Quote: "These 2 therapists and all patients were blinded in relation to active PEMF or placebo PEMF treatment." Comment: Participants, who self-reported some outcomes, were blinded
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "Finally, the examiner (D.G.F.) was blind to the group assignment of the patients and did not participate in the interventions." Comment: Assessor of objective outcomes was blinded

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "At 3 months, 4 subjects in the active PEMF group and 6 subjects in the placebo PEMF group were lost during follow-up. Therefore, all per-protocol data analyses were performed with 22 subjects in the active PEMF group and 24 subjects in the placebo PEMF group." Quote: "After the per-protocol data analysis, an intention-to-treat analysis was performed using the mean value obtained from the remaining subjects of each group." Quote: "The results of the intention-to-treat analysis were consistent with the per-protocol analysis, providing evidence that the missing data had no substantial influence on the overall results." Comment: The number and reasons for attrition were balanced between groups, so attrition is unlikely to have biased the results
Selective reporting (reporting bias)	Low risk	Comment: Trialists only specified strength as an outcome in the ClinicalTrials.gov registry entry (NCT01452204), yet reported data for pain and function in the manuscript. However, both pain and function are important outcomes to measure, so their addition to the trial is unlikely to be a reporting bias issue
Other bias	Low risk	Comment: No other sources of bias identified

Giombini 2006

Methods	**Study design**: Parallel group RCT **Setting:** Athletes who attended the Physiotherapy Department of the Sport Science Institute, Italy **Intervention 1:** Therapeutic ultrasound **Intervention 2:** Microwave diathermy **Intervention 3:** Exercise **Source of funding:** Not reported
Participants	**Diagnostic label used by trialists:** Supraspinatus tendinopathy **Criteria for defining the shoulder condition being treated:** diagnosis of supraspinatus tendinopathy of the dominant shoulder based on following 3 criteria: • impingement with a positive Hawkins sign in internal rotation or impingement in 90 degrees of forward flexion with forced external rotation;

	• pain with supraspinatus muscle testing in the 'empty can' position; • ultrasonographic evidence of nonhomogenous signal intensity without a frank tear in the supraspinatus tendon **Inclusion Criteria (not listed above)** • Gradual onset of pain • Participant engaged in sport at county, regional, national or international level and training in chosen sport at least 3 times a week • All participants were secondary referrals to the fellowship-trained sports physicians or orthopaedic surgeons with a special interest in sports traumatology or shoulder surgery from family practitioners or physical therapists, as well as tertiary referrals from other orthopaedic surgeons or sports physicians. All participants had undergone nonoperative management, including complete or modified rest from their sports, and several (3-8) 1-week cycles of NSAIDs. **Exclusion Criteria (not listed above)** • Athletes without full passive range of motion of the affected shoulder • Supraspinatus tendinopathy after a single traumatic episode • Severe neck pain, frozen shoulder, calcific tendinopathy, degenerative joint disease of the acromioclavicular or glenohumeral joint • Intra-articular or subacromial injections of corticosteroids • Clinical or ultrasonographic diagnosis of a rotator cuff tear • Previous surgery in the affected or contralateral shoulder **Baseline characteristics** *Intervention 1: Therapeutic ultrasound* Number randomised: 12 Mean (SD, range) age: 28.6 ± 6.6 years, range 19-43 years Sex: F/M 4/8 Duration of symptoms: not reported *Intervention 2: Microwave diathermy* Number randomised: 14 Mean (SD, range) age: 25.3 ± 4.8 years, range 19-37 years Sex: F/M 2/12 Duration of symptoms: not reported *Intervention 3: Exercises* Number randomised: 11 Mean (SD, range) age: 26.3 ± 6.2 years, range 20-38 years Sex: F/M 2/9 Duration of symptoms: not reported
Interventions	**Intervention 1: Therapeutic ultrasound** *Components of intervention*: continuous ultrasound was administered with the participant in the same position as participants receiving hyperthermia and by slowly moving the transducer in a circular fashion along the area distal to the anterior border of the acromion and the inferior third of a line between the glenoid fossa and the humeral head. A gel complant was used between the ultrasound transducer and the skin of the area undergoing treatment. A Level 730 device was used. It was equipped with an emission probe of 1-MHz frequency, a sound head with an effective radiating area of 10 cm^2 and a maximum output power of 22 W *Dose*: 1 MHz at an intensity of 2.0 W/cm^2; each session lasted 15 min *Frequency of administration*: 3 times a week for 4 weeks

	Intervention 2: Microwave diathermy *Components of intervention*: an ALBA Hyperthermia System was used which was equipped with a 433.92-MHz microwaves generator with a maximum output power of 100 W; a microstrip antenna applicator, with a curve shape specific for semicylindrical joint volumes of 20 to 30 cm in diameter and with a total radiating area of 240 cm^2 and an effective field size; and a pad of silicone 0.5 cm thick, filled with thermostatic deionized water that allows the greatest energy transfer to be achieved while preventing overheating of superficial tissues near the radiant source. A hydraulic thermoregulation and 1 or 2 skin temperature sensors were also used. The thermocouple was placed on the shoulder with the participant lying supine and the arm at 60 degrees of abduction and externally rotated. It was placed over the middle third of the joint line between the glenoid fossa and the humeral head. The thermocouple on the skin was perpendicular to the electromagnetic field *Dose*: 434 MHz; administered at a power between 50 and 70 W, a pilot temperature on the skin between 38 and 40 degrees centigrade, and a water pad temperature between 35 and 37 degrees centigrade according to the depth of the subcutaneous fat of each participant. Each session lasted 30 min *Frequency of administration*: 3 times a week for 4 weeks **Intervention 3: Exercises** *Components of intervention*: supervised and home exercises, consisting of pendular swinging in the prone position in flexion and extension of the shoulder and passive glenohumeral stretching exercises to tolerance *Frequency of administration*: supervised exercises once a week for 4 weeks; home exercises 5 min per day, every day for 4 weeks
Outcomes	Outcomes assessed at 4 weeks and 10 weeks • Function measured by Constant-Murley score (0-100) • Rest pain measured on a 0-10 VAS • Global assessment of treatment success: measured by number of participants who felt ready to return to sport at the end of the experimental period • Night pain measured on a 0-10 VAS (no outcome data reported) • Pain on activity measured on a 0-10 VAS (no outcome data reported) • Pain with resisted movement measured on a 4-point scale (0 = no pain, 1 = slight pain but full strength, 2 = moderate pain and reduced strength; 3 = severe pain and inability to exert any strength against minimal manual resistance); measured with active resisted abduction in the neutral position, active abduction in external rotation and active resisted abduction in internal rotation (no usable outcome data reported) • Adverse events
Notes	**Conflicts of interest:** the authors stated that they had no conflicts of interest **Funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Subjects were randomised into 3 groups using a computer-generated list." Comment: An adequate method was used

Giombini 2006 (*Continued*)

		to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "The subjects were assessed by fully trained sports physicians who had never seen the patients and were unaware as to which intervention the patients had been allocated." Comment: Assessor of objective outcome was likely blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: There was no loss to follow-up and all randomised participants were analysed
Selective reporting (reporting bias)	High risk	Comment: Data for pain on resisted movement was reported in figure only as means with no error bars. No data for night pain, pain on movement, rest pain and painful arc were reported, despite being listed as outcomes in the methods section of the trial report
Other bias	Low risk	Comment: No other sources of bias were identified

Grymel-Kulesza 2007

Methods	**Study design**: Parallel group RCT **Setting:** Rehabilitation centre, Poland **Intervention 1:** Therapeutic ultrasound plus TENS plus exercise plus massage **Intervention 2:** Cryotherapy plus exercise plus massage **Source of funding:** Not reported

Participants	**Diagnostic label used by trialist:** Chronic rotator cuff injuries **Criteria for defining the shoulder condition being treated** • Confirmed painful shoulder syndrome caused by rotator cuff injuries • Muscle damage assessed using Jobe's test for the supraspinatus and anterior part of the rotator cuff, test for infraspinatus, test for the biceps muscle of the arm, and test for the teres major muscle **Any restriction on duration of symptoms:** 1-7 months history of shoulder pain **Inclusion Criteria (not listed above)** • None **Exclusion Criteria (not listed above)** • History of rheumatic disease (rheumatoid arthritis, ankylosing spondylitis) • Congenital defects of the shoulder girdle • History of upper limb injuries during the 6 months preceding the study • Shoulder joint neoplasms • Discopathy and spondylosis of the cervical spine • Cervical vein or artery disease • Iatrogenic disease of the shoulder joint • Pain radiating below the elbow joint • Rest pain • Pharmacological treatment for shoulder problems within the last six months **Baseline characteristics** *Intervention 1: Therapeutic ultrasound plus TENS plus exercise plus massage* Number randomised: 15 Number included in analyses: 15 Age: mean: 57.6 years; range: 50-65 years Sex: male: 4; female: 11 Duration of symptoms: mean: 4.6 months; range: 1-7 months *Intervention 2: Cryotherapy plus exercise plus massage* Number randomised: 15 Number included in analyses: 15 Age: mean: 57.5 years; range: 50-65 years Sex: male: 3; female: 12 Duration of symptoms: mean: 4.2 months; range: 2-7 months
Interventions	**Intervention 1: Therapeutic ultrasound plus TENS** *Description of modality used*: therapeutic ultrasound and TENS covered 4 muscles i.e. the supraspinatus, the infraspinatus, the teres major muscle and the biceps muscle of arm • Therapeutic ultrasound: the ultrasound transducer was the active electrode connected to the negative pole. It was applied directly to trigger points. The passive electrode was affixed to the opposite arm. The first procedure always lasted 10 seconds per trigger point, with 10 seconds per trigger point added during each of the subsequent 4 procedures. Starting from the sixth procedure, another 5 seconds per trigger point were allowed, so finally each trigger point was treated for 75 seconds. Individual participants had different numbers of active trigger points. When the trigger points were not detected, the procedure was applied to an area where they were likely to be located. • TENS: participants were treated with alternating, triangular, symmetric TENS-type waveforms. The amperage was adjusted to the participant's sensory perceptions to produce pleasant, distinct tingling. The current did not induce pain or muscle

	contraction. The passive electrode (positive), 25 cm^2 in area, was made of conductive carbon rubber *Dose* • Therapeutic ultrasound: not reported • TENS: frequency 100 Hz, pulse duration: 50 µs *Frequency of administration*: 10 sessions over 2 weeks **Intervention 2: Cryotherapy** *Description of modality used*: painful shoulder joints were cooled with CO_2 vapours at -75 degrees Celsius for 3 min *Frequency of administration*: 10 sessions over two weeks **Both groups: Exercise and massage** *Description of modality used*: massage and non-weight bearing exercises as well as self-assisted exercises according to a uniform programme. Each massage procedure covered the entire shoulder girdle, including the painful joint. Kinesitherapy included non-weight bearing and self-assisted exercises. Treatment started with ultrasound plus TENS or cryotherapy followed 15-20 min later by therapeutic exercises for 20 min followed by massage for 15-20 min *Frequency of administration*: every day for 2 weeks
Outcomes	Outcomes assessed at 2 weeks • Active and passive range of motion (abduction, extension, internal rotation, external rotation) measured using a goniometer • Strength measured by Lovett's scale; 5-level scale; muscles tested: supraspinatus, subscapularis, infraspinatus, biceps (tested indirectly), teres minor muscle (tested indirectly) • Night pain (dichotomised as any versus no night pain)
Notes	**Conflicts of interest:** not reported **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: They were randomly assigned to two subgroups (A and B)." Comment: There was no information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention

Grymel-Kulesza 2007 (*Continued*)

Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Unclear risk	Comment: There was no information on whether the assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: There were no losses to follow-up. Data presented were based on the number of randomised participants
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Johansson 2005

Methods	**Study design**: Parallel group RCT **Setting:** Outpatient urban primary health care centres, Sweden **Intervention 1:** Therapeutic ultrasound plus home exercises **Intervention 2:** Acupuncture plus home exercises **Source of funding:** "This study was supported by funding and facilities provided by the County Council of Ostergotland and Linkopings Universitet, Sweden."
Participants	**Diagnostic label used by trialist:** Subacromial impingement syndrome **Criteria for defining the shoulder condition being treated** • Clinical signs of probable impingement syndrome, described as pain during abduction and pain located in the proximal lateral aspects of the upper arm, especially during arm elevation • Positive Neer impingement test (subacromial injection of anaesthetic) • Positive on 3 of the following 4 tests: Hawkins-Kennedy impingement sign, Jobe supraspinatus muscle tear (in 90 degrees of abduction in the scapular plane), Neer impingement sign, painful arc between 60 degrees and 120 degrees of active abduction **Any restriction on duration of symptoms:** at least 2 months' duration of the current episode **Inclusion Criteria (not listed above)** • Age: between 30 and 65 years **Exclusion Criteria (not listed above)** • Radiological findings: malignancy, osteoarthritis of the glenohumeral joint,

	skeletal abnormalities decreasing the subacromial space (bony spurs, osteophytes) • Known or suspected polyarthritis, rheumatoid arthritis or diagnosed fibromyalgia • Previous fractures of any bone in the shoulder complex or shoulder surgery on the affected side • Dislocation of the glenohumeral joint or the clavicular joints on the affected side • History of current clinical findings of instability in any joint of the shoulder complex (negative apprehension sign-relocation test for exclusion of ventral instability of the glenohumeral joint) • Suspicions of frozen shoulder: time-dependent decreased range of movements following the capsular pattern (external rotation-abduction-internal rotation) and pain during intra-articular mobilisation • Problems from the cervical spine: shoulder symptoms reproduced with neck movements or a positive test for the foramina intervertebralia (pain or neurological symptoms during manual extension combined with manual lateral flexion and rotation toward the tested side) • Having received any of the treatment alternatives in the study earlier for the current problem • Having received a corticosteroid injection during the last 2 months for the current problem • A clinical picture of ruptured rotator cuff (trauma, pronounced weakness, atrophy) • Acute subacromial bursitis, making a clinical examination impossible due to pain • Difficulty participating in data collection due to communication problems **Baseline characteristics** *Intervention 1: Therapeutic ultrasound plus home exercises* Number randomised: 41 Number included in analyses: 30 Age: mean: 49 years; SD: 8 years Sex: female: 27; male: 14 Duration of symptoms: 2-3 months (n = 11); 4-6 months (n = 10); 7-12 months (n = 11); > 12 months (n = 9) *Intervention 2: Acupuncture plus home exercises* Number randomised: 44 Number included in analyses: 44 Age: mean: 49 years; SD: 7 years Sex: female: 32; male: 12 Duration of symptoms: 2-3 months (n = 13); 4-6 months (n = 8); 7-12 months (n = 10) ; > 12 months (n = 13)
Interventions	**Intervention 1: Therapeutic ultrasound** *Description of modality used*: continuous ultrasound with gel coupling administered by 4 physical therapists at the same primary health care centre. The size of the transducer was 4 cm^2, and the skin area treated was twice this size, covering an area of about 8-10cm^2inferior to the anterior and lateral part of the acromion. The transducer head was moved in small circles covering the area. The participants were seated with the glenohumeral joint extended and medially rotated in order to make the muscle insertion of the supraspinatus muscle appear beneath and anterior to the acromion. This joint position was maintained by placing the arm behind the back of the chair. The equipment used was a Phyaction 190 ultrasound device

	Dose: frequency = 1 MHz, spatial-average intensity = 1 W/cm^2; 10 min duration *Frequency of administration*: twice a week for 5 weeks **Intervention 2: Acupuncture** *Description of modality used*: standardised needle placement at 4 local points (L1 14 (Binao), L1 15 (Jianyu), LU 1 (Zhongfu), and TE 14 (Jianliao)) and 1 distal point (L1 4 (Hegu)). All physical therapists were trained to locate these points. The type of needle used was a HEGU sterile and single-packaged one-time needle no. 8 (30 mm long and 0.30 mm in diameter). The participants lay on a treatment table on their unaffected side. After insertion into the defined points, the needle was rotated a few seconds until "de qui" (described as sensation of heaviness, numbness and radiating paraesthesia) was experienced by the participant. In total 3 stimulations were performed (at insertion, after 15 min and after 30 min). De qi was to be experienced at every stimulation at each acupuncture point, if not the needle was adjusted until this was the case *Frequency of administration*: 10 treatment sessions in total. 30 min treatment sessions repeated twice a week for 5 weeks **Both groups: Home exercises** *Description of modality used*: 2-step home exercise programme. Part 1: exercises targeted to maintain or restore motion as well as to stimulate circulation in the rotator cuff using many repetitions of low-intensity exercises, without provoking pain from involved tissues. Part 2: exercises targeted to strengthen the rotator cuff muscles with the upper arm in a neutral position to avoid impingement. In all exercises, the position of a retracted shoulder was emphasised. At the first treatment visit, the participants received instructions from the physical therapist and practiced the exercises in part one of the programme. They were instructed to perform the programme daily for 5 weeks. After the first half of the treatment period, the participants received instruction and practiced the second part of the exercise programme. All rotations were performed with a pillow in the axilla to decrease the activity in the deltoid muscle. Pain during the exercises was not to last more than 10-15 min after the programme. If pain persisted longer than that, the participants were instructed to decrease either the resistance or the force produced. Adherence to the exercise programme was monitored by a home-exercise adherence log, and the use of additional medications was reported *Frequency of administration*: daily for 5 weeks. Exercises repeated every other day in the fourth and fifth weeks
Outcomes	Outcomes assessed at 6 weeks and 3, 6 and 12 months • Function: mean of 3 measures - Constant-Murley total score, UCLA and Adolfsson-Lysholm Score - score 0-100 with higher scores denoting better function) • Adverse events
Notes	**Conflicts of interest:** not reported **Funding:** County Council of Ostergotland and Linkopings Universitet, Sweden

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Concealed randomization, based on a random list, with the treatment alternative in envelopes was carried out be-

		forehand. The intervention was then introduced and performed by 4 physical therapists at the same primary health care center" Comment: An adequate method was likely used to generate the allocation sequence
Allocation concealment (selection bias)	Low risk	Comment: An adequate method was likely used to conceal the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "The research physical therapist, who performed the examinations and all assessments, was uninformed of treatment group assignments throughout the study." Comment: Assessor of objective outcomes was blind to treatment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All patients were adherent to the study protocol (no missed or additional interventions) during the 5 weeks of acupuncture or ultrasound. At the 3-, 6-, and 12-month visits, the number of patients who were adherent to the study protocol changed, as shown in Figure 2. In total, 64 patients were adherent to the study protocol throughout the study. The data were analyzed both for the group adhering to the study protocol and with an "intention-to-treat" (ITT) application model for analysis of data for clinical trials. The latter analysis included all patients who were randomly assigned to groups. The principle of last observation carried forward (LOCF) was used in both analyses, using the scores recorded just prior to the missing scores in case of missing posttreatment values. The number of patients where LOCF was used

Johansson 2005 (*Continued*)

		is illustrated in Figure 2." Quote: "The between-group analysis, including the mean scores from all 4 assessment visits (after 5 weeks of acupuncture or ultrasound and at 3, 6, and 12 months), showed a larger change (P.045, ANCOVA) in the combined score for the acupuncture group, analyzed with those adhering to the study protocol. This effect was seen already at the first assessment visit and was maintained over time. In the ITT analyses, no differences were found across the 4 data collection periods." Comment: Loss to follow-up was slightly different between groups but an appropriate analysis was used to deal with attrition
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Kelle 2014

Methods	**Study design**: Parallel group quasi-randomised trial **Setting:** Physical Medicine and Rehabilitation outpatient clinic, Turkey **Intervention 1**: Low-level laser treatment (LLLT) plus home exercises **Intervention 2:** Glucocorticoid injection plus home exercises **Control:** Sham LLLT plus home exercises **Source of Funding:** Scientific Research Projects Coordination Unit of Cukurova University (grant number TF2006LTP19)
Participants	**Diagnostic label used by trialists:** Subacromial impingement syndrome **Criteria for defining the shoulder condition being treated** • Neer, Hawkins-Kennedy and empty can tests were positive • Positive magnetic resonance imaging (MRI) findings for stage I or II subacromial impingement syndrome **Any restriction on duration of symptoms** • At least 1 month **Inclusion Criteria (not listed above)** • Age older than 18 years • VAS score greater than 40 mm

	Exclusion Criteria (not listed above) • Major trauma to the shoulder • Stage III subacromial impingement syndrome • Diabetes mellitus • Hypothyroidism • Calcific tendinitis • Adhesive capsulitis (forward flexion < 160°, horizontal abduction < 160°) • Installation of cardiac pacemaker • Attendance of any physical therapy session and local corticosteroid injections during the previous six months **Baseline characteristics** *Intervention 1: LLLT plus home exercises* Number randomised: 45 Number included in analyses: 45 Age: 50.7 (range 29-74) years old Sex: F/M 36/9 Duration of symptoms: 15 (range 2-120) months *Intervention 2: Glucocorticoid injection plus home exercises* Number randomised: 45 Number included in analyses: 45 Age: 48.7 (range 18-77) years old Sex: F/M 35/10 Duration of symptoms: 16.6 (range 1-120) months *Contol: Sham LLLT plus home exercises* Number randomised: 45 Number included in analyses: 45 Age: 48 (range 19 to 76) years old Sex: F/M 34/11 Duration of symptoms: 18.7 (range 1-120) months
Interventions	**Intervention 1: LLLT** *Description of modality used*: Gallium arsenide laser at a wavelength of 904 nm was administered using the direct contact technique, with a 90-degree angle on the subacromial space and the most painful area of the affected shoulder accessible to palpation. During LLLT, the laser device was positioned so that the participant could not see it, and both the participant and the therapist wore protective eyewear *Dose*: 2 J/cm^2, 3,500 Hz, for 150 seconds *Frequency of administration*: 3 times weekly for 3 weeks (total of 9 sessions) **Intervention 2: Glucocorticoid injection** *Description of modality used*: betamethasone dipropionate and betamethasone sodium phosphate with lidocaine (3 ml, 1%) were injected into the subacromial region of the affected shoulder. The injection was administered via the lateral approach. The lateral side of the acromion was palpated, and the injection was administered from below the acromion and was directed upward *Dose*: Betamethasone dipropionate (6.43 mg) and betamethasone sodium phosphate (2.63 mg) *Frequency of administration*: twice (second injection delivered 10 days after the first) **Control: Sham LLLT** *Description of modality used*: Same as LLLT group, except the laser device was not turned

	on *Dose*: none *Frequency of administration*: 3 times weekly for 3 weeks (total of 9 sessions) **All groups: Home exercises** *Description of modality used*: a home exercise programme, including shoulder pendulum exercises, posterior capsule stretching, and range of motion and isometric shoulder exercises *Dose*: 10 repetitions during each session *Frequency of administration*: twice daily for 3 weeks *Any additional treatment*: all of the participants were allowed to use up to 1000 mg of paracetamol per day for analgesia when necessary
Outcomes	Outcomes assessed at 3 weeks, 3 months and 6 months • Function: University of California at Los Angeles rating score (UCLA), scored from 2-35 with higher values indicating better function • Rest pain: VAS 0-100 • Pain on motion VAS 0-100 • Quality of life: Nottingham Health Profile (NHP) scale, with 6 sub-scales for pain, physical mobility, energy level, sleep, emotional reaction and social isolation, each scored from 0-100 with higher values indicating poorer quality of life. Only data for pain and physical mobility was reported • Adverse events
Notes	**Conflict of interest:** "The authors declare that there are no conflicts of interest." **Funding:** Scientific Research Projects Coordination Unit of Cukurova University (grant number TF2006LTP19)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Quote: "The patients were allocated to three groups according to their order of admission. The first patient was allocated to group I, the second was allocated to group II, and so on." Comment: Alternation (a quasi-random method of allocation) was used
Allocation concealment (selection bias)	High risk	Comment: Alternation (a quasi-random method of allocation) was used, so the allocation sequence could not be concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Neither the patients nor the assessor and therapist were blinded in the study. " Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different ex-

Kelle 2014 (*Continued*)

		pectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Quote: "Neither the patients nor the assessor and therapist were blinded in the study. " Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	High risk	Quote: "Neither the patients nor the assessor and therapist were blinded in the study. " Comment: Assessor of objective outcomes was not blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "A total of 135 patients with stage I or stage II subacromial impingement syndrome were included in the study. The patients had normal routine laboratory results. Although 114 patients completed the study, the data analysis was performed on an intention-to-treat basis, so we included all 135 patients. Seven patients in groups II [sham LLLT] and III [LLLT] did not complete the sessions. Additionally, seven patients in group II [sham LLLT] did not come to their follow-up visits." Quote: "In our trial, there was a high dropout rate in the sham laser group, whereas the dropout rate in the low-level laser treatment group was acceptable in comparison. This outcome might have been due to the slower improvement in the sham laser group, as evidenced by the lack of dropouts in the local corticosteroid injection group." Comment: There were no losses to follow-up in the glucocorticoid injection group, 7 in the LLLT group, and 14 in the sham LLLT group. Reasons for loss to follow-up were not recorded, but the amount per group suggests that dropout was related to the intervention. It is unclear what method was used to impute missing data in the intention-to-treat analysis

Selective reporting (reporting bias)	High risk	Comment: Outcome data were fully reported for all outcomes specified in the methods section of the publication except for 4 of the 6 sub-scales of the Nottingham Health Profile, which were only reported as not significantly different between groups. Also, without a trial protocol it is unclear whether other outcomes were measured but not reported based on the results
Other bias	Low risk	Comment: No other sources of bias identified

Kocyigit 2012

Methods	**Study design**: Parallel group RCT **Setting:** University, Turkey **Intervention:** Transcutaneous electrical nerve stimulation (TENS) **Control:** Sham TENS **Source of funding:** Not reported
Participants	**Diagnostic label used trialist:** Subacromial impingement syndrome **Criteria for defining the shoulder condition being treated** • At least 3 positive provocative tests out of 4: Neer impingement sign, Hawkins test, Jobe Test, and painful arc test • Absence of pain at rest and painful shoulder internal rotation • Shoulder pain on a 100-mm VAS of at least 40 mm **Any restriction on duration of symptoms** • None **Inclusion Criteria (not listed above)** • Aged 25-65 years old • No previous history of electrotherapy • No previous history of fracture, dislocation, or surgery on the shoulder region • Absence of lesions or medications that can affect cerebral perfusion and oxygenation (arteriovenous malformation, tranquillisants) **Exclusion Criteria (not listed above)** • Contraindications for TENS application or fMRI (presence of pacemakers, cardiac implants, dysrhythmias, cochlear implants) **Baseline characteristics** *Intervention: TENS* Number randomised: 10 Number included in analyses: 10 Age mean (range): 49.2 (40-55) years Sex: F/M 5/5 Duration of symptoms mean (range): 5.5 (1.5-12) months *Control: Sham TENS* Number randomised: 10 Number included in analyses: 10

Kocyigit 2012 (*Continued*)

	Age mean (range): 44.7 (24 - 64) years Sex: F/M 7/3 Duration of symptoms mean (range): 7.8 (1-24) months
Interventions	**Intervention: TENS** *Description of modality used*: Low-frequency TENS. 2 carbon silicone electrodes were placed on the anterior and the posterior aspect of the shoulder. The participants were observed for displacement of electrodes, and continuation of muscle contraction during the TENS treatment *Dose*: 3 Hz, 250 μs, for 30 min. Intensity of the current was chosen as submaximal value causing visible muscle contractions. In one of the participants, the current intensity was changed because of discontinuation of contractions or irritation of the current Frequency of administration: once **Control: Sham TENS** *Description of modality used*: 2 carbon silicone electrodes were placed on the anterior and the posterior aspect of the shoulder. No current was passed through these electrodes *Dose*: none over a 30 min session *Frequency*: once
Outcomes	Outcomes assessed immediately post-treatment (day 1) • Overall pain measured on a 0-100 VAS with a higher score indicating worse pain
Notes	**Conflict of interest:** not reported **Funding: n**ot reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomized to receive either low-frequency TENS or sham TENS by random number table." Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "There is the possibility of unblinding in TENS studies as it delivers electrical current through the skin. There are several attempts to decrease unblinding in the literature: inclusion of patients who were not applied TENS previously, and the use of devices that display an activator light but do not deliver current. In this study, both the strategies were applied to decrease the risk of unblinding. Patients who did not

Kocyigit 2012 (*Continued*)

		have any kind of electrotherapy earlier were included in the study. The timer of the device was set in the sham TENS group so an indicator light was on during which time the electrodes were connected. All the patients were told that they may or may not feel contractions during application. All the patients were inspected on separate days, so the patients did not see other patients." Comment: Participants were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported the outcome of interest of our review
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: There was no loss to follow-up in this study
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Korkmaz 2010

Methods	**Study design**: Parallel group RCT **Setting:** Outpatient physical therapy and rehabilitation clinic, Turkey **Intervention 1:** Transcutaneous electrical nerve stimulation (TENS) plus exercise **Intervention 2:** Pulsed radiofrequency treatment plus exercise **Source of funding:** "We have no financial relationship for this study".
Participants	**Diagnostic label used by trialist:** Supraspinatus tendinopathy or partial tears of the supraspinatus tendon **Criteria for defining the shoulder condition being treated** • No specific criteria reported other than "Ultrasonography and anterior-posterior X-rays were used for the diagnoses" **Any restriction on duration of symptoms** • At least three months **Inclusion Criteria (not listed above)** • Age: 18-85 years old **Exclusion Criteria (not listed above)** • Inflammatory arthritis • Active synovitis in the joints

	• History of shoulder surgery • History of nerve blocks to the surgery • Intra-articular injection within the last 3 months • Trauma of physical therapy within the last 6 months • Advanced osteoarthritis • Referred pain in the shoulder • Neurological impairment (stroke, Parkinson's disease, paresis) • Severe cardiovascular disease (acute myocardial infarction, congestive heart failure or uncontrolled hypertension) • Unstable chronic or terminal illness (diabetes mellitus, malignancies) • Bleeding problems • Major depression • Severe cognitive impairment • Severe musculoskeletal impairment **Baseline characteristics** *Intervention 1: TENS plus exercise* Number randomised: 20 Number included in analyses: 20 Age: mean: 55.80 ± 9.82 years Sex: female: 14; male: 6 Diagnosis: supraspinatus tendinopathy: 10; partial tears of the supraspinatus tendon: 9; acromioclavicular joint osteoarthritis: 1 Duration of symptoms: mean: 8.85 ± 9.05 months *Intervention 2: Pulsed radiofrequency plus exercise* Number randomised: 20 Number included in analyses: 20 Age: mean: 54.80 years ± 12.09 Sex: female: 14; male: 6 Diagnosis: supraspinatus tendinopathy: 11; partial tears of the supraspinatus tendon: 9; acromioclavicular joint osteoarthritis: 0 Duration of symptoms: mean: 10.45 ± 8.31 months
Interventions	**Intervention 1: TENS** *Description of modality used:* TENS (Enraf Nonius Sonopuls 492) on the anterior and posterior aspects of the joint *Dose*: mean frequency of 100 Hz, 15 mA amplitude, 150 μsn; 20 min session *Frequency of administration*: 5 times per week for 4 weeks (20 sessions) **Intervention 2: Pulsed radiofrequency** *Description of modality used*: procedure performed in an operating room with sterile conditions maintained. Each participant was placed in the prone position and the skin within the operation area was prepared and draped. Fluoroscopy was adjusted to show the scapular notch at approximately 15 degrees lateral and 30 degrees of the cephalocaudal angle. The entry point was marked, and local anaesthesia was applied. A radiofrequency needle was introduced through the skin 3 cm along the line of the spine in the upper, outer quadrant, and then guided to the edge of the suprascapular notch with the use of an image intensifier. With 2 Hz motor stimulation (< 0.5 V), a 5 cm long radiofrequency needle with a 0.5 cm active tip was advanced under fluoroscopic guidance. Motor stimulation muscle response was observed, and the correct entry of the needle was confirmed again by a 50 Hz sensorial stimulation (< 0.7 V). Finally, a placement of the needle was verified

	by both imaging and stimulations. After determining that the needle was in the correct position, pulse radiofrequency was applied to participants *Dose*: 45 V, 200 msn, 42 degrees; total treatment time: 4 min *Frequency of administration*: once **Both groups: Exercise** *Description of modality used*: supervised exercise programme. All participants in both groups were recommended the following exercises: exercises for increasing the range of motion (active-passive range of motion, stretching exercise); strengthening exercises; Codman exercises; pulley exercises; and finger ladder exercises. For each of these, participants were provided with simple, step-by-step written instructions with illustrations *Frequency of administration*: exercises were performed 5 days a week for a period of 4 weeks at the rehabilitation unit. Each participant completed the exercise programme on a daily basis and it lasted at least 30 min
Outcomes	Outcomes assessed at 1, 4 and 12 weeks • Function measured by the Shoulder Pain and Disability Index (SPADI) total score 0-130, higher score indicates more disability • Rest pain measured on a 10 cm VAS • Pain on motion measured on a 10 cm VAS • Night pain measured on a 10 cm VAS • Quality of life measured by the Short form-36 • Active and passive range of motion (flexion, extension, abduction, external rotation, internal rotation) • Global assessment of treatment success measured by participant and blinded physician; 1 = minor effect, 2 = moderate effects; 3 = good results; 4 = very good results • Adverse events
Notes	**Conflicts of interest:** authors state that they have no financial relationship for this research **Funding:** No specific funding for this trial

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Forty patients were randomized.. .by using double randomization from the random number table" Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	Comment: An adequate method was used to conceal the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention

Korkmaz 2010 (*Continued*)

Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "A physician blinded to the treatment protocols performed the following assessments before and after the procedure." Comment: Assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: There was no loss to follow-up
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication except for global assessment of treatment success, but this did not appear to be related to the lack of statistical significance for this outcome (as many other non-significant outcomes were fully reported). However, without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Kurtai Gursel 2004

Methods	**Study design**: Parallel group RCT **Setting:** Outpatient clinic, The Netherlands **Intervention:** Therapeutic ultrasound plus hot pack plus interferential current plus exercise **Control:** Sham ultrasound plus hot pack plus interferential current plus exercise **Source of funding:** Not reported
Participants	**Diagnostic label used by trialist:** Supraspinatus tendinosis, subacromial bursitis, rotator cuff tear or bicipital tendinosis **Criteria for defining the shoulder condition being treated** • Diagnosis of soft tissue disorders of the shoulder (e.g. supraspinatus tendinosis, bicipital tendinosis, rotator cuff tendinosis (including rotator cuff tears), subacromial bursitis) by ultrasonography or magnetic resonance imaging (through which calcific tendinitis was excluded) **Any restriction on duration of symptoms** • At least 4 weeks prior to the study **Inclusion Criteria (not listed above)**

	• Absence of direct trauma to the shoulder or the memory of trauma (to exclude probable fractures or resorbing haematoma) • Absence of underlying neurologic, inflammatory rheumatic disease, notably rheumatoid arthritis, systemic lupus erythematosus, or extrinsic diseases such as cervical spondylosis with referring pain to the shoulder • No physical therapy for the shoulder was given in the 4-5 weeks prior to the study **Exclusion Criteria (not listed above)** • Calcific tendinitis **Baseline characteristics** *Intervention: Therapeutic ultrasound plus other physical therapy* Number randomised: 20 Number included in analyses: 19 Age: mean: 54.16 ± 8.22 years; range: 38-69 Sex: female: 12; male: 7 Diagnosis: supraspinatus tendinosis: 6; supraspinatus partial rupture: 11; rotator cuff rupture: 1; biceps tendinosis: 8 Duration of symptoms: mean: 8.68 ± 8.84 months; range: 1-36 months *Control: Sham ultrasound plus other physical therapy* Number randomised: 20 Number included in analyses: 19 Age: mean: 54.00 ± 9.8; range: 35-69 Sex: female: 14; male: 5 Diagnosis: supraspinatus tendinosis: 6; supraspinatus partial rupture: 7; rotator cuff rupture: 3; biceps tendinosis: 7 Duration of symptoms: mean: 8.11 ± 10.81 months; range: 1-42 months
Interventions	**Intervention: True ultrasound** *Description of modality used*: continuous ultrasound using a Petsan 250 device. The transducer head had an area of 6.2 cm^2, an effective radiating area of 5 cm^2, and a beam non-uniformity ratio of 1:6. While sitting on a table, each participant placed an arm with the hand supinated on his or her lap. Using slow circular movements, the treating physical therapist applied the transducer head over the superior and anterior periarticular regions of the participant's glenohumeral joint, covering an area of approximately 15 cm^2 *Dose*: frequency of 1 MHz, intensity of 1.5 W/cm^2. The treatment duration was 10 min *Frequency of administration*: 15 days (5 days each week) **Comparator: Sham ultrasound** *Description of modality used*: the ultrasound device was set to "off" mode. The transducer was applied to the same area as the real ultrasound group and Aquasonic transmission gel was used *Dose*: none *Frequency of administration*: 15 days (5 days each week for 3 weeks) **Both groups: Other physical therapy interventions** *Description of modality used* • Superficial heat: hot packs (60 degrees C) for ten min • Electrical stimulation: interferential current was delivered using Medi-Link Model 71, which operated with a carrier frequency of 4000 Hz, with an amplitude-modulated frequency of 100 Hz. Rubber bipolar plate electrodes (6 x 8 cm) were placed again over the superior and anterior periarticular regions of the glenohumeral joint. The intensity

	was set according to the sensory threshold level of each participant, and the treatment duration was 15 min • Exercises for the shoulder girdle. At the start of therapy or when a subject had severe pain, passive restricted ROM exercises and gentle stretching were used. At a later phase or when pain lessened, active ROM exercises and gradually isometric and dynamic resistance exercises were added. Exercises were applied to all participants by the same physical therapist. The duration of exercise was a minimum of 15 min and a maximum of 30 min *Frequency of administration*: 15 days (5 days each week) *Any additional treatment during trial*: paracetamol (500 - 1000 mg maximum daily) if needed
Outcomes	Outcomes assessed at 3 weeks • Function measured by the Dutch Shoulder Disability Questionnaire (SDQ), 0-100 where higher = more disability • Rest pain measured on a 4-point Likert scale; 0 = no pain; 1 = mild pain; 2 = moderate pain; 3 = severe pain • Pain on motion measured on a 4-point Likert scale; 0 = no pain; 1 = mild pain; 2 = moderate pain; 3 = severe pain • Active and passive range or motion (flexion, extension, abduction, adduction, external and internal rotation) measured using a goniometer
Notes	**Conflicts of interest:** not reported **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "...were randomly assigned by the use of random numbers." Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	High risk	Quote: "The selector, who did not perform any assessment, was aware of the randomisation scheme and opened the codes at the statistical evaluation stage." Comment: The allocation sequence was not concealed from the person allocating participants to groups
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The subjects were not informed about the true nature of the US application. The treating physical therapist was aware of the nature of this intervention and the physical findings of the subjects, but did not change the intervention according to the symptoms during the study"

Kurtai Gursel 2004 (*Continued*)

		Comment: Participants were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "The assessor and the subjects, however, were not informed about the true nature of US application" Comment: Assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "One subject from the true-US group and 1 subject from the sham-US group withdrew from the study because they could not spare time for the physical therapy sessions. Another subject from the true-US group and 2 other subjects from the sham-US group withdrew without any explanation" Comment: The amount of attrition was low and relatively equal between groups so was unlikely to have biased the results
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Leduc 2003

Methods	**Study design**: Parallel group RCT **Setting:** Ambulatory academic hospital in Quebec, Canada **Intervention:** Acetic acid iontophoresis plus thermotherapy plus exercises **Control:** Sham iontophoresis plus thermotherapy plus exercises **Source of funding:** Not reported
Participants	**Diagnostic label used by trialist:** Calcifying tendinitis of the shoulder **Criteria for defining the shoulder condition being treated** • Symptomatic (painful) tendinitis of the shoulder and at least 1 calcification of the shoulder visible on radiography **Any restriction on duration of symptoms** • None

	Inclusion Criteria (not listed above) • 18 years of age or older **Exclusion Criteria (not listed above)** • Pregnancy • Oral or local injection corticosteroid therapy administered during the previous 2 months • Cutaneous contraindications to the application of 5% acetic acid • Adhesive capsulitis of the shoulder • Arthropathy of the shoulder • Any other medical condition accompanied by pain **Baseline characteristics** *Intervention: Acetic acid iontophoresis* Number randomised: 18 Number included in analyses: 17 Age: mean: 51.5 years; range: 39-71 years Sex: female: 10; male: 7 Duration of symptoms: mean: 27.5 months; range: 3-144 months **Control: Sham iontophoresis** Number randomised: 18 Number included in analyses: 10 Age: mean: 47.9 years; range: 31-63 years Sex: female: 8; male: 5 Duration of symptoms: mean: 33 months; range: 3-120 months
Interventions	**Intervention: Acetic acid iontophoresis** *Description of modality used*: an electrotherapy apparatus, Dynaplus 421, was used to administer the treatment. The participant was seated with their arm resting on a table. The active electrode (cathode) was made of easily malleable lead, had a surface of 5 x 7.5 cm and was placed on three compresses saturated with 20 mL of 5% acetic acid applied approximately at the site of calcification of the shoulder. The second electrode (anode) , also of malleable lead, had a 4 x 5 cm surface and was fixed to the anterior side of the distal segment of the ipsilateral arm. The acetic acid iontophoresis material was prepared by physiotherapist A who used 2 different techniques. Once the shoulder and arm of all subjects of both groups had been wrapped with identical elastic bandage, the acetic acid iontophoresis treatment was administered by physiotherapist B. After the treatment was completed, the iontophoretic material was removed by physiotherapist A *Dose*: a galvanic current of 5 mA for 15-20 min was administered *Frequency of administration*: 10 sessions: 3 per week for 2 weeks followed by 1 per week for 4 weeks (6 weeks in total) **Control: Sham iontophoresis** *Description of modality used*: same as acetic acid iontophoresis group except a plastic film was used to cover the upper surface of the active electrode, and the compresses that were saturated with acetic acid were placed above the active electrode and not between the skin and the electrode, as technically required to ensure iontophoresis *Dose*: none *Frequency of administration*: 10 sessions: 3/week for 2 weeks followed by 1/week for 4 weeks (6 weeks in total) **Both groups: Thermotherapy and exercises** *Description of modality used*: thermotherapy (no details provided) and range of motion

Leduc 2003 (*Continued*)

	exercises *Frequency of administration*: 10 sessions: 3/week for 2 weeks followed by 1/week for 4 weeks (6 weeks in total) *Any additional treatment during trial*: paracetamol if needed
Outcomes	Outcomes assessed at 6 weeks • Function measured using Shoulder Pain and Disability Index (SPADI): score: 0-100; 0 being best function, 100 being worst function • Active range of motion (flexion, abduction, external rotation, internal rotation) using a manual goniometer
Notes	**Conflicts of interest:** "No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit upon the authors (s) or upon any organization with which the author(s) is/are associated" **Funding:** Centre Hospitalier Universitaire de Montreal Foundation, Physiatry Division

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "...the participants were divided randomly according to a stratified randomisation table..." Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Physiotherapist A prepared and installed the material needed for the acetic acid iontophoresis treatment of all participants in both groups; neither the participants nor physiotherapist B were aware of the true nature of the treatments (acetic acid iontophoresis or placebo) administered to participants; physiotherapist B administered the treatments, followed by thermotherapy and ROM exercises. At all times, only the main investigator and physiotherapist A were aware of the actual allocation of patients." Comment: Participants were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes

Leduc 2003 (*Continued*)

Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "...neither the participants nor physiotherapist B were aware of the true nature of the treatments (acetic acid iontophoresis or placebo) administered to participants..." Quote: "...The amplitude of active anterior flexion, abduction, and external and internal rotation of the shoulder was assessed by physiotherapist B by using a manual goniometer" Comment: Assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Thirty-six subjects fitting the inclusion criteria were recruited and randomized in 2 equal groups of 18 participants Quote: "Nine participants were removed from the study, 5 from the control group for superficial second-degree burns under the negative electrode; 2 participants were removed after being treated with cortisone injection in the shoulder, and 2 patients failed to show up for the posttreatment radiography. Therefore, a total of 27 subjects remained in the study, 17 in the treatment group and 10 in the control group" Comment: The amount of attrition is unbalanced (higher in the placebo) and authors only reported a per-protocol analysis, which is likely to have yielded biased results
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Montes-Molina 2012a

Methods	**Study design**: Parallel group RCT **Setting:** Physiotherapy Unit and Rehabilitation Department of Ramon y Cajal University Hospital, Spain **Intervention:** Interferential laser therapy **Comparator:** Continuous laser therapy **Source of funding:** Instituto de Salud Carlos III, Fondo de Investigacion Sanitaaria (FIS)
Participants	**Diagnostic label used by trialists:** Rotator cuff tendinitis, bicipital tendinitis, calcific tendinitis, rotator cuff partial tears, impingement syndrome, frozen shoulder, or bursitis **Criteria for defining the shoulder condition being treated** • Unilateral acute or chronic shoulder pain of musculoskeletal origin, with or without restriction in range of motion. participants were diagnosed using X-rays, nuclear magnetic resonance or ultrasound **Any restriction on duration of symptoms** • None **Inclusion Criteria (not listed above)** • 18 years or older **Exclusion Criteria (not listed above)** • Shoulder pain associated with radicular cervical spine conditions • Implanted osteosynthesis material • Central or peripheral neurological diseases • Pacemakers • Tumours • Brachial plexus palsy • Fibromyalgia **Baseline characteristics** *Intervention: Interferential laser therapy* Number randomised: 99 Number included in analyses: 86 Age: mean: 57 years old; range: 52-63 years Sex: male: 26; female: 73 Diagnosis: rotator cuff tendinitis (53%), bicipital tendinitis (3%), calcific tendinitis (25%), rotator cuff partial tears (16%), impingement syndrome (5%), frozen shoulder (5%), dislocations (10%), bursitis (5%) Duration of symptoms: acute (< 90 days): 8; chronic (> 90 days): 91 *Control: Continuous laser therapy* Number randomised: 99 Number included in analyses: 83 Age: mean: 54 years old; range: 48-62 years Sex: male: 24; female: 75 Diagnosis: rotator cuff tendinitis (50%), bicipital tendinitis (5%), calcific tendinitis (13%), rotator cuff partial tears (17%), impingement syndrome (8%), frozen shoulder (3%), dislocations (10%), bursitis (3%) Duration of symptoms: acute (< 90 days): 6; chronic (> 90 days): 93
Interventions	**Intervention: Interferential laser therapy** *Description of modality used*: two independent identical infra-red GaAIAs diode lasers (Sys Stim 540), Mettler Electronics Corp, Anaheim, CA, USA) with a wavelength 810 +/- 10 nm, pulse width of 100 milliseconds and maximum power output of 100 +/- 10

	mW were used. This type of laser has an elliptical beam spot with an irradiation area of 9.2 mm^2 at the aperture and the treatment area is illuminated with three 7400-nm blue light-emitting diodes. One applicator was placed perpendicular to the painful arm of the shoulder and the other was placed on the opposite side. Both lasers were switched on with the hand-held probes pressed against the skin. The area was treated in 5 different points: 1 at the site of maximal pain and the other 4 at adjacent locations immediately above, below, right and left of the central point. Both probes were active and both lasers delivered the same dose at the same time. Participants were seated with the shoulder at rest in adduction and medial rotation *Dose:* laser was applied using continuous wave mode at a power density of 1.1 W/cm^2. The energy dose per point was 7 J in 70 seconds. The energy density was 1.4 J/cm^2. Total energy delivered per session was 70 J *Frequency of administration*: 10 treatment sessions in total, 3 per week (4 weeks) *Any additional treatment during trial*: some participants performed supervised shoulder exercises. The exercises were the same for all participants - Codman, finger-stair and shoulder wheels **Control: Continuous laser therapy** *Description of modality used*: same as above, except one applicator was placed perpendicular to the painful area of the shoulder and the other applicator was switched off and placed on the opposite side. Both probes were pressed against the skin, as in the interferential group. The same points were treated as the interferential group. Participants were seated with the shoulder at rest in adduction and medial rotation *Dose*: total energy delivered per session was 35 J. *Frequency of administration*: 10 treatment sessions in total, 3 per week (4 weeks) *Any additional treatment during trial*: some participants performed supervised shoulder exercises. The exercises were the same for all participants - Codman, finger-stair and shoulder wheels
Outcomes	Outcomes assessed at 4 weeks • Function measured by the Shoulder Pain and Disability Index (SPADI); score: 0-100, higher score indicates worse function • Rest pain measured on a 10 cm VAS, score: 0-10; 0 = no pain, 10 = unbearable pain • Night pain measured on a 10 cm VAS, score: 0-10; 0 = no pain, 10 = unbearable pain • Adverse events
Notes	**Conflicts of interest:** "None declared". **Funding:** Instituto de Salud Carlos III, Fondo de Investigación Sanitaria (FIS), Project no. PI 07/0046 and FEDER funds

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Before starting the study, a randomisation list was produced using a random generator. Patients were assigned to one of two groups."

		Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Patient blinding was implemented in two ways. First, the laser protective goggles worn by the patients prevented them from noticing if one or both laser applicators were active. Second, laser equipment was placed behind the subjects, preventing them from seeing the probes. The observer was also blinded to the group allocation. Only the physiotherapist who applied the laser therapy knew which treatment was received by each patient." Comment: participants were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported all outcomes
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "The initial number of 100 patients in each group was reduced to 99 because one patient in each group did not sign the informed consent form. In addition, 16 subjects in the conventional group and 13 subjects in the interferential group dropped out of laser treatment before completion of the 10 sessions. Considering these losses, the number of patients actually studied was 83 in the conventional group and 86 in the interferential group." Comment: The number of losses to follow-up are relatively similar between groups but no reasons are reported
Selective reporting (reporting bias)	Low risk	Comment: Outcome data were fully reported for all outcomes specified in the ClinicalTrials.gov registry entry (NCT00694538)
Other bias	Low risk	Comment: No other sources of bias identified

Montes-Molina 2012b

Methods	**Study design:** Parallel group RCT **Setting:** Physical Medicine and Rehabilitation Service (Unit of Physiotherapy) at of Ramon y Cajal University Hospital, Spain **Intervention:** Interferential light therapy generated by 2 light probes **Comparator:** Conventional light therapy generated by 1 light probe **Source of funding:** This work was supported by the Carlos III Health Institute and the Feder Funds, with grant number PI 07/0046
Participants	**Diagnostic label used by trialists:** Rotator cuff tendinitis, calcific tendinitis or partial rotator cuff tears **Inclusion criteria** • participants above 18 years old with acute shoulder pain or chronic participants with an acute episode of recurrent pain from tendinopathy. The diagnosis was alternatively evaluated by ultrasonography, X-ray and magnetic resonance image **Exclusion criteria** • participants with shoulder pain associated with radicular cervical spine, implanted prostheses, central neurological aetiology affectation, fractures, tumours, braquial plexus palsy, fibromyalgia, other musculoskeletal shoulder disorders • Undergoing an exercise-based treatment programme within the period of the study **Baseline characteristics** Total n randomised = 30 participants Total n analysed = 26 participants *Intervention: Interferential light therapy* Number randomised: 15 randomised; Number completed: 13 Sex: F/M 12/3 Mean ± SD (range) age: 59.2 ± 11.0 years Mean ± SD (range) duration of symptoms: not reported *Control: Conventional light therapy* Number randomised: 15 randomised Number completed: 13 Sex: F/M 10/5 Mean ± SD (range) age: 9.0 ± 8.9 years Mean ± SD (range) duration of symptoms: not reported
Interventions	The therapy was applied in all cases with 2 independent and identical devices (Mettler Electronics Sys Stim 540, Anaheim, CA, USA) equipped with a multi-diode cluster applicator combining 7 light-emitting diodes at 660 nm and 12 superluminescent diodes at 950 nm wavelength, with a peak power of 500 mW and an average power of 310 mW. Diodes were distributed on each applicator in a circular arrangement covering an area of 4.50 cm^2. The output activation was achieved by using a capacitance switch on the handheld applicator **Intervention: Interferential light therapy generated by two light probes** *Components of intervention:* two applicators were active and placed on opposite sides of the shoulder joint, covering the pain-affected zone. In each session, treatment was applied in 2 successive applications. After the first application, the pair of applicators were slightly moved a short distance, and a second application was made. The energy delivered in each application was 84 J, 42 J per applicator with a power density of 67

	mW/cm^2. The resulting energy density at the skin was 10.3 J/cm^2 in all cases. The total energy dose per session (two applications) was 168 J. The accumulated energy delivered during the entire treatment was 1680 J **Comparator: Conventional light therapy** *Components of intervention*: for blinding purposes of the study, the procedure was the same as in the interferential group, except that now only 1 of the 2 applicators was active, so the total dose per session (in 2 applications) was 84 J. The accumulated energy delivered in this case during the entire treatment was 840 J **Both groups:** The treatment technique chosen in both groups was the contact mode, applying the cluster probes and holding them firmly pressed to the skin. Participants were always in a seated position with the shoulder at rest and in medial rotation. The mode selected was pulsed, and the pulse modulation frequency was automatically applied step-by-step by the device along 10 interval values, from 10 Hz to 5 kHz, with a cycle duration of 10 seconds, 1 second at each step. The sessions were given over 2 weeks, at a rate of 5 per week
Outcomes	Outcomes assessed at 2 weeks • Function using the University of California-Los Angeles (UCLA) Shoulder Rating Scale, scored from 1-35 with high scores indicating better function • Rest pain using a 10 cm VAS, with 0 indicating "no pain" and 10 indicating "unbearable pain" • Night pain using a 10 cm VAS, with 0 indicating "no pain" and 10 indicating "unbearable pain" • Adverse events
Notes	**Conflicts of interest:** no specific conflicts of interest reported **Funding:** Carlos III Health Institute (contract number PI 07/0046) and FEDER funds

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "For the allocation of the 30 remaining participants, block randomization was made by a computer-generated random number list of elements with two possible random values (1 or 2), prepared by an investigator with no clinical involvement in the trial. The selected patients were consecutively assigned a number on the random list when they first came for treatment. Patients assigned with 1 received interferential light therapy (group 1) and those assigned with 2 received conventional light therapy (group 2)." Comment: An adequate method was used to generate the allocation sequence

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Allocation concealment (selection bias)	Unclear risk	Quote: "To preserve the allocation concealment, the random list was handled only by the non-clinical investigator, who was also responsible for giving the daily sequence of treatments to the physiotherapist." Comment: Insufficient information was reported to determine whether an adequate method of allocation concealment was used
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: For blinding purposes of the study, the procedure was the same as in the interferential group, except that now only one of the two applicators was active." Quote: "The patient-blinding procedure consisted in a twofold action. First, the two applicators were applied to all patients, regardless of whether one or both of them were active. Patients wore a pair of goggles that besides giving protection, prevented them from seeing the light spot of the applicator that was switched on. The front panel of the power supply was located behind the patients and outside their visual field." Comment: participants were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported pain and function
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "Evaluations were performed by a physiotherapist who was not informed about the technique each patient received. " Comment: Assessor of objective outcomes (i.e. objectively measured components of UCLA shoulder scale) was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "A total of 30 patients were randomized, assigning 15 to each group. Two subjects per group dropped out over the six-month period of the study, leaving 13 patients per group to be analysed." Comment: The participants' flow diagram shows that in each group, 1 participant was lost to follow-up and 1 discontinued treatment. Thus, the number of drop-outs and reasons for drop-out were balanced between groups and are unlikely to have bi-

Montes-Molina 2012b (*Continued*)

		ased the results
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Nykänen 1995

Methods	**Study design**: Parallel group RCT **Setting:** Inpatient rehabilitation centre, Finland **Intervention:** Therapeutic ultrasound plus massage plus exercises **Control:** Placebo ultrasound plus massage plus exercises **Source of funding:** Not reported
Participants	**Diagnostic label used by trialist:** Painful arc or supraspinatus tendinopathy/tendinitis **Criteria for defining the shoulder condition being treated:** Shoulder pain with one of the following: • a painful arc of between 40-120 degrees of abduction • other painful movement plus pain in the supraspinatus test (participant upright, shoulder 90 degrees of abduction, 30 degrees of horizontal adduction, and full internal rotation) **Any restriction on duration of symptoms** • At least 2 months **Inclusion Criteria (not listed above)** • None **Exclusion Criteria (not listed above)** • Suspected biceps-tendinitis (prominent pain on biceps-sulcus and pain during resisted elbow flexion) • Prominent tenderness over the acromioclavicular joint • Frozen shoulder (adhesive capsulitis) • Apparent rupture of rotator cuff (marked weakness or inability of active abduction not due to pain) • Participants with shoulder problems associated with hemiplegia • Cases of altered anatomy or function (including states with nerve or bone lesions) • Participants with inflammatory rheumatoid diseases • Participants with unresolved compensation claims **Baseline characteristics** *Intervention: Therapeutic Ultrasound* Number randomised: 36 Number included in analyses: 35 Age: 66 ± 6 years old

	Sex: F/M 6/29 Duration of symptoms: not reported *Control: Placebo ultrasound* Number randomised: 37 Number included in analyses: 37 Age: 67 ± 9 years old Sex: F/M: 5/32 Duration of symptoms: not reported
Interventions	**Intervention: Therapeutic ultrasound** *Description of modality used*: pulsed ultrasound using a EST301-machine with Ultra-Phone ultrasonic coupling medium *Dose*: Pulsed on-to-off ratio 1:4, frequency 1.0 mHz, intensity 1.0 W/cm^2, pulse repetition rate 100 mHz, pulse duration 2 ms, radiating area 5 cm^2 over a 10-min treatment period *Frequency of administration*: 10-12 treatments over 3-4 weeks **Control: Placebo ultrasound** *Description of modality used*: same as above except the transducer plug was manipulated to leave it off during the sessions *Dose*: none for 10 min *Frequency*: 10-12 treatments over 3-4 weeks **Both groups: Massage and exercises** *Description of modality used*: neck and shoulder massage and group gymnastics attempting to stretch and strengthen the humero-scapular and cervical musculature. Analgesia and NSAIDs were kept to a minimum but given for pain disturbing sleep
Outcomes	Outcomes assessed at 3-4 weeks, 4 months and 12 months • Function: ADL index scored 3-14, with a higher score indicating worse function • Overall pain: Pain Index scored 4-20, with a higher score indicating worse pain
Notes	**Conflicts of interest:** not reported **Funding: n**ot reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "...the subjects were randomly assigned to groups A or B" Comment: There was no information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Before treatment the therapist chose a transducer plug labelled either A or B according to the respective group of patients. A technician, also responsible for the

Nykänen 1995 (*Continued*)

		regular checking of the ultrasonic output of the machines, had made the other plug nonfunctioning. Apart from him, no other person knew which plug was manipulated. Manipulation affected only the function of the applicator head, with no difference in machine appearance" Comment: participants were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported all outcomes
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "Seventy-two patients (35 in the ultrasound group and 37 in the placebo group) completed the treatment period (one patient suffered a fatal myocardial infarction after one week's treatment). At the 4-month follow-up, 67 responded (32 in the ultrasound group and 35 in the placebo group) and at one-year follow-up, 68 responded (30 and 37, respectively)" Comment: The experimental group had a larger loss to follow-up, but reasons for this were not reported. Therefore it is unclear if attrition biased the results
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Otadi 2012

Methods	**Study design**: Parallel group RCT **Setting:** Physiotherapy ward (by referral from orthopaedic surgeon or rheumatologist), Iran **Intervention:** Low-level laser therapy (LLLT) plus therapeutic ultrasound plus exercise **Control:** Therapeutic ultrasound plus exercise **Source of funding:** Not reported

Participants	**Diagnostic label used by trialist:** Shoulder tendinitis **Criteria for defining the shoulder condition being treated** • Local pain in supraspinatus and/or long head of biceps tendons • Painful arc in abduction movement • Pain in isometric resistance and passive stretch in supraspinatus and biceps • Tenderness over the involved tendons • Positive Speed's sign or impingement test **Any restriction on duration of symptoms** • None **Inclusion Criteria (not listed above)** • Female • MRI and/or CT support for diagnosis if required **Exclusion Criteria (not listed above)** • History of steroid injections to the tendons • Rupture of the tendons • Calcifications in the tendons • Bursitis • Previous operation in the shoulder region • Neck and shoulder osteoarthritis • Thoracic outlet syndrome **Baseline characteristics** *Intervention: LLLT, US, exercise and laser* Number randomised: 23 Number included in analyses: 21 Age: 49.48 ± 8.5 years old Sex: all female Duration of symptoms: not reported *Control: US and exercise* Number randomised: 21 Number included in analyses: 21 Age: 48.05 ± 7.9 years old Sex: all female Duration of symptoms: not reported
Interventions	**Intervention: LLLT** *Description of modality used*: LLLT with Class 3B solid state GA-AS-AI infrared laser (Endolaser 476, Enraf Nonius, Holland, type 1476.751) with pencil probe. Laser treatment applied over 1 cm^2 areas marked out with a dematographic pencil *Dose*: Wavelength 830 nm, power 30 mW, 1 J/cm^2, beam diameter 4 mm, 1 mm at 10 mm from the probe, angle of divergence 2.5° *Frequency of administration*: 3 sessions per week for 10 sessions (4 weeks) **Control: no placebo LLLT delivered** **Both Groups:** *Description of modality used* • Therapeutic ultrasound: pulsed ultrasound carried out using slow circular movements over the supraspinatus tendon just medial to its insertion on the greater tuberosity of the humerus. If bicipital tendons involved, the device was used over the bicipital groove or lower insertion • Supervised and home exercises: pendulum exercises without weights were used to

	cause pain-inhibiting grade II joint distraction and oscillation motions. Pain-free, low intensity, multiple angle isometrics and protected exercises were instructed to appropriate muscle groups (scapulothoracic muscles, infraspinatus, subscapularis, and teres minor, supraspinatus, deltoid and biceps). These exercises initiated in inner range, through range, outer range and into functional positions. Later, these exercises progressed to dynamic resistance exercises such as concentric and eccentric exercise *Dose* • Ultrasound: Frequency 1 mHz, intensity 1 W/cm^2, pulsed mode duty cycle of 2: 8, transducer area of 5 cm^2 for 5 min • Exercises: number of repetitions or duration not reported *Frequency of administration* • Ultrasound: 3 sessions per week for 10 sessions (4 weeks) • Exercise: twice daily 4 weeks
Outcomes	Outcomes assessed at 4 weeks and 12 weeks • Function: Constant-Murley Score of 0-100 with higher scores indicating better function • Overall pain: VAS ranging from 0 (no pain) to 10 (worst imaginable pain) categorised as "greatly improved" (reduction from baseline > 5 points), "much improved" (reduction from baseline between 5 and 3 points), "somewhat improved" (reduction from baseline between 3 and 1 points), "about the same" (1 point lower or higher from baseline) or "worse" (increase from baseline > 1 point) • Strength: manual muscle testing with 5 grades (0, no function and 5, complete range of motion with maximum resistance)
Notes	**Conflicts of interest:** not reported **Funding:** not reported Trial registered in the Iranian Registry of Clinical Trials (IRCT138712101719N1)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "...were randomly assigned into two groups, using unmarked envelopes in clinic to achieve simple randomisation. There were 50 envelopes, 25 of which contained the word 'US and exercise' and 25 of which contained the word 'adding laser"' Comment: An adequate method was likely to used to generate the allocation sequence
Allocation concealment (selection bias)	Low risk	Comment: An adequate method was likely to used to conceal the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each inter-

Otadi 2012 (*Continued*)

		vention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "The staff that assessed the outcomes was differed from the staff that administered the treatments; and they were blinded to the type of treatments" Comment: Assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Two diabetic patients reported increase of pain in adding laser group and then withdrew from the study." Comment: The attrition may be related to the laser intervention, but the amount is small so is unlikely to have biased the results
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Ozgen 2012

Methods	**Study design**: Parallel group RCT **Setting:** Pamukkale University School of Medicine, Physical Medicine and Rehabilitation, Turkey **Intervention 1:** Transcutaneous electrical nerve stimulation (TENS) plus therapeutic ultrasound plus hot pack plus home exercises **Intervention 2:** Sodium hyaluronate injection plus home exercises **Source of funding:** Not reported
Participants	**Diagnostic label used by trialist:** Supraspinatus tendinitis **Criteria for defining the shoulder condition being treated** • Shoulder pain • Limitation of movement • MRI confirming supraspinatus tendinitis **Any restriction on duration of symptoms** • None

	Inclusion Criteria (not listed above) • None **Exclusion Criteria (not listed above)** • Younger than 18 • Dislocation or fracture of the shoulder joint • Rotator cuff laceration • Cervical radiculopathy • Inflammatory joint disease • Malignity • Pregnancy • Coagulation disease • Having received therapy for a similar condition in the last 3 months **Baseline characteristics** *Intervention 1: TENS plus therapeutic ultrasound plus hot pack plus home exercises* Number randomised: 12 Number included in analyses: 11 Mean (SD) age: 52.50 (8.83) years old Sex: F/M 9/3 Duration of symptoms: 9.17 ± 9.90 months *Intervention 2: Sodium hyaluronate injection plus home exercises* Number randomised: 12 Number included in analyses: 10 Mean (SD) age: 58.67 (9.80) years old Sex: F/M 9/3 Duration of symptoms: 8.75 ± 4.96 months
Interventions	**Intervention 1: TENS plus therapeutic ultrasound plus hot pack** *Description of modality used* • TENS administered conventionally with an ITO-Trio 300 electro-stimulation device by adjusting the flow frequency at 60 Hz, flow duration at 60 μsn, the amplitude in a way that would not disturb the participant and on a level that would reside below the motor threshold • Therapeutic ultrasound applied using direct shoulder contact technique with shoulder pain zone, using a SONICATOR 730 capped device with Sonotact US gel • hot packs: fabric bags filled with silicate gel residing in a TESA hot pack heater at 75°C were applied to the shoulder by wrapping a towel on them *Dose* • TENS: 60 Hz flow frequency, 60 μsn flow duration and below motor threshold amplitude for 20 min • Therapeutic ultrasound: 1.5 W/cm^2 for 5 min/10 cm^2 • hot packs: 20 min *Frequency*: not reported (assumed 3 weeks in total) **Intervention 2: Sodium hyaluronate injection** *Description of modality used*: administered to the shoulder joint by posterior approach. The administration zone cleaned with 10% polyvinylpyrrolidone iodine solution, then a 2 ml (16 mg) of G-F 20 preparation with a molecular weight of 6 x 10^6 was administered into the joint cavity using a 21-gauge injector *Dose*: 2 ml (16 mg) of G-F 20 preparation with a molecular weight of 6 x 10^6 *Frequency of administration*: 3 times with weekly intervals

	Both groups: Home exercises *Description of modality used*: range of motion, stretching and strengthening exercises
Outcomes	Outcomes assessed at 3 weeks, 3 months and 4 years • Function: function portion of the Society of the American Shoulder and Elbow Surgeons Rating Scale, ranging from 0-60 with a higher score indicating better function • Rest pain: 10 cm VAS with a higher score equating to worse pain • Pain on motion: 10 cm VAS with a higher score equating to worse pain • Night pain: 10 cm VAS with a higher score equating to worse pain • Global assessment of treatment success: participants' global effectiveness evaluation on Likert scale of 1-4 with 1 = poor, 2 = moderate, 3 = good and 4 = excellent, using scores of 3 or 4 to indicate success • Active and passive range of motion (abduction, flexion, extension, internal rotation, external rotation) using a goniometer • Adverse events
Notes	**Conflicts of interest:** not reported **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "They were randomized into two groups." Comment: There was no information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Unclear risk	Comment: There was no information on whether the assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "On the other hand, we determined that the effectiveness of treatment in the remaining 11 people in Group I and 10

Ozgen 2012 (*Continued*)

		people in Group II who could be reached was evaluated as 'very good"' Comment: The amount of attrition was small and unlikely to have biased the results
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Pan 2003

Methods	**Study design**: Parallel group RCT **Setting:** Outpatient clinics, Taiwan **Intervention 1:** Transcutaneous electric nerve stimulation (TENS) **Intervention 2:** Extracorporeal shock wave therapy (ESWT) **Source of funding:** Not reported
Participants	**Diagnostic label used by trialist:** Chronic calcific tendinitis **Criteria for defining the shoulder condition being treated** • Radiographically and sonographically verified calcific tendinitis **Any restriction on duration of symptoms** • Continuous pain for 6 months **Inclusion Criteria (not listed above)** • Moderate pain required (above or equal to 4 on a VAS from 0-10) **Exclusion Criteria (not listed above)** • Systemic diseases • Cardiac pacemaker or other implanted device • Neuropathic, malignant or infectious causes of pain • Rotator cuff tear • Previous surgery for calcification • Percutaneous needle aspiration • Glucocorticoid injection of the shoulder within three months • Pregnant **Baseline characteristics** *Intervention 1: TENS* Number randomised: 30 shoulders in 28 participants Number included in analyses: 29 shoulders in 27 participants Age: 58.00 ± 1.83 years Sex: F/M 19/9 Duration of symptoms: 23.90 ± 5.32 months *Intervention 2: ESWT*

Pan 2003 (*Continued*)

	Number randomised: 33 shoulders in 32 participants Number included in analyses: 33 shoulders in 32 participants Age: 55.21 ± 2.01 years Sex: F/M 20/12 Duration of symptoms: 24.55 ± 6.45 months
Interventions	**Intervention 1: TENS** *Description of modality used*: Hydrocollator pack and Neurosan50 electrostimulator (TENS) delivered constant square-wave pulse stimulation current with a 0.5 ms pulse width and a 10 ms interval length to an active electrode secured firmly on the skin at the subacromion painful area *Dose*: frequency of 95 Hz and intensity increased until local contraction of adjacent muscles. Total session time was around 20 min *Frequency*: 3 times a week for 4 weeks **Intervention 2: ESWT** *Description of modality used*: The Orthospec^{TM} was used to deliver ESWT. The Orthospec^{TM} is a spark gap generator in a mobile unit. The therapeutic zone is ellipsoid in shape, 95 mm in height and 25 mm in diameter. There is about 0.29 mJ/cm^2 of energy density at the edge of the therapeutic zone. The contact head was positioned at the marked painful area, which was defined by sonography before each treatment so that the acoustic shock wave could be transmitted effectively *Dose*: 2 Hz with 2000 shock waves and the energy level ranged from 0.26 mJ/mm^2 to 0.32 mJ/mm^2, depending on the intensity, which was adjusted to the participant's tolerance *Frequency of administration*: 2 sessions over 4 weeks
Outcomes	Outcomes assessed at 2 weeks, 4 weeks and 12 weeks • Function: Constant-Murley total score, 0 to 100 points with a higher score indicating better function • Overall pain: VAS from 0 to 10 with a higher score indicating more pain • Strength: Manual muscle test (0-5 scale dichotomised as "improved" or not) • Adverse events
Notes	**Conflicts of interest:** not reported **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "All patients were randomly assigned to ESWT or TENS groups by draw" Comment: An adequate method was likely used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed

Pan 2003 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Unclear risk	Comment: There was no information on whether the assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "With the exception of 1 patient in the TENS group who dropped out after the first session because of severe pain, all patients completed the scheduled treatments and follow-up" Comment: The very small amount of attrition is unlikely to have biased the results
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Perron 1997

Methods	**Study design**: Parallel group RCT **Setting:** General community, private practice, Canada **Intervention:** Acetic acid iontophoresis plus therapeutic ultrasound **Control:** No treatment **Source of funding:** Not reported
Participants	**Diagnostic label used by trialist:** Calcifying tendinitis **Criteria for defining the shoulder condition being treated** • Confirmed diagnosis of symptomatic calcifying tendinitis • Area of calcium density of 50 mm^2 or larger (Type I or Type II lesion was also determined) **Any restriction on duration of symptoms**

	• None **Inclusion Criteria (not listed above)** • Adults **Exclusion Criteria (not listed above)** • If presented with secondary conditions (e.g. systemic disease) • X-rays were contraindicated • Participants received secondary benefits (e.g. worker's compensation) **Baseline characteristics** *Intervention: Acetic acid iontophoresis plus therapeutic ultrasound* Number randomised: 11 Number included in analyses: 11 Age: 43 years (32-57) Sex: F/M 7/4 Diagnosis: Type I lesion: 3, Type II lesion: 8 Duration of symptoms: 45 (0.2-180) months *Control: No Treatment* Number randomised: 11 Number included in analyses: 10 Age: 40 years (33-50) Sex: F/M 8/2 Diagnosis: Type I lesion n = 2, type II lesion n = 8 Duration of symptoms: 31 (0.5 - 120) months
Interventions	**Intervention: Acetic acid iontophoresis plus therapeutic ultrasound** *Description of modality used* • Acetic acid iontophoresis (AAI) using a 48 cm^2 carbon rubber electrode connected to the negative pole (active electrode). The cathode was inserted into a sponge soaked in 5% acetic acid solution and fixed to the area to be treated with an elastic bandage. The hand of the uninvolved arm was placed away from the anode (indifferent electrode) in a tub of tap water. A Dynatron 406 was used to deliver a galvanic current • Continuous ultrasound using a Sonopuls 434 applied over the same area *Dose* • AAI: Current amplitude set to 5 mA (which corresponds to a current density of less than 1 mA per square inch) administered over 20 min • US: Frequency 1 mHz to reach 2 - 4 cm in depth, intensity 0.8 W/cm^2, for 5 min *Frequency of administration*: 3 treatments per week for 3 weeks **Control: No Treatment** **Both Groups** Asked to avoid activities requiring overhead arm movements or repetitive tasks with the involved shoulder
Outcomes	Outcomes assessed at 1, 2, and 3 weeks • Pain on motion: Present Pain Index, which ranges from 0-5 with a higher score indicating worse pain • Passive range of motion (abduction) measured using a goniometer
Notes	**Conflicts of interest:** not reported **Funding:** Ordre des Physiotherapeutes du Quebec Outcome data extracted from Figures using DigitizeIt software

Perron 1997 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "The patients in each stratum were then randomly assigned to th experimental (EXP) or control (CTL) groups". Comment: There was no information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "Four physiotherapists participated in the functional evaluations, but each patient was reevaluated by the same physiotherapist. Evaluators were unaware of the group assignment, and the patients were reminded not to make any statement that would unblind the evaluators" Comment: Assessors of objective outcomes were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Although all 22 patients completed the study, results from one patient were rejected because the incidence of X-ray films taken at each evaluation did not allow a fair comparison of the CD area." Comment: One participant did not complete evaluation, and was removed due to technical problems with their X-rays. This is unlikely to have biased the results
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear

		whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Polimeni 2003

Methods	**Study design**: Parallel group RCT **Setting:** Ambulatory academic hospital, Canada **Intervention 1:** Therapeutic ultrasound plus mobilisation plus exercises **Intervention 2:** Diadynamic current plus mobilisation plus exercises **Intervention 3:** Radar plus mobilisation plus exercises **Control:** Mobilisation plus exercises **Source of funding:** Not reported
Participants	**Diagnostic label used by trialist:** Supraspinatus tendinitis or biceps tendinitis **Criteria for defining the shoulder condition being treated:** • Participants referred with painful shoulder syndrome assessed by history and physical examination, including 6 clinical signs (Yocum, Jobe, Impingement test, Yergason, Palm up and Apley) **Any restriction on duration of symptoms** • Less than 3 months **Inclusion Criteria (not listed above)** • Pain not due to traumatic injury • No NSAID use in the 15 days prior to assessment **Exclusion Criteria (not listed above)** • None **Baseline characteristics** *Overall cohort of participants* Number randomised: 18 into each group Number included in analyses: not reported Age (mean and SD, or range): 56 ± 16 years Number of men and women: F/M 36/14 Duration of symptoms: not reported
Interventions	**Intervention 1: Therapeutic ultrasound** *Description of modality used*: no details reported *Dose*: frequency not reported; intensity 1.5 W/cm^2 *Frequency of administration*: 10 days **Intervention 2: Diadynamic current** *Description of modality used*: no details reported *Dose*: long interval of 7 min per session *Frequency*: 10 days **Intervention 3: Radar** *Description of modality used*: no details reported *Dose*: 60 W/cm^2 in increasing 1min steps per day *Frequency*: 10 days

	Control: Nothing other than mobilisation plus exercises, which all groups received **All Groups: Mobilisation plus exercises** *Description of modality used*: mobilisation of all planes of movement, passive and active assisted exercises *Dose*: 10 min of passive exercises, 20 min of active assisted exercises *Frequency of administration*: 10 days
Outcomes	Outcomes assessed at 5 days, 10 days, and 40 days • Function: Constant-Murley total score: 0-100 scale with a higher score indicating better function
Notes	**Conflicts of interest:** not reported **Funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The patients were randomly assigned to 4 groups" Comment: There was no information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported all outcomes of interest to this review
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: Trialists did not report whether there were any dropouts, losses to follow-up or exclusions, or the number of participants included in each analysis
Selective reporting (reporting bias)	Unclear risk	Comment: Medians with no measures of variation reported for the Constant-Murley score, however this was not related to the lack of statistical significance for this outcome. Without a trial protocol it is unclear whether other outcomes were mea-

Polimeni 2003 (*Continued*)

		sured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Rabini 2012

Methods	**Study design**: Parallel group RCT **Setting:** Outpatient clinic of the Department of Orthopaedics and Traumatology, University Hospital, Rome, Italy **Intervention 1:** Microwave diathermy **Intervention 2:** Glucocorticoid injection **Source of funding:** Not reported
Participants	**Diagnostic label used by trialist:** Rotator cuff tendinopathy, with or without partial thickness tendon tears **Criteria for defining the shoulder condition being treated** • Shoulder pain • Degenerative rotator cuff tendinopathy on clinical exam (abduction at 0 degrees or 30 degrees, external or internal rotation, positive Kennedy-Hawkin's sign) • Evidence of tendinopathy on X-ray in anteroposterior, axillary or outlet views • Confirmation of diagnosis on MRI **Any restriction on duration of symptoms** • At least 3 months **Inclusion Criteria (not listed above)** • Aged over 18 **Exclusion Criteria (not listed above)** • Inability or unwillingness to sign informed consent • Full thickness tear of the rotator cuff and/or of the subscapularis tendon • Degenerative arthritis of the glenohumeral joint • Symptomatic arthritis of the acromioclavicular joint • Previous surgery on the affected shoulder • Inflammatory or neurological disease involving shoulder girdles • Anticoagulant treatment • Chronic NSAID drug or steroid treatment • Cognitive or psychiatric disorders • Pregnancy or breastfeeding • Previous treatment with one of the two interventions • Contraindications to the treatments • Contraindications to MRI **Baseline characteristics** *Intervention 1: Microwave diathermy* Number randomised: 46 Number included in analyses: 40 Age: 59.2 ± 7.1 years Sex: F/M 30/16 Duration of symptoms: 15.5 ± 20.4 months

	Intervention 2: Glucocorticoid injection Number randomised: 46 Number included in analyses: 42 Age: 56.6 ± 11.6 years Sex: F/M 31/15 Duration of symptoms: 13.1 ± 9.1 months
Interventions	**Intervention 1: Microwave diathermy** *Description of modality used*: administered using a Smarterapia Sigma Hyperthermia System with a 434 mHz microwave generator and a maximum output power of 100 W. It also utilised a microstrip antenna applicator specific for semicylindrical joint volumes of 20 to 30 cm in diameter. It had a total radiating area of 240 cm^2 and an effective field size on a surface of 96 cm^2. A 0.5 cm thick silicone pad filled with thermostatic deionised water was applied on the shoulder to allow the greatest energy transfer to be achieved. The pad was placed over the middle third of the joint line (between the glenoid and humeral head) with the participant supine and arm at 60 degrees of abduction and externally rotated *Dose*: 40 W power with silicone pad temperature of 38°C. The aim was to achieve 1.5° C difference between cutaneous and deep temperature according to the thickness of the cutaneous fat of each participant. Each session lasted 30 min *Frequency*: 3 sessions per week for 4 weeks **Intervention 2: Glucocorticoid injection** *Description of modality used*: experienced physician injected at the subacromial space of the affected shoulder, using a 21-gauge needle, aseptic conditions, through a posterolateral access *Dose*: 1 mL 40 mg methylprednisolone acetate containing 10 mg lidocaine chlorhydrate *Frequency of administration*: 1 injection every 2 weeks for total of 3 injections
Outcomes	Outcomes assessed at 4 weeks, 12 weeks and 24 weeks • Function: Constant-Murley total score measured from 0-100 (higher score denotes better function) • Overall pain: VAS score ranging from 0 (the absence of pain) to 100 (most severe pain) • Adverse events
Notes	**Conflicts of interest:** not reported **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomly assigned…using a random sequence generator (www.random.org)" Comment: An adequate method was used to generate the allocation sequence

Allocation concealment (selection bias)	Low risk	Quote: "The randomization list was kept by an independent researcher not involved in the study. Allocation concealment was performed using closed envelopes, and the assignment code of each patient was revealed to the researcher who performed the treatment only at the beginning of the therapeutic protocol" Comment: An adequate method was used to conceal the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "Primary and secondary outcome measures were determined at baseline and follow-up visits by an investigator blind to participants' allocation" Comment: Assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Missing data at follow-up were managed according to the last-observation-carried-forward (LOCF) method. Data were analysed according to the intention-to-treat principle" Quote: "A total of 8 participants (8.7%) were lost to follow-up, 2 in the corticosteroid group and 6 in the hyperthermia group. The follow-up was thus completed in 82 patients (89%)" Quote: "Finally, reasons for lack of follow-up were not recorded. However, only a few participants were lost to follow-up (8.7%) and dropouts occurred to a similar extent in the 2 treatment groups, which did not substantially affect the results" Comment: The small amount of attrition is unlikely to have biased the results

Rabini 2012 (*Continued*)

Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

San Segundo 2008

Methods	**Study design**: Parallel group RCT **Setting:** Outpatient rehabilitation service, Spain **Intervention:** Therapeutic ultrasound plus exercise **Control:** Placebo ultrasound plus exercise **Source of funding:** Not reported
Participants	**Diagnostic label used by trialist:** Rotator cuff tendinitis or partial rotator cuff tears **Criteria for defining the shoulder condition being treated** • Ultrasonography or MRI showing tendinitis or partial rotator cuff tears. **Any restriction on duration of symptoms** • Greater than 3 months **Inclusion Criteria (not listed above)** • Aged between 18 and 70 years • No contraindications to either treatment • Participant gave informed consent **Exclusion Criteria (not listed above)** • Traumatic causes of pain • Rheumatic or neurological causes • Complete rupture of any of the tendons of the rotator cuff • Participants with a normal MRI or ECO • Calcifying tendinitis • Adhesive capsulitis (frozen shoulder) • Shoulder infiltration in the past 3 month **Baseline characteristics** *Intervention: Therapeutic ultrasound plus exercise* Number randomised: 17 shoulders Number included in analyses: 16 shoulders Age (mean and SD, or range): 52.6 (10.9) years old Number of men and women: F/M 80%/20% Diagnosis: tendinitis: 88.2%; partial rotator cuff tear: 11.8% Duration of symptoms (SD): 10.2 (11.4) months *Control: Placebo ultrasound plus exercise* Number randomised: 17 shoulders Number included in analyses: 15 shoulders Age (mean and SD, or range): 56.9 (9.4) years

	Number of men and women: F/M 87.5%/12.5% Diagnosis: tendinitis: 82.3%; partial rotator cuff tear: 17.7% Duration of symptoms (SD): 12.6 (11.1) months
Interventions	**Intervention: Ultrasound plus exercises** *Description of modality used*: pulsed ultrasound delivered with standard technique *Dose*: intensity 2 W/cm^2 1:4 at frequency 1 mHz for 7 min *Frequency of administration*: 3 days a week for 3 weeks **Control: Placebo Ultrasound plus exercises** *Description of modality used*: application of non-functioning ultrasound device *Dose*: none *Frequency of administration*: 3 days a week for 3 weeks *Any additional treatment during trial*: analgesia if required **Both groups** *Description of modality used*: active assisted exercises for mild mobility impairment and strengthening exercises for rotator cuff, using an elastic band *Dose*: not reported *Frequency of administration*: daily sessions for 3 weeks followed by sessions twice a week for an additional 2 weeks once the ultrasound sessions were finished
Outcomes	Outcomes assessed at time points: baseline, 3 weeks, 5 weeks, 3 months and 6 months • Function: Constant-Murley total score, 0-100 with higher score indicating better function • Rest pain: VAS 0-100 with a higher score indicating worse pain • Night pain: VAS 0-100 with a higher score indicating worse pain
Notes	**Conflicts of interest:** not reported **Funding:** not reported Article is written in Spanish but translated into English using https://translate.google.com.au/

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The patients included were assigned by a third person, one of the two treatment groups in a sequence generated by a random number table. In patients with bilateral shoulder each shoulder was assigned to a group, randomized consecutively" Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Initially, both the physician and the therapist and the patient were blinded to the type of treatment assignment. However, once started the study found that it was possible to blinding therapists who performed the treatment, since the proceeding routine device check told him when the U. S. is not functioning. " Comment: Participants were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Comment: According to the above quote, the physician (who was the outcome assessor) was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All 29 patients completed the study at 5 weeks, but at 3 and 6 months the percentage of patients lost was very high (44.1% overall, 23.5% in group 1 and 20. 6 % in group 2), so results could not be analyzed" Comment: There was no attrition at short-term follow-up, and authors decided not to analyse data at 3- and 6-month follow-up due to high attrition at this later time point
Selective reporting (reporting bias)	Unclear risk	Comment: Due to the high attrition rate, the authors chose not to publish data for their planned 3- and 6-month follow-up. However, outcome data were fully reported for all outcomes specified in the methods section of the publication at short-term follow-up. Though without a trial protocol it is unclear if other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Santamato 2009

Methods	**Study design**: Parallel group RCT **Setting:** Outpatients in a university hospital, Italy **Intervention 1:** High intensity laser therapy **Intervention 2:** Therapeutic ultrasound **Source of funding:** "Work was supported by the Italian Longitundinal Study on Aging (ILSA) - Italian National Research Council"
Participants	**Diagnostic label used by trialist:** Subacromial impingement syndrome **Criteria for defining the shoulder condition being treated** • Presence of shoulder pain • Pain on abduction of the shoulder with a painful arch • Positive impingement sign (Hawkins) • Positive impingement test (relief of pain within 15 min after injection of local anaesthetic into the subacromial space) • Confirmation of Neer stage I or II impingement by MRI or ultrasound **Any restriction on duration of symptoms** • Minimum 4 weeks **Inclusion Criteria (not listed above)** • 18 years or older **Exclusion Criteria (not listed above)** • Anaesthetic or corticosteroid injections within 4 weeks of study • Surgery or previous fracture of the humeral head on the affected side • Impaired rotation of the glenohumeral joint • History of acute trauma • Known osteoarthritis in the glenohumeral or acromioclavicular joint • Calcifications exceeding 2 cm in the rotator cuff tendons • Signs of a rupture of the cuff • Cervical myofascial pain syndrome • Radicular pain • Inflammatory rheumatic disease • SLE, diabetes mellitus, thyroid dysfunction or neurological pathologies • A pacemaker • Anxiety-depression syndromes **Baseline characteristics** *Intervention 1: High intensity laser therapy* Number randomised: 35 Number included in analyses: 35 Age (mean and SD, or range): 54.2 years (8.2 SD) Number of men and women: F/M 20/15 Duration of symptoms: 8.7 months (8.8 SD) *Intervention 2: Therapeutic ultrasound* Number randomised: 35 Number included in analyses: 35 Age (mean and SD, or range): 54.0 years (9.8 SD) Number of men and women: F/M 22/13 Duration of symptoms: 8.1 months (10.8 SD)
Interventions	**Intervention 1: High intensity laser therapy** *Description of modality used*: high intensity laser therapy with a neodymium yttrium aluminum garnet laser that has a pulsating waveform produced by an HIRO 1.0 device.

	Administered by a physiatrist using a standard handpiece endowed with fixed spacers, with consistent distance from the skin, verticality of 90 degrees to the treatment zone and a bright spot diameter of 5 mm. Each session involved 3 phases: • a fast manual scanning (100 cm^2/30 seconds) of the zones of muscular contracture (particularly for the upper trapezius and deltoid muscles and anteriorly for the pectoralis minor muscle) in both transverse and longitudinal directions with the arm positioned in internal rotation and extension to expose the rotator cuff. In this phase, 1000 J was administered; • an intermediate phase involving applying the handpiece with fixed spacers vertically to 90 degrees on the trigger points until a pain reduction of 70% to 80% was achieved. In this phase, 50 J was administered; • a final phase involved slow manual scanning (100 cm^2/60 s) of the same areas treated in the initial phase until a total energy dose of 1000 J was achieved *Dose*: the treatment consisted of a high peak power (1 kW), a wavelength of 1064 nm, a maximum energy for a single impulse of 150 mJ, an average power of 6 W, a fluency of 760 mJ/cm^2, and a duration for the single impulse of less than 150 ms. Three steps were predicted in the starting/initial and nal phases of the treatment; the fi uencies used were 510, 610, and 710 mJ/cm2, respectively. Therefore, the total dose of energy administered was approximately 2050 J over 10 min *Frequency of administration*: 5 days a week for 2 weeks **Intervention 2: Therapeutic ultrasound** *Description of modality used*: continuous ultrasound using a Sonopuls 492 with a 5.8 cm^2 transducer head and an effective radiating area of 4.6 cm^2. The treating physical therapist, using the technique of slow circular movements, applied the transducer head over the superior and anterior periarticular regions of the participant's glenohumeral joint and on the shoulder trigger points, covering an area of approximately 20 cm^2 *Dose*: frequency of 1 MHz and an intensity of 2 W/cm^2 with a duty cycle of 100%. Duration 10 min *Frequency of administration*: 5 days a week for 2 weeks
Outcomes	Outomes assessed at 2 weeks • Function: Constant-Murley total score (0-100 with a higher score indicating better function) • Overall pain: VAS from 0 ("no shoulder pain") to 10 ("worst pain ever")
Notes	**Conflicts of interest:** authors stated that the funding agencies had no role in the design, conduct or reporting of the study **Funding:** Italian Longitudinal Study on Aging (ILSA) (Italian National Research Council-CNR-Targeted Project on Aging grants 9400419PF40 and 95973PF40

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Concealed allocation was performed with random numbers generated from the Web site http://www.random.org/ before the beginning of the study. The procedure Random Integer

		Generator allowed us to generate random integers. A priori it generated 100 random integers and, before the beginning of the study, the randomization number was already present." Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Low risk	Quote: "Individual, sequentially numbered index cards with the random assignments were prepared. The index cards were folded and placed in sealed opaque envelopes. A physician who was unaware of the baseline examination findings opened the envelopes to attribute the interventions according to the group assignments." Comment: An adequate method was used to conceal the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "...the physicians who performed the clinical evaluations of the participants were unaware of the group assignments" Comment: Assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All 70 participants completed the trial and were included in the analysis." Comment: There was no attrition
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results

Santamato 2009 (*Continued*)

Other bias	Low risk	Comment: No other sources of bias identified

Saunders 1995

Methods	**Study design**: Parallel group RCT **Setting:** Physiotherapy department, UK **Intervention:** Low level laser therapy (LLLT) **Control:** Placebo laser **Source of funding:** Not reported
Participants	**Diagnostic tool used by trialist:** Supraspinatus tendinitis **Criteria for defining the shoulder condition being treated** • General practitioner or rheumatologist's diagnosis of supraspinatus tendinitis • Full passive range of shoulder movement, but with impingement on full elevation • Pain leading to secondary weakness in isometric contraction of the supraspinatus muscle with the arm in 1.57 rad (90°) of abduction, 0.52 rad of flexion and medially rotated so that the participant's thumb points directly downwards • Tenderness on palpation of the tendon medial to the point of insertion on the head of the humerus **Any restriction on duration of symptoms** • Over four weeks' duration **Inclusion Criteria (not listed above)** • 35-65 years of age; and • no treatment during the last four weeks; • no other painful musculoskeletal or neurological condition **Exclusion Criteria (not listed above)** • None **Baseline characteristics** *Overall cohort of participants* Number of men and women: F/M 12/12 *Intervention: LLLT* Number randomised: 12 Number included in analyses: 12 Age mean (SD): 49.8 (8.12) years old Number of men and women: not reported Duration of symptoms: 3.86 (2.4 SD) months *Control: Placebo LLLT* Number randomised: 12 Number included in analyses: 12 Age mean (SD): 50.7 (8.31 SD) years old Number of men and women: not reported Duration of symptoms: 3.32 (1.9 SD) months
Interventions	**Intervention: LLLT** *Description of modality used*: a 50 mW, 820 nm (infrared) laser probe was pressed firmly into the tissue, at an angle of 1.57 radian to the tendon. Two areas were irradiated: • the anterior shoulder, at the point of maximum tenderness just medial to the

	tendon's insertion with the arm at the side and the forearm resting on the abdomen, and • the tendon just below the acromion with the participant's hand placed behind the back at the L3 level *Dose*: 40 mW, 30 J/cm^2 treatment, operated for 90 seconds at a frequency of 5000 Hz for both areas (i.e. 180 seconds in total) *Frequency of administration*: 9 treatments over 3 weeks (3 treatments per week) Any additional treatment during trial: none reported **Control: Placebo LLLT** *Description of modality used*: same as above except laser device switched off *Dose*: Zero power *Frequency of administration*: 9 treatments over 3 weeks (3 treatments per week) **Both Groups: Advice** *Description of modality used*: a recording of a physiotherapist explaining to the participants how to use their arms, and a transcript of the recording *Frequency of administration*: the tape was played once, but the transcript was the participant's to keep
Outcomes	Outcomes assessed at 3 weeks • Overall pain: pain diary asking about pain at rest and when using the arm at different times of the day (6 questions in total, summed and categorised as "improved", "no change" or "worsened) • Strength: muscle force measured using a myometer
Notes	**Conflicts of interest:** Not reported **Funding:** Not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "The subjects were randomly assigned to two treatment groups" Comment: There was no information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The standardized treatments were administered by two physiotherapy helpers who had been given on-the-job training and training on laser safety procedures. The helpers used probe A or B depending on the treatment group of the patient. The helpers did not know which of the probes was real and which was the dummy" Quote: "There was no way for the helpers or therapists to distinguish between the

Saunders 1995 (*Continued*)

		probes" Comment: Participants and personnel were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "The subjects were tested by the same independent 'blind' assessor before and after the course of nine treatments" Comment: Assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: No attrition was reported, and outcome data were based on the number of randomised participants
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the Methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Shehab 2000

Methods	**Study design**: Parallel group RCT **Setting:** Outpatient rehabilitation unit, Kuwait **Intervention 1:** Trancutaneous electrical nerve stimulation (TENS) plus exercise plus cold pack **Intervention 2:** Therapeutic ultrasound plus exercise plus cold pack **Source of funding:** Not reported
Participants	**Diagnostic label used by trialist:** Supraspinatus tendinitis, subdeltoid bursitis or bicipital tendinitis **Criteria for defining the shoulder condition being treated** • Painful shoulder movement of at least one month's duration • Confirmation of supraspinatus tendinitis, subdeltoid bursitis or bicipital tendinitis based on physical examination of the shoulders and the cervical spine, including assessment of the range of motion and use of provacative testing **Any restriction on duration of symptoms** • At least 1 month **Inclusion Criteria (not listed above)** • Adults

	• Female • Not on drug therapy **Exclusion Criteria (not listed above)** • Inflammatory arthritis • Calcific tendinitis • Fracture **Baseline characteristics** *Overall cohort of participants* Number randomised: 50 (26 in TENS group and 24 in ultrasound group) Number included in analyses: 50 Age mean and SD, or range): 50 ± 5.89 years old Number of men and women: all women Diagnosis: most had supraspinatus tendinitis, subdeltoid bursitis or bicipital tendinitis Duration of symptoms: at least 1 month
Interventions	**Intervention 1: TENS** *Description of modality used*: TENS through electrodes applied to the anterior and posterior shoulder area *Dose*: frequency 50 Hz for 30 min *Frequency of administration*: 3-5 times per week for 13 sessions (i.e. 3-5 weeks) **Intervention 2: Therapeutic ultrasound** *Description of modality used*: ultrasound around the glenohumeral joint (not reported whether continuous or pulsed) *Dose*: Intensity 0.5 W/cm^2 increasing by 0.1 each session; frequency not reported; duration 10 min *Frequency of administration*: 3-5 times per week for 13 sessions (i.e. 3 -5 weeks) **Both groups:** cold packs for 20 min and stretching and range of motion exercises for the shoulder after each treatment
Outcomes	Outcomes assessed at 3-5 weeks • Overall pain: VAS 0-10, with a higher score indicating worse pain • Range of motion (flexion and abduction) using a goniometer (unclear if active or passive)
Notes	**Conflicts of interest:** Not reported **Funding:** Not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly assigned to one of two groups." Comment: There was no information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed

Shehab 2000 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	High risk	Quote: "We realize that not having the outcome measures blinded is a limitation of the study" Comment: Assessor of objective outcomes was not blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: Trialists did not report whether there were any dropouts, losses to follow-up or exclusions, or the number of participants included in each analysis
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Vecchio 1993

Methods	**Study design**: Parallel group RCT **Setting:** Outpatient rheumatology clinics, UK **Intervention:** Low-level laser therapy (LLLT) plus exercise **Control:** Placebo LLLT plus exercise **Source of funding:** No specific source of funding reported but the authors acknowledge "CM Medico for use of their laser equipment"
Participants	**Diagnostic label used by trialist:** Rotator cuff tendinitis **Criteria for defining the shoulder condition being treated** • Typical rotator cuff tendinitis (criteria of Cyriax) • Painful arc of abduction between 40 and 120 degrees • Painful resisted movement in at least one of: abduction, internal rotation or external rotation

	Any restriction on duration of symptoms • None **Inclusion Criteria (not listed above)** • None **Exclusion Criteria (not listed above)** • Participants with frozen shoulder, acromioclavicular arthritis or clinical rotator cuff tears • Pregnancy or breast-feeding • Subacromial steroids in the 3 months prior to treatment • Systemic diseases (e.g. rheumatoid arthritis) • Participants who had received physiotherapy for their shoulder lesion **Baseline characteristics** *Overall cohort of participants* Number randomised: 35 Number included in analyses: 35 Age mean (range): 54.4 years (17-77) Number of men and women: F/M 25/10 Duration of symptoms: 14.9 months (4-48) *LLLT plus exercise* Number randomised: 19 Number included in analyses: 19 Age (mean and SD, or range): not reported Number of men and women: F/M 11/8 Duration of symptoms: not reported *Placebo LLLT plus exercise* Number randomised: 16 Number included in analyses: 16 Age (mean and SD, or range): not reported Number of men and women: F/M 14/2 Duration of symptoms: not reported
Interventions	**Intervention: LLLT** D*escription of modality used*: continuous irradiation laser with a CB Medico Master III hand held single probe laser (Gallium aluminium arsenide diode of class 3B). Each session consisted of three pulses (3 J) to each of a maximum of 5 tender points found on clinical examination. As far as possible, treatment was concentrated in the subacromial or anterior shoulder regions. The laser was held perpendicular to the body and skin contact delivered without pressure *Dose*: 3 pulses (3 J); wavelength of 830 nm; mean power of 30 mW with a wavelength divergence of ± 1.5 nm and a beam diameter of 3 mm *Frequency of administration*: twice weekly for 8 weeks **Control: Placebo LLLT** *Description of modality used*: same as above except laser device switched off *Dose*: none *Frequency*: twice weekly for 8 weeks **Both groups: Supervised exercises** *Description of modality used*: exercises including pendular swing and wall climbing exercises. A physiotherapist taught exercises on the first session. Pendular swinging was performed in flexion and extension, abduction and adduction. Participants were also

	asked to stand facing a wall with both hands placed on the wall and shoulder elevation gradually increasing bilaterally (wall climbing exercises). On their second visit, participants were asked to repeat the exercises as shown previously to determine whether or not the participant had performed them correctly and if not, they were reinstructed *Dose*: not reported *Any additional treatment during trial*: paracetamol to a maximum of 2 g per day
Outcomes	Outcomes assessed at 2 weeks, 4 weeks, 6 weeks and 8 weeks. However, data were analysed at 4 weeks and 8 weeks only • Function: VAS from 0 (full function) to 10 (severely limited function) • Rest pain: VAS from 0 (no pain) to 10 (severe pain) • Pain on motion: VAS from 0 (no pain) to 10 (severe pain) • Night pain: VAS from 0 (no pain) to 10 (severe pain) • Pain on resisted abduction: categorical rating scale (0 = no pain; 1 = mild pain, full power; 2 = moderate pain, reduced power; 3 = severe pain) • Total range of motion using a goniometer (unclear if active or passive) • Adverse events
Notes	**Conflicts of interest:** not reported **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised to treatment..." Comment: There was no information on how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "One physiotherapist set up the appropriate probe (active or placebo) whilst the second 'blinded' physiotherapist administered the treatment." Comment: Participants and personnel were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "Patients were assessed by another observer unaware of the treatment code" Comment: Assessor of objective outcomes was blinded

Vecchio 1993 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: Trialists did not report whether there were any dropouts, losses to follow-up or exclusions, or the number of participants included in each analysis
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Yavuz 2014

Methods	**Study design**: Parallel group RCT **Setting:** Outpatient physical medicine and rehabilitation clinic, Turkey **Intervention 1**: Low-level laser therapy (LLLT) plus hot pack plus exercises **Intervention 2:** Therapeutic ultrasound plus hot pack plus exercises **Source of Funding:** Not reported
Participants	**Diagnostic label used by trialists:** Subacromial impingement syndrome **Criteria for defining the shoulder condition being treated** • Pain during abduction of the shoulder with a painful arc and presence of positive impingement signs (Hawkins and Neer tests) • A positive impingement test (subacromial injection of anaesthetic) • Diagnosis of Stage I or II impingement confirmed by MRI **Any restriction on duration of symptoms:** At least 4 weeks **Inclusion Criteria (not listed above)** • 30-65 years of age **Exclusion Criteria (not listed above)** • Had previous fractures of any bone in the shoulder complex or shoulder surgery on the affected side • Neurologic or inflammatory diseases • A rotator cuff tear on MRI (Stage III impingement) • Referring pain due to neck pathologies • Had received a subacromial injection within 6 months **Baseline characteristics** *Intervention 1: LLLT* Number randomised: 16 Number included in analyses: 16 Age: 44.2 ± 8.2 years old Sex: F/M 7/9 Duration of symptoms: 6.7 ± 4.8 months *Intervention 2: Therapeutic ultrasound*

	Number randomised: 15 Number included in analyses: 15 Age: 45.3 ± 9.8 years old Sex: F/M 7/8 Duration of symptoms: 6.3 ± 5.2 months
Interventions	**Intervention 1: LLLT** *Description of modality used:* a gallium-aluminum-arsenide (GaAlAs, infrared laser) diode laser device (Chattanooga Group, USA) with a wavelength of 850 nm, a power output of 100 mV, continuous wave, and a 0.07 cm^2 spot area laser was used for the laser therapy. The LLLT was applied at a maximum of 5 painful points for 1 min at each point over the subacromial region of the shoulder *Dose*: 3 J/cm^2 to 5 painful points (total 15 J); power output of 100 mV; duration 5 min *Frequency of administration*: 5 times a week for 2 weeks (10 sessions) **Intervention 2: Therapeutic ultrasound** *Description of modality used*: administered to the area over the subacromial region of the shoulder using a technique of slow circular movement, with continuous mode *Dose*: frequency 1 MHz; intensity 2 W/cm2; duration 5 min *Frequency of administration*: 5 times a week for 2 weeks (10 sessions) **Both groups: Hot pack and exercises** *Description of modality used*: hot pack therapy was applied to all participants in both groups for 10 min. In addition, all participants received an exercise programme. These exercises included range of motion, stretching, and progressive resistive exercises *Dose*: hot pack for 10 min; each exercise was performed once a day with 10 repetitions *Frequency of administration*: 5 times a week for 3 weeks (10 sessions)
Outcomes	Outcomes assessed at 1 and 3 months • Function: Shoulder Pain and Disability Index (SPADI) 0-100, where higher scores indicate worse function • Overall pain: VAS from 0 ("no pain at all") to 100 ("the most severe pain that I can imagine")
Notes	**Conflict of interest:** "The authors declare that there is no conflict of interest." **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "These participants were randomly assigned into two groups via a numbered-envelope system: "LLLT" or "US therapy" was written on a piece of paper in each sealed envelope, and each patient selected one envelope" Comment: An adequate method was used to generate the allocation sequence

Yavuz 2014 (*Continued*)

Allocation concealment (selection bias)	Low risk	Quote: "These participants were randomly assigned into two groups via a numbered-envelope system: "LLLT" or "US therapy" was written on a piece of paper in each sealed envelope, and each patient selected one envelope" Comment: An adequate method was used to conceal the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Given the nature of the interventions, participants were not blind to treatment, and may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants, who may have had different expectations about the benefits of the intervention they received, self-reported all outcomes of interest to the review
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All of the 31 participants completed the trial and were included in the analysis." Comment: All randomised participants were analysed
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Yeldan 2009

Methods	**Study design**: Parallel group RCT **Setting:** Outpatients recruited from the Medicine Faculty of Istanbul, University of Istanbul, Turkey **Intervention:** Low-level laser therapy (LLLT) plus exercise plus cold pack **Control:** Placebo LLLT plus exercise plus cold pack **Source of funding:** Not reported

Participants	**Diagnostic label used by trialist:** Subacromial impingement syndrome **Criteria for defining the shoulder condition being treated:** at least 3 of the folllowing: • positive Neer test; • positive Hawkin's test; • pain with active shoulder elevation; • pain with isometric resisted abduction **Any restriction on duration of symptoms** • Not reported **Inclusion Criteria (not listed above)** • None **Exclusion Criteria (not listed above)** • Presence of direct trauma to the shoulder • Frozen shoulder, acromioclavicular arthritis or rotator cuff tear • Underlying neurological, inflammatory rheumatic or extrinsic disease (e.g. cervical spondylosis referring pain to the shoulder) • Physical therapy given in 6 months prior to the study • Receiving intra-articular or subacromial steroids in the 3 months prior to treatment **Baseline characteristics** *Intervention: LLLT plus exercise plus cold pack* Number randomised: 34 Number included in analyses: 34 Age: 55.32 ± 8.73 years old Sex: F/M 25/9 Duration of symptoms: 6.5 ± 4.52 months *Control: Placebo LLLT plus exercise plus cold pack* Number randomised: 33 Number included in analyses: 26 Age: 55.0 ± 8.75 years old Sex: F/M 22/4 Duration of symptoms: 6.42 ± 4.79 months
Interventions	**Intervention: LLLT** *Description of modality used*: application of GaAs diode laser instrument (Roland Serie Elettronica Pagani), with wavelength 904 nm, frequency range of 5-7000 Hz and maximum peak power of 27, 50 or 27 x 4 W). Laser was applied while sitting on a chair; each participant placed an arm with the hand supinated in his or her lap. The transducer head was placed on the superior and anterior periarticular parts of glenohumeral joint, covering an area of approximately 15 cm^2. Three pulses (3 J) were applied to a maximum of 5 tender points found on clinical examination (pain with palpation). As far as possible, treatment was concentrated on the subacromial and anterior shoulder regions. The laser was held perpendicular to the skin without pressure *Dose*: 90 seconds at each location with a frequency of 2000 Hz. The treatment duration was approximately 8 min *Frequency of administration*: 5 days per week for 3 weeks **Control: Placebo LLLT** *Description of modality used*: same as above except the device was set to "off" mode *Dose*: none *Frequency*: 5 days per week for 3 weeks

	Both groups: Supervised and home exercises and cold pack *Description of modality used*: progressive exercise programme including range of motion exercises, strengthening and stretching exercises, followed by a cold pack application. Exercises were performed under supervision in the clinic and at home. First week exercises included inferior and posterior capsule stretching, wand exercises (shoulder flexion, abduction, extension, internal and external rotation), active-assisted range of motion exercises and internal rotator exercise (with a towel). In later weeks, these were performed actively and with Theraband resistance (The Hygenic Corporation). In the second and third weeks, supraspinatus exercise (empty can) was added. The cold pack was applied around the shoulder. To promote compliance with the therapy, participants were asked to write a diary of the exercise programme which was reviewed weekly *Dose*: between 15 and 30 min of exercise and 15 min of cold pack *Frequency*: twice daily for 3 weeks
Outcomes	Outcomes assessed at 3 weeks • Function: Constant-Murley total score 0-100, with a higher score indicating better function • Rest pain: VAS from 0 (no pain) to 10 (very severe pain) • Pain on motion: VAS from 0 (no pain) to 10 (very severe pain) • Night pain: VAS from 0 (no pain) to 10 (very severe pain) • Strength (flexion, abduction, external rotation and internal rotation force) using a handheld dynamometer • Range of motion (flexion, extension, abduction, external rotation and internal rotation) using a goniometer (unclear if active or passive) • Adverse events
Notes	**Conflicts of interest:** not reported **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Randomisation was done using Microsoft Excel 'RAND()' function. Command was =IF(RAND()<=0.5;"laser group";"placebo laser group")." Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	High risk	Quote: "The selector (ARO), who did not perform any assessment, was aware of the randomisation scheme." Comment: The allocation sequence was not concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The subjects were not informed about the true nature of laser application" Quote:"The treating physical therapist

		(EC) was aware of the nature of this intervention, the physical findings of subjects and the treatment group to which subjects had been allocated." Comment: Participants were blinded
Blinding of outcome assessment (detection bias) Self-reported outcomes	Low risk	Comment: Blinded participants self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Low risk	Quote: "The assessor (IY) was blind to which group the subjects had been allocated." Comment: Assessor of objective outcomes was blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Seven patients in the placebo laser group were unable to complete the therapy; 26 patients were able to complete the study. The reasons for dropping out of the study were surgery (2 subjects), scheduling problems (n=3) or personal circumstances that prevented weekly visits (n=2)." Comment: The dropouts were all in the placebo group, however the reasons for loss to follow-up were all given. These were unrelated to the study treatments. Therefore, the results are unlikely to be biased due to this attrition
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data were fully reported for all outcomes reported in the methods section of the publication, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Yildirim 2013

Methods	**Study design:** Parallel group RCT **Setting:** Outpatient clinic of the Istanbul Physical Therapy and Rehabilitation Education and Research Hospital, Turkey **Intervention:** Therapeutic ultrasound for 4 min plus superficial heat plus TENS plus exercise **Control:** Therapeutic ultrasound for 8 min plus superficial heat plus TENS plus exercise **Source of funding:** Not reported
Participants	**Diagnostic label used by trialists:** Subacromial impingement syndrome **Criteria for defining the shoulder condition being treated** • Subacromial impingement syndrome diagnosed based on clinical diagnostic tests, including the Neer, Hawkins, painful arc, drop arm, Yergeson, Jobe and supraspinatus tests, and MRI • Had findings compatible with nerve compression on physical examination • Passive range of motion was less than 30% compared to the unaffected side **Any restriction on duration of symptoms** • At least 6 months **Inclusion Criteria (not listed above)** • Aged above 40 years **Exclusion Criteria (not listed above)** • Systemic inflammatory rheumatic diseases, decompensated heart failure • Neurologic deficits and had undergone shoulder and neck surgery • Received physical therapy and steroid injections for their shoulder pain • Findings consistent with calcific tendinitis and bursitis on conventional XR images • Complete lacerations on MRI images • Adhesive capsulitis or shoulder instability **Baseline characteristics** *Intervention: Therapeutic ultrasound for 4 min plus other physical therapy* Number randomised: 50 Number included in analyses: 50 Age: mean: 55.4 ± 7.63 years old Sex: female: 34; male: 16 Duration of symptoms: mean: 8.34 ± 4.86 months *Control: Therapeutic ultrasound for 8 min plus other physical therapy* Number randomised: 50 Number included in analyses: 50 Age: mean: 54.7 ± 8.67 years Sex: female: 27; male: 23 Duration of symptoms: mean: 6.66 ± 4.91 months
Interventions	**Intervention: Therapeutic ultrasound for 4** min *Components of intervention*: continuous ultrasound applied using circular motions. A Chattanooga brand ultrasound machine with a transducer head size of 5 cm^2 was used *Dose*: 4 min duration; intensity 1.5 W/cm^2; frequency not reported *Frequency of administration*: 5 times a week for 3 weeks **Control: Therapeutic ultrasound for 8** min *Components of intervention*: continuous ultrasound applied using circular motions. A Chattanooga brand ultrasound machine with a transducer head size of 5 cm^2 was used

	Dose: 8 min duration; intensity 1.5 W/cm^2; frequency not reported *Frequency of administration*: 5 times a week for 3 weeks **Both groups: Superficial heat plus TENS plus exercise** *Components of intervention*: TENS, infrared therapy, and exercises. The initial exercise programme consisted of Codman's pendulum exercises, passive range of motion exercises and stretching exercises. Posterior capsular stretching exercises and wall walking exercises were also performed. The exercises were taught to the participants at the beginning of the physical therapy programme. After the participants achieved full or nearly full range of motion, shoulder strengthening exercises were performed. participants were instructed to not to use their affected arm for daily activities, in particular overhead activities, in order to properly rehabilitate their shoulders. After the participants' shoulders were properly strengthened, they were allowed to abduct their shoulder greater than 90 degrees and use their arm for daily activities. The exercises were performed under observation in the outpatient clinic, twice a week, and the participants were instructed to carry out the exercise programme at home twice a day with 20 repetitions per exercise *Dose*: TENS (30 min, no other details reported); infrared therapy (20 min, no other details reported); exercises (20 repetitions per exercise) *Frequency of administration*: TENS (unclear); infrared therapy (unclear); exercises (twice a week for 3 weeks in clinic, and twice a day for 3 weeks at home)
Outcomes	Outcomes assessed at 5 weeks • Function: Constant-Murley total score (0-100 with higher scores denoting better function) • Function: UCLA shoulder rating scale (34-35 points were classed as excellent, 29-33 points as good and less than 29 points as poor) • Overall pain: VAS 0-10 (0 = no pain, 10 = worst pain) • Active range of motion in flexion, abduction, external rotation, internal rotation (Constant-Murley sub-scores) • Strength (Constant-Murley sub-score)
Notes	**Conflicts of interest:** "The writers have no conflict of interest to declare." **Funding:** not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "The 100 patients included in this study were divided into 2 groups each consisting of 50 patients using consecutive sequential randomization" Comment: An adequate method was used to generate the allocation sequence
Allocation concealment (selection bias)	Unclear risk	Comment: There was no information on how the allocation sequence was concealed

Yildirim 2013 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "A prospective, randomized, single-blind study was performed" Comment: The trialists did not specify who was blinded in this trial (participants, personnel or outcome assessors). It is likely participants were not blinded (and personnel certainly were not blinded). Participants may have had different expectations about the benefits of each intervention
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Comment: Unblinded participants who may have had different expectations about the benefits of the intervention they received self-reported some outcomes
Blinding of outcome assessment (detection bias) Objectively rated outcomes	Unclear risk	Quote: "A prospective, randomized, single-blind study was performed" Comment: The trialists did not specify who was blinded in this trial (participants, personnel or outcome assessors). It is therefore unclear whether assessors of objective outcomes were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: No losses to follow-up, withdrawals or post-randomisation exclusions were reported, and outcome data is analysed based on all randomised participants
Selective reporting (reporting bias)	Unclear risk	Comment: Outcome data for all outcomes specified in the methods section of the publication were fully reported, but without a trial protocol it is unclear whether other outcomes were measured but not reported based on the nature of the results
Other bias	Low risk	Comment: No other sources of bias identified

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Ainsworth 2007	Ineligible condition: 29% of participants were classified as "capsular pattern positive", suggesting that they had adhesive capsulitis. We were unable to obtain data for the subgroup of participants with rotator cuff disease

(*Continued*)

Dickens 2005	Ineligible intervention: multi-modal physiotherapy, where effect of electrotherapy modality could not be isolated
Ginn 2005	Ineligible intervention: multi-modal physiotherapy, where effect of electrotherapy modality could not be isolated
Hay 2003	Ineligible intervention: multi-modal physiotherapy, where effect of electrotherapy modality could not be isolated
Herrera-Lasso 1993	Ineligible condition: 31% of participants had periarthritis and we were unable to obtain data for the subgroup of participants with rotator cuff disease
Taverner 2014	Ineligible condition: participants were only reported as having "shoulder pain", and it was unclear if participants with adhesive capsulitis, myofascial neck and shoulder pain condition, rheumatoid arthritis or pain due to trauma were excluded
Van der Heijden 1999b	Ineligible condition: most participants had pain radiating below the elbow, ~10% had shoulder pain caused by trauma, and the number of participants with adhesive capsulitis unclear

Characteristics of studies awaiting assessment *[ordered by study ID]*

Dal Conte 1990

Methods	Requires translation
Participants	
Interventions	
Outcomes	
Notes	

Gudmundsen 1987

Methods	Requires translation
Participants	
Interventions	
Outcomes	
Notes	

Güler 2009

Methods	Requires translation
Participants	
Interventions	
Outcomes	
Notes	

Jiménez-García 2008

Methods	Requires translation
Participants	
Interventions	
Outcomes	
Notes	

Knorre 1990

Methods	Requires translation
Participants	
Interventions	
Outcomes	
Notes	

DATA AND ANALYSES

This review has no analyses.

ADDITIONAL TABLES

Table 1. Characteristics of electrotherapy modalities

Therapeutic ultrasound					
Study ID	**Dose**	**Session duration**	**No. sessions per week**	**No. weeks treatment**	**Total no. sessions**
Al Dajah 2014	Frequency: 3 MHz Intensity: 0.5 W/cm2	10 minutes	1	1	1
Bansal 2011	Frequency: 1 MHz Intensity: 0.6 W/cm2	6-8 minutes	10	1.5	10
Berry 1980	Frequency: NR Intensity: NR	10 minutes	2	4	8
Calis 2011	Frequency: 3 MHz Intensity: 1.5 W/cm2	5 minutes	7	2	15
Celik 2009	Frequency: 1 MHz Intensity: 1 W/cm2	4 minutes	5	3	15
Clews 1987	Frequency: NR Intensity: 0.8 W/cm2	15 minutes	3	0.5	3
Downing 1986	Frequency: 1 MHz Intensity: 1.2 W/cm2	6 minutes	3	4	12
Ebenbichler 1999	Frequency: 0.89 MHz Intensity: 2.5 W/cm2	15 minutes	3 to 5	6	24
Giombini 2006	Frequency: 1 MHz Intensity: 2 W/cm2	15 minutes	3	4	12
Grymel-Kulesza 2007	Frequency: NR Intensity: NR	NR	5	2	10

Table 1. Characteristics of electrotherapy modalities (*Continued*)

Johansson 2005	Frequency: 1 MHz Intensity: 1 W/cm2	10 minutes	2	5	10
Kurtai Gursel 2004	Frequency: 1 MHz Intensity: 1.5 W/cm2	10 minutes	5	3	15
Nykanen 1995	Frequency: 1 MHz Intensity: 1 W/cm2	10 minutes	3	3 to 4	10 to 12
Ozgen 2012	Frequency: NR Intensity: 1.5 W/cm2	5 minutes	NR	3	NR
Perron 1997	Frequency: 1 MHz Intensity: 0.8 W/cm2	5 minutes	3	3	9
Polimeni 2003	Frequency: NR Intensity: 1.5 W/cm2	NR	7	1.5	10
San Segundo 2008	Frequency: 1 MHz Intensity: 2 W/cm2	7 minutes	3	3	9
Santamato 2009	Frequency: 1 MHz Intensity: 2 W/cm2	10 minutes	5	2	10
Shehab 2000	Frequency: NR Intensity: 0.5 W/cm2	10 minutes	3 to 5	3 to 5	13
Yavuz 2014	Frequency: 1 MHz Intensity: 2 W/cm2	5 minutes	5	2	10
Yildirim 2013	Frequency: NR Intensity: 1.5 W/cm2	4 or 8 minutes	5	3	15
Low-level laser therapy (LLLT)					
Study ID	**Dose**	**Session duration**	**No. sessions per week**	**No. weeks treatment**	**Total no. sessions**
Abrisham 2011	Wavelength: 890 nm Power: 7-10 W Frequency: 80-1500 Hz	6 minutes	5	2	10

Table 1. Characteristics of electrotherapy modalities (*Continued*)

	Intensity: 2 to 4 J/cm2				
Bal 2009	Wavelength: 904 nm Power: 27 W Frequency: 5500 Hz Intensity: 1.6 J/cm2	10 minutes	5	2	10
Bingol 2005	Wavelength: 904 nm Power: 50 W Frequency: 2000 Hz Intensity: 2.98 J/cm2	5 minutes	5	2	10
Calis 2011	Wavelength: 904 nm Power: 6 mW Frequency: 16 Hz Intensity: 1 J/cm2	2 minutes	7	2	15
Dogan 2010	Wavelength: 850 nm Power: 100 mV Frequency: NR Intensity: 3 J/cm2	5-6 minutes	5	3	14
England 1989	Wavelength: 904 nm Power: 10 W Frequency: 4000 Hz Intensity: NR	5 minutes	3	2	6
Eslamian 2012	Wavelength: 830 nm Power: 100 mW Frequency: NR Intensity: 4 J/cm2	5 minutes	3	3 to 4	10
Kelle 2014	Wavelength: 904 nm Power: NR Frequency: 3500 Hz Intensity: 2 J/cm2	2.5 minutes	3	3	9

Table 1. Characteristics of electrotherapy modalities (*Continued*)

Montes-Molina 2012a	Wavelength: 810 nm Power: 100 mW Frequency: NR Intensity: 1.4 J/cm2	NR	3	4	10
Otadi 2012	Wavelength: 830 nm Power: 30 mW Frequency: NR Intensity: 1 J/cm2	NR	3	4	10
Saunders 1995	Wavelength: 820 nm Power: 40 mW Frequency: 5000 Hz Intensity: 30 J/cm2	3 minutes	3	3	9
Vecchio 1993	Wavelength: 830 nm Power: 30 mW Frequency: NR Intensity: NR	NR	2	8	16
Yavuz 2014	Wavelength: 850 nm Power: 100 mW Frequency: NR Intensity: 3 J/cm2	5 minutes	5	2	10
Yeldan 2009	Wavelength: 904 nm Power: NR Frequency: 2000 Hz Intensity: NR	8 minutes	5	3	15
Transcutaneous electrical nerve stimulation (TENS)					
Study ID	**Dose**	**Session duration**	**No. sessions per week**	**No. weeks treatment**	**Total no. sessions**
Baskurt 2006	Frequency: 100 Hz Pulse duration: 0.1 ms	20 minutes	1	1	1

Table 1. Characteristics of electrotherapy modalities (*Continued*)

Eyigor 2010	Frequency: 100 Hz Pulse duration: 150 µsn	NR	5	3	15
Grymel-Kulesza 2007	Frequency: 100 Hz Pulse duration: 50 µs	NR	5	2	10
Kocyigit 2012	Frequency: 3 Hz Pulse duration: 250 µs	30 minutes	1	1	1
Korkmaz 2010	Frequency: 100 Hz Pulse duration: 150 µsn	20 minutes	5	4	20
Ozgen 2012	Frequency: 60 Hz Pulse duration: 60 µsn	20 minutes	NR	3	NR
Pan 2003	Frequency: 95 Hz Pulse duration: 0.5 ms	20 minutes	3	4	12
Shehab 2000	Frequency: 50 Hz Pulse duration: NR	30 minutes	3 to 5	3 to 5	13
Pulsed electromagnetic field (PEMF)					
Study ID	**Dose**	**Session duration**	**No. sessions per week**	**No. weeks treatment**	**Total no. sessions**
Aktas 2007	Frequency: 50 Hz Intensity: 30 G	25 minutes	5	3	15
Binder 1984	Frequency: 73 ± 2 Hz Intensity: NR	5-9 hours	7	8	56
Chard 1988	Frequency: 72 ± 3 Hz Intensity: NR	2 or 8 hours	7	8	56
Galace de Freitas 2014	Frequency: 50 Hz Intensity: 200 G	30 minutes	3	3	9
Microwave diathermy					

Table 1. Characteristics of electrotherapy modalities (*Continued*)

Study ID	Dose	Session duration	No. sessions per week	No. weeks treatment	Total no. sessions
Akyol 2012	Power: 100 W Temperature: NR	20 minutes	5	3	15
Rabini 2012	Power: 40 W Temperature: 38°C	30 minutes	3	4	12
Acetic acid iontophoresis					
Study ID	**Dose**	**Session duration**	**No. sessions per week**	**No. weeks treatment**	**Total no. sessions**
Leduc 2003	Current: 5 mA	15-20 minutes	1 to 2	6	10
Perron 1997	Current: 5 mA	20 minutes	3	3	9
High intensity laser therapy					
Study ID	**Dose**	**Session duration**	**No. sessions per week**	**No. weeks treatment**	**Total no. sessions**
Santamato 2009	Wavelength: 1064 nm Power: 6 W Frequency: NR Intensity: 760 mJ/cm2	10 minutes	5	2	10
Light therapy					
Study ID	**Dose**	**Session duration**	**No. sessions per week**	**No. weeks treatment**	**Total no. sessions**
Montes-Molina 2012b	Wavelength: 950 nm Power: 310 mW Frequency: NR Intensity: 10.3 J/cm2	NR	5	2	10
Microcurrent electrical stimulation					
Study ID	**Dose**	**Session duration**	**No. sessions per week**	**No. weeks treatment**	**Total no. sessions**

Table 1. Characteristics of electrotherapy modalities (*Continued*)

Atya 2012	Intensity: 30-40 mA Pulse frequency: 10 Hz	20 minutes	3	6	18

NR = Not reported

Table 2. Outcome matrix

Study ID	Overall pain	Function	Pain on motion	Global assessment	Quality of life	Adverse events
Abrisham 2011	X					X
Aktas 2007	X	X	X			
Akyol 2012	X	X	X		X	X
Al Dajah 2014	X					
Atya 2012		X	X			
Bal 2009		X		X		X
Bansal 2011	X					
Baskurt 2006	X					
Berry 1980	X			X		X
Binder 1984	X			X		X
Bingol 2005	X					X
Calis 2011	X	X	X			
Celik 2009	X	X				
Chard 1988	X		X	X		
Clews 1987	X					
Dogan 2010	X	X				X
Downing 1986	X	X		X		
Ebenbichler 1999	X	X	X	X	X	X

Table 2. Outcome matrix (*Continued*)

England 1989	X	X				
Eslamian 2012	X	X				
Eyigor 2010	X	X	X	X	X	
Galace de Freitas 2014	X	X				
Giombini 2006	X	X	X	X		X
Grymel-Kulesza 2007						
Johansson 2005		X				X
Kelle 2014	X	X	X		X	X
Kocyigit 2012	X					
Korkmaz 2010	X	X	X	X	X	X
Kurtai Gursel 2004	X	X	X			
Leduc 2003		X				
Montes-Molina 2012a	X	X				X
Montes-Molina 2012b	X	X				X
Nykanen 1995	X	X				
Otadi 2012	X	X				
Ozgen 2012	X	X	X	X		X
Pan 2003	X	X				X
Perron 1997			X			
Polimeni 2003		X				
Rabini 2012	X	X				X
San Segundo 2008	X	X				

Table 2. Outcome matrix (*Continued*)

Santamato 2009	X	X				
Saunders 1995	X					
Shehab 2000	X					
Vecchio 1993	X	X	X			X
Yavuz 2014	X	X				
Yeldan 2009	X	X	X			X
Yildirim 2013	X	X				
FREQUENCY	**40**	**33**	**15**	**10**	**5**	**19**

Table 3. Therapeutic ultrasound versus placebo

Study ID: Berry 1980
Participants: Rotator cuff lesions
Intervention: Therapeutic ultrasound
Control: Placebo ultrasound plus placebo tolmetin sodium

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-100, 0 = no pain) at 2 weeks	33.7	34	12	29.4	23.6	12	4.30 (-19.12, 27.72)
Overall pain (VAS 0-100, 0 = no pain) at 4 weeks	41.2	36.6	12	22	28.6	12	19.20 (-7.08, 45.48)
Range of shoulder abduction (degrees, unclear if active or passive) at 2 weeks	96.3	34.2	12	107.3	25.1	12	-11.00 (-35.00, 13.00)
Range of shoulder abduction	95.6	37.1	12	120.8	30.1	12	-25.20 (-52.23, 1.83)

Table 3. Therapeutic ultrasound versus placebo (*Continued*)

(degrees, unclear if active or passive) at 4 weeks							
	Events	**Total**		**Events**	**Total**		**Risk ratio (95% CI)**
Global assessment of treatment success (participant does not need a glucocorticoid injection, according to clinician) at 4 weeks	6	12		9	12		0.67 (0.35, 1.28)

Study ID: Ebenbichler 1999
Participants: Calcific tendinitis
Intervention: Therapeutic ultrasound
Control: Placebo ultrasound

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Overall pain (Binder's pain score 0-52, 0 = no pain) change from baseline to 6 weeks	-14.9	9.71	32	-6.3	9.73	29	-8.60 (-13.48, -3.72)
Overall pain (Binder's pain score 0-52, 0 = no pain) change from baseline to 9 months	-13.7	12.54	31	-11.3	12.84	25	-2.40 (-9.09, 4.29)
Function (Constant-Murley total score 0-100, higher	17.8	16.09	32	3.7	18.40	29	14.10 (5.39, 22.81)

Table 3. Therapeutic ultrasound versus placebo (*Continued*)

= better function) change from baseline to 6 weeks							
Function (Constant-Murley total score 0-100, higher = better function) change from baseline to 9 months	15.7	19.63	31	12.4	18.41	25	3.30 (-6.69, 13.29)
Quality of life (VAS 0-10, 0 = excellent quality) change from baseline to 6 weeks	2.6	2.50	32	0.4	2.63	29	2.20 (0.91, 3.49)
Quality of life (VAS 0-10, 0 = excellent quality) change from baseline to 9 months	2.4	3.27	31	1.9	2.66	25	0.50 (-1.05, 2.05)
	Events	**Total**		**Events**	**Total**		**Risk ratio (95% CI)**
Global assessment of treatment success ("clinical improvement", not defined) at 6 weeks	29	32		15	29		1.75 (1.21, 2.53)
Global assessment of treatment success ("clinical improvement", not defined) at 9 months	24	31		14	25		1.38 (0.93, 2.05)
Requring surgery during 9 month treat-	Zero events in both groups						

Table 3. Therapeutic ultrasound versus placebo (*Continued*)

ment and follow-up period	
Total adverse events during 9 month treatment and follow-up period	Zero events in both groups
Work status	"…the number of days lost from work during treatment and follow-up were moderate...nine patients missed work (four and five, respectively)"

Table 4. Therapeutic ultrasound as add-on to other physical therapy

Study ID: Calis 2011
Participants: Subacromial impingement syndrome
Intervention: Therapeutic ultrasound plus exercise plus hot pack
Control: Exercise plus hot pack

Outcome	Intervention			Control			Effect Estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-10, 0 = no pain) at 3 weeks	2.21	2.09	21	3.96	2.71	16	-1.75 (-3.35, -0.15)
Function (Constant-Murley total score: 0-100, higher score = better function) at 3 weeks	62.85	6.85	21	56.25	13.12	16	6.60 (-0.46, 13.66)
Pain on motion (VAS 0-10, 0 = no pain) at 3 weeks	4.24	2.26	21	5.51	1.89	16	-1.27 (-2.61, 0.07)
Night pain (VAS 0-10, 0 = no pain) at 3 weeks	3.74	2.18	21	4.84	2.72	16	-1.10 (-2.73, 0.53)

Table 4. Therapeutic ultrasound as add-on to other physical therapy (*Continued*)

Shoulder abduction (degrees, unclear if active or passive) at 3 weeks	155.95	9.21	21	150.37	5.03	16	5.58 (0.93, 10.23)
Shoulder flexion (degrees, unclear if active or passive) at 3 weeks	177.04	3.74	21	172.18	6.93	16	4.86 (1.11, 8.61)
Shoulder internal rotation (degrees, unclear if active or passive) at 3 weeks	74.85	7.29	21	69.18	7.67	16	5.67 (0.79, 10.55)
Shoulder external rotation (degrees, unclear if active or passive) at 3 weeks	81.66	5.82	21	78.25	6.72	16	3.41 (-0.72, 7.54)

Study ID: Celik 2009
Participants: Subacromial impingement syndrome
Intervention: Therapeutic ultrasound plus TENS plus exercise
Control: Placebo ultrasound plus TENS plus exercise

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Overall pain (VAS 0-10, 0 = no pain) at 3 weeks	3	NR	20	2	NR	16	1 (95% CI not estimable)
Overall pain (VAS 0-10, 0 = no pain) at 6 weeks	2	NR	20	1	NR	16	1 (95% CI not estimable)

Table 4. Therapeutic ultrasound as add-on to other physical therapy (*Continued*)

Function (Constant-Murley score 0-100, higher score = better function) at 3 weeks	58.3	9.07	20	61.06	8.06	16	-2.76 (-8.36, 2.84)
Function (Constant-Murley score 0-100, higher score = better function) at 6 weeks	65.65	7.65	20	65.25	7.61	16	0.40 (-4.61, 5.41)
Shoulder forward elevation (degrees) at 3 weeks	170.2	9.87	20	174.38	8.94	16	-4.18 (-10.34, 1.98)
Shoulder forward elevation (degrees) at 6 weeks	175.55	6	20	177.38	4.43	16	-1.83 (-5.24, 1.58)
Shoulder internal rotation (degrees) at 3 weeks	75.2	14.93	20	84.19	7.57	16	-8.99 (-16.51, -1.47)
Shoulder internal rotation (degrees) at 6 weeks	83.15	10.9	20	87.06	6.77	16	-3.91 (-9.73, 1.91)
Shoulder external rotation (degrees) at 3 weeks	77.15	13.36	20	79.75	14.6	16	-2.60 (-11.84, 6.64)
Shoulder external rotation (degrees) at 6 weeks	84.35	9.61	20	84.63	8.36	16	-0.28 (-6.16, 5.60)

Table 4. Therapeutic ultrasound as add-on to other physical therapy (*Continued*)

Study ID: Clews 1987
Participants: Rotator cuff tendinitis
Intervention: Therapeutic ultrasound plus ice
Control: Placebo ultrasound plus ice

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Pain after strength test (VAS 0-10) at 3 days	3.2	1.2	6	2.7	1.9	6	0.50 (-1.30, 2.30)
Strength (maximal isometric force production, measured in peak force) % change from baseline to 3 days	11	9.5	6	-1.5	9	6	12.50 (2.03, 22.97)

Study ID: Downing 1986
Participants: Supraspinatus tendinitis or subacromial bursitis
Intervention: Therapeutic ultrasound plus exercise plus NSAID
Control: Placebo ultrasound plus exercise plus NSAID

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (4-point categorical rating scale, 0 = no pain) at 4 weeks	"No significant difference between the sham and true US groups, however, existed in the proportion of patients who improved"						
Function (any vs no interference with sleep, dress, work, grooming and sports)	"Approximately one half of the patients in both groups improved in each category but, again, no significant difference existed between the mean scores of the sham and true US groups"						

Table 4. Therapeutic ultrasound as add-on to other physical therapy (*Continued*)

at 4 weeks							
Global assessment of treatment success at 4 weeks	"Both the patients and the physician recorded that 50% of the patients improved their overall status."						
Shoulder flexion (degrees, unclear if active or passive) at 4 weeks	87	6.63	11	89	3	9	-2.00 (-6.38, 2.38)
Shoulder abduction (degrees, unclear if active or passive) at 4 weeks	85	13.27	11	80	9	9	5.00 (-4.80, 14.80)
Shoulder internal rotation (degrees, unclear if active or passive) at 4 weeks	76	23.22	11	58	27	9	18.00 (-4.35, 40.35)
Shoulder external rotation (degrees, unclear if active or passive) at 4 weeks	75	39.80	11	72	24	9	3.00 (-25.27, 31.27)

Study ID: Kurtai Gursel 2004
Participants: Supraspinatus tendinosis, subacromial bursitis, rotator cuff tear or bicipital tendinosis
Intervention: Therapeutic ultrasound plus hot pack plus interferential current plus exercise
Control: Sham ultrasound plus hot pack plus interferential current plus exercise

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Rest pain (0-3 categorical rating scale, 0 = no pain) at 3 weeks	1	0.1	17	1.3	0.4	16	-0.30 (-0.50, -0.10)

Table 4. Therapeutic ultrasound as add-on to other physical therapy (*Continued*)

Function (Dutch SDQ 0-100, higher = worse function) at 3 weeks	41.5	20.3	17	38.2	15.6	16	3.30 (-9.01, 15.61)
Pain on motion (0-3 categorical rating scale, 0 = no pain) at 3 weeks	1.9	0.2	17	2.1	0.2	16	-0.20 (-0.34, -0.06)
Active shoulder abduction (degrees) at 3 weeks	150.2	20	17	162.2	16.7	16	-12.00 (-24.54, 0.54)
Active shoulder flexion (degrees) at 3 weeks	156.4	12.6	17	160.3	12	16	-3.90 (-12.29, 4.49)
Active shoulder extension (degrees) at 3 weeks	51.7	9	17	57.2	7.9	16	-5.50 (-11.27, 0.27)
Active shoulder external rotation (degrees) at 3 weeks	81.4	15.5	17	87.8	5.4	16	-6.40 (-14.23, 1.43)
Active shoulder internal rotation (degrees) at 3 weeks	71.4	18.7	17	72.2	13.4	16	-0.80 (-11.85, 10.25)

Study ID: Nykanen 1995
Participants: Painful arc or supraspinatus tendinopathy/tendinitis
Intervention: Therapeutic ultrasound plus massage plus exercises
Control: Sham ultrasound plus massage plus exercises

Outcome	Intervention	Control	Effect estimate

Table 4. Therapeutic ultrasound as add-on to other physical therapy (*Continued*)

	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (Pain Index 1-5, higher score = worse pain) at 3-4 weeks	2.5	0.7	35	2.4	0.9	37	0.10 (-0.27, 0.47)
Overall pain (Pain Index 4-20, higher score = worse pain) at 4 months	13	5	32	13	4	35	0.00 (-2.18, 2.18)
Overall pain (Pain Index 4-20, higher score = worse pain) at 12 months	13	5	30	13	4	37	0.00 (-2.21, 2.21)
Function (ADL-score 2-10, higher score = worse function): at 3-4 weeks	4.2	1.3	35	4.4	1.4	37	-0.20 (-0.82, 0.42)
Function (ADL-score 3-14, higher score = worse function): at 4 months	6.9	2.4	32	7.4	2	35	-0.50 (-1.56, 0.56)
Function (ADL-score 3-14, higher score = worse function): at 12 months	7	2.4	30	7.3	2.3	37	-0.30 (-1.43, 0.83)

Study ID: Polimeni 2003
Participants: Supraspinatus tendinitis or biceps tendinitis
Intervention: Therapeutic ultrasound plus mobilisation plus exercises
Control: Mobilisation plus exercises

Table 4. Therapeutic ultrasound as add-on to other physical therapy (*Continued*)

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Function (Constant-Murley total score 0-100, higher = better function) at 10 days	No usable outcome data, though difference between groups not statistically significant						
Function (Constant-Murley total score 0-100, higher = better function) at 40 days	No usable outcome data, though difference between groups not statistically significant						

Study ID: San Segundo 2008
Participants: Rotator cuff tendinitis or partial rotator cuff tears
Intervention: Therapeutic ultrasound plus exercises
Control: Placebo ultrasound plus exercises

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Rest pain (VAS 0-100, 0 = no pain) at 3 weeks	40.1	20.7	16	44.6	20.3	15	-4.50 (-18.94, 9.94)
Rest pain (VAS 0-100, 0 = no pain) at 5 weeks	35.5	21.1	16	44.9	18.9	15	-9.40 (-23.48, 4.68)
Function (Constant-Murley total score 0-100, higher = better function) at 3	57.4	18.1	16	50.1	15.6	15	7.30 (-4.57, 19.17)

Table 4. Therapeutic ultrasound as add-on to other physical therapy (*Continued*)

weeks							
Function (Constant-Murley total score 0-100, higher = better function) at 5 weeks	61.3	17.8	16	51.1	16.1	15	10.20 (-1.74, 22.14)
Night pain (VAS 0-100, 0 = no pain) at 3 weeks	20.7	21.6	16	25.2	32.5	15	-4.50 (-24.06, 15.06)
Night pain (VAS 0-100, 0 = no pain) at 5 weeks	15.6	20.6	16	21.6	26.3	15	-6.00 (-22.70, 10.70)

NR = not reported

Table 5. Therapeutic ultrasound versus another active intervention

Study ID: Al Dajah 2014 **Participants: Shoulder impingement syndrome** **Intervention: Therapeutic ultrasound** **Control: Soft tissue mobilisation and proprioceptive neuromuscular facilitation**							
Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Overall pain (VAS 0-10) immediately after 1 treatment session (day 1)	5.23	0.72	15	3.8	0.79	15	1.43 (0.89, 1.97)
External rotation (degrees, unclear if active or passive) immediately after 1 treatment session (day 1)	40.33	5.6	15	52.4	4.9	15	-12.07 (-15.84, -8.30)

Table 5. Therapeutic ultrasound versus another active intervention (*Continued*)

Study ID: Bansal 2011
Participants: Supraspinatus tendinitis
Intervention: Therapeutic ultrasound plus Codman's exercises
Control: Deep friction massage technique plus Codman's exercises

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-10) at 10 days	2.1	NR	20	1.4	NR	20	0.7 (95% CI not estimable)
Active shoulder abduction (degrees) at 10 days	105.65	NR	20	107.15	NR	20	-1.5 (95% CI not estimable)

Study ID: Berry 1980
Participants: Rotator cuff lesions
Intervention: Therapeutic ultrasound
Control: Glucocorticoid injection plus tolmetin sodium

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-100, 0 = no pain) at 2 weeks	33.7	34	12	26.2	21.3	12	7.50 (-15.20, 30.20)
Overall pain (VAS 0-100, 0 = no pain) at 4 weeks	41.2	36.6	12	29.2	24.3	12	12.00 (-12.86, 36.86)
Range of shoulder abduction (degrees, unclear if active or passive) at 2 weeks	96.3	34.2	12	95.2	22.9	12	1.10 (-22.19, 24.39)

Table 5. Therapeutic ultrasound versus another active intervention (*Continued*)

Range of shoulder abduction (degrees, unclear if active or passive) at 4 weeks	95.6	37.1	12	93.2	25.7	12	2.40 (-23.14, 27.94)
	Events	**Total**		**Events**	**Total**		**Risk ratio (95% CI)**
Global assessment of treatment success (participant does not need a glucocorticoid injection, according to clinician) at 4 weeks	6	12		5	12		1.20 (0.50, 2.88)

Study ID: Berry 1980
Participants: Rotator cuff lesions
Intervention: Therapeutic ultrasound
Control: Glucocorticoid injection plus placebo tolmetin sodium

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Overall pain (VAS 0-100, 0 = no pain) at 2 weeks	33.7	34	12	20.6	20.5	12	13.10 (-9.36, 35.56)
Overall pain (VAS 0-100, 0 = no pain) at 4 weeks	41.2	36.6	12	26.6	22.5	12	14.60 (-9.71, 38.91)
Range of shoulder abduction (degrees, unclear if active or passive) at 2 weeks	96.3	34.2	12	107.2	34.5	12	-10.90 (-38.39, 16.59)

Table 5. Therapeutic ultrasound versus another active intervention (*Continued*)

Range of shoulder abduction (degrees, unclear if active or passive) at 4 weeks	95.6	37.1	12	100.6	37.7	12	-5.00 (-34.93, 24.93)
	Events	**Total**		**Events**	**Total**		**Risk ratio (95% CI)**
Global assessment of treatment success (participant does not need a glucocorticoid injection, according to clinician) at 4 weeks	6	12		6	12		1.00 (0.45, 2.23)

Study ID: Berry 1980
Participants: Rotator cuff lesions
Intervention: Therapeutic ultrasound
Control: Acupuncture

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Overall pain (VAS 0-100, 0 = no pain) at 2 weeks	33.7	34	12	38.6	26.7	12	-4.90 (-29.36, 19.56)
Overall pain (VAS 0-100, 0 = no pain) at 4 weeks	41.2	36.6	12	34.1	27.2	12	7.10 (-18.70, 32.90)
Range of shoulder abduction (degrees, unclear if active or passive) at 2 weeks	96.3	34.2	12	95.5	27.6	12	0.80 (-24.07, 25.67)

Table 5. Therapeutic ultrasound versus another active intervention (*Continued*)

Range of shoulder abduction (degrees, unclear if active or passive) at 4 weeks	95.6	37.1	12	103.5	36.6	12	-7.90 (-37.39, 21.59)
	Events	**Total**		**Events**	**Total**		**Risk ratio (95% CI)**
Global assessment of treatment success (participant does not need a glucocorticoid injection, according to clinician) at 4 weeks	6	12		5	12		1.20 (0.50, 2.88)

Study ID: Clews 1987
Participants: Rotator cuff tendinitis
Intervention: Therapeutic ultrasound plus ice
Control: Massage plus ice

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Pain after strength test (VAS 0-10 at strength testing) at 3 days	3.2	1.2	6	2.8	1.2	6	0.40 (-0.96, 1.76)
Strength (maximal isometric force production, measured in peak force) % change from baseline to 3 days	11	9.5	6	9.8	8.8	6	1.20 (-9.16, 11.56)

Table 5. Therapeutic ultrasound versus another active intervention (*Continued*)

Study ID: Giombini 2006 **Participants: Supraspinatus tendinopathy** **Intervention: Therapeutic ultrasound** **Control: Supervised and home exercises**							
Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Rest pain (VAS 0-10, 0 = no pain) at 4 weeks	5.8	0.96	12	5.3	0.65	11	0.50 (-0.17, 1.17)
Rest pain (VAS 0-10, 0 = no pain) at 10 weeks	5.15	0.87	12	4.9	0.88	11	0.25 (-0.47, 0.97)
Function (Constant-Murley total score, 0-100, higher = better function) at 4 weeks	60	3.21	12	61.2	4.28	11	-1.20 (-4.31, 1.91)
Function (Constant-Murley total score, 0-100, higher = better function) at 10 weeks	61.75	4.18	12	63.27	5.56	11	-1.52 (-5.57, 2.53)
	Events	**Total**		**Events**	**Total**		**Risk ratio (95% CI)**
Global assessment of treatment success (ready to return to sport) at 4 weeks	6	12		4	11		1.38 (0.52, 3.61)
Global assessment of treatment success (ready to re-	4	12		4	11		0.92 (0.30, 2.81)

Table 5. Therapeutic ultrasound versus another active intervention (*Continued*)

turn to sport) at 10 weeks						
Adverse events	Zero events in both groups					
Study ID: Johansson 2005 **Participants: Subacromial impingement syndrome** **Intervention: Therapeutic ultrasound plus home exercises** **Control: Acupuncture plus home exercises**						
Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Function (combined Constant-Murley, Adolfsson-Lysholm shoulder score and UCLA-score, 0-100, higher score = better function) at 6 weeks	76	11	41	79	9	44	-3.00 (-7.29, 1.29)
Function (combined Constant-Murley, Adolfsson-Lysholm shoulder score and UCLA-score, 0-100, higher score = better function) at 6 months	83	15	41	83	17	44	0.00 (-6.81, 6.81)
Function (combined Constant-Murley, Adolfsson-Lysholm	85	14	41	88	13	44	-3.00 (-8.75, 2.75)

Table 5. Therapeutic ultrasound versus another active intervention (*Continued*)

shoulder score and UCLA-score, 0-100, higher score = better function) at 12 months							
Total adverse events during 12-month follow-up period	Zero events in both groups						

NR = not reported

Table 6. LLLT versus placebo

Study ID: England 1989
Participants: Supraspinatus or bicipital tendinitis
Intervention: Low-level laser therapy (LLLT)
Control: Placebo LLLT

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Median difference (95% CI)**
Overall pain (VAS 0-10, higher score = more pain) at 2 weeks	NR	NR	< = 10	NR	NR	< = 10	2.5 (2.01, 3)
Function (VAS 0-10, higher score = worse function) at 2 weeks	NR	NR	< = 10	NR	NR	< = 10	1.5 (-0.01, 3.99)
Active shoulder abduction (degrees) at 2 weeks	NR	NR	< = 10	NR	NR	< = 10	20 (10, 40)
Active shoulder flexion (degrees) at 2 weeks	NR	NR	< = 10	NR	NR	< = 10	15 (5, 29)

Table 6. LLLT versus placebo (*Continued*)

Active shoulder extension (degrees) at 2 weeks	NR	NR	< = 10	NR	NR	< = 10	6 (0, 20)

Study ID: Saunders 1995
Participants: Supraspinatus tendinitis
Intervention: Low-level laser therapy (LLLT)
Control: Placebo LLLT

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Strength (muscle force (N)) at 3 weeks	172.01	40.70	12	125.55	27.44	12	46.46 (18.69, 74.23)
	Events	**Total**		**Events**	**Total**		**Risk ratio (95% CI)**
Overall pain (number of participants with "improved" pain) at 3 weeks	10	12		5	12		2.00 (0.98, 4.09)

NR = not reported

Table 7. LLLT as add-on to other physical therapy

Study ID: Abrisham 2011
Participants: Rotator cuff and bicep tendinitis
Intervention: Low-level laser therapy (LLLT) plus exercise
Control: Placebo LLLT plus exercise

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Overall pain (10 point scale, 0 = no pain) at 2 weeks	2.1	0.5	40	3	1	40	-0.90 (-1.25, -0.55)

Table 7. LLLT as add-on to other physical therapy (*Continued*)

Active abduction (degrees) at 2 weeks	102.6	6.8	40	87.9	7.9	40	14.70 (11.47, 17.93)
Active flexion (degrees) at 2 weeks	102.6	6.6	40	88	6	40	14.60 (11.84, 17.36)
Active external rotation (degrees) at 3 weeks	51.3	5	40	49.4	4.8	40	1.90 (-0.25, 4.05)
Total adverse events during 2-week intervention period	Zero events in both groups						

Study ID: Bal 2009
Participants: Subacromial impingement syndrome
Intervention: Low-level laser therapy (LLLT) plus home exercises
Control: Home exercises

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Function (SPADI total score 0-100 where higher = worse function) change from baseline to 2 weeks	-16.2	17.73	20	-23.2	17.14	20	7.00 (-3.81, 17.81)
Function (SPADI total score 0-100 where higher = worse function) change from baseline to 12 weeks	-32.7	18.58	20	-37.2	21.28	20	4.50 (-7.88, 16.88)
Night pain (VAS 0-100, 0 = no	-22.7	24.36	20	-21.7	-19.21	20	-1.00 (-14.60, 12.60)

Table 7. LLLT as add-on to other physical therapy (*Continued*)

pain) change from baseline 2 weeks							
Night pain (VAS 0-100, 0 = no pain) change from baseline 12 weeks	-54.7	24.68	20	-31.5	27.77	20	-23.20 (-39.48, -6.92)
	Events	**Total**		**Events**	**Total**		**Risk ratio (95% CI)**
Global assessment of treatment success ("excellent" or "good" result on UCLA) at 2 weeks	4	20		3	20		1.33 (0.34, 5.21)
Global assessment of treatment success ("excellent" or "good" result on UCLA) at 12 weeks	17	20		13	20		1.31 (0.90, 1.89)
Total adverse events at 2 weeks	Zero events in both groups						
Total adverse events at 12 weeks	Zero events in both groups						
Study ID: Bingol 2005 **Participants: Rotator cuff disease** **Intervention: Low-level laser therapy (LLLT) plus exercise** **Control: Placebo LLLT plus exercise**							
Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**Range**	**n**	**Mean**	**Range**	**n**	**Mean difference (95% CI)**

Table 7. LLLT as add-on to other physical therapy (*Continued*)

Overall pain (VAS 0-10, 0 = no pain) at 2 weeks	5.65	(1-9)	20	5.96	(0-9)	20	-0.31 (95% CI not estimable)
Active shoulder abduction (degrees) at 2 weeks	147.5	(80-80)	20	149.5	(60-180)	20	-2 (95% CI not estimable)
Active shoulder flexion (degrees) at 2 weeks	158.5	(120-180)	20	160.5	(120-180)	20	-2 (95% CI not estimable)
Active shoulder extension (degrees) at 2 weeks	54	(30-60)	20	55.5	(40-60)	20	-1.5 (95% CI not estimable)
Active shoulder internal rotation (degrees) at 2 weeks	63	(25-70)	20	61.75	(30-70)	20	1.25 (95% CI not estimable)
Active external rotation (degrees) at 2 weeks	69.5	(30-90)	20	75	(30-90)	20	-5.5 (95% CI not estimable)
Active adduction (degrees) at 2 weeks	44.75	(40-45)	20	43.5	(25-45)	20	1.25 (95% CI not estimable)
Total adverse events	Zero events in both groups						

Study ID: Calis 2011
Participants: Subacromial impingement syndrome
Intervention: Low-level laser therapy (LLLT) plus exercise plus hot pack
Control: Exercise plus hot pack

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**

Table 7. LLLT as add-on to other physical therapy (*Continued*)

Overall pain (VAS 0-10, 0 = no pain) at 3 weeks	2.56	2.28	15	3.96	2.71	16	-1.40 (-3.16, 0.36)
Function (Constant-Murley total score: 0-100, higher score = better function) at 3 weeks	64.6	16.18	15	56.25	13.12	16	8.35 (-2.06, 18.76)
Pain on motion (VAS 0-10, 0 = no pain) at 3 weeks	3.73	2.37	15	5.51	1.89	16	-1.78 (-3.30, -0.26)
Night pain (VAS 0-10, 0 = no pain) at 3 weeks	3.68	2.85	15	4.84	2.72	16	-1.16 (-3.12, 0.80)
Shoulder abduction (degrees, unclear if active or passive) at 3 weeks	155.8	7.35	15	150.37	5.03	16	5.43 (0.97, 9.89)
Shoulder flexion (degrees, unclear if active or passive) at 3 weeks	174.46	6.94	15	172.18	6.93	16	2.28 (-2.61, 7.17)
Shoulder internal rotation (degrees, unclear if active or passive) at 3 weeks	70.93	6.06	15	69.18	7.67	16	1.75 (-3.10, 6.60)
Shoulder external rotation (degrees, unclear if active or passive) at 3	83.13	5.23	15	78.25	6.72	16	4.88 (0.66, 9.10)

Table 7. LLLT as add-on to other physical therapy (*Continued*)

weeks							

Study ID: Dogan 2010
Participants: Subacromial impingement syndrome
Intervention: Low-level laser therapy (LLLT) plus exercise plus ice
Control: Placebo LLLT plus exercise plus ice

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-10, 0 = no pain) at 3 weeks	3.76	1.45	30	4.63	2.1	22	-0.87 (-1.89, 0.15)
Function (SPADI total score 0-100, higher score = worse function) at 3 weeks	44.33	2.8	30	36.39	20.53	22	7.94 (-0.70, 16.58)
Shoulder flexion (degrees, unclear if active or passive) at 3 weeks	168	22.65	30	174.31	14.98	22	-6.31 (-16.55, 3.93)
Shoulder extension (degrees, unclear if active or passive) at 3 weeks	42.66	3.4	30	42.95	3.98	22	-0.29 (-2.35, 1.77)
Shoulder abduction (degrees, unclear if active or passive) at 3 weeks	166.66	21.38	30	172.72	16.67	22	-6.06 (-16.41, 4.29)
Shoulder adduction (degrees, unclear if active	42	4.27	30	42.04	5.26	22	-0.04 (-2.72, 2.64)

Table 7. LLLT as add-on to other physical therapy (*Continued*)

or passive) at 3 weeks							
Shoulder internal rotation (degrees, unclear if active or passive) at 3 weeks	49.33	9.62	30	49.77	4.49	22	-0.44 (-4.36, 3.48)
Shoulder external rotation (degrees, unclear if active or passive) at 3 weeks	44.83	5.64	30	44.09	1.97	22	0.74 (-1.44, 2.92)
Total adverse events during 3-week treatment period	Zero events in both groups						

Study ID: Eslamian 2012
Participants: Rotator cuff tendinitis
Intervention: Low-level laser therapy (LLLT) plus therapeutic ultrasound, TENS and exercise programme
Control: Placebo LLLT plus therapeutic ultrasound, TENS and exercise programme

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Overall pain (VAS 0-10, 0 = no pain) at 6 weeks	3.16	2.21	25	5	2.67	25	-1.84 (-3.20, -0.48)
Function (Croft SDQ 0-22 scale, higher score = greater disability) at 6 weeks	4.44	3.15	25	8.25	5.13	25	-3.81 (-6.17, -1.45)
Active shoulder abduction (degrees) at 6 weeks	144.92	31.6	25	132.8	31.3	25	12.12 (-5.31, 29.55)

Table 7. LLLT as add-on to other physical therapy (*Continued*)

Active shoulder external rotation (degrees) at 6 weeks	76.32	19.1	25	78.04	19.5	25	-1.72 (-12.42, 8.98)

Study ID: Kelle 2014
Participants: Subacromial impingement syndrome
Intervention: Low-level laser therapy (LLLT) plus home exercises
Control: Sham LLLT plus home exercises

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Rest pain (VAS 0-100) at 3 weeks	11.1	11.6	45	18.4	12.1	45	-7.30 (-12.20, -2.40)
Rest pain (VAS 0-100) at 6 months	11.5	13.8	45	16.3	9.5	45	-4.80 (-9.70, 0.10)
Function (UCLA 2-35, higher = better function) at 3 weeks	25.9	4.6	45	20.2	5.5	45	5.70 (3.61, 7.79)
Function (UCLA 2-35, higher = better function) at 6 months	26.1	5.6	45	19.9	5.5	45	6.20 (3.91, 8.49)
Pain on motion (VAS 0-100) at 3 weeks	32.6	17.6	45	43.3	17.6	45	-10.70 (-17.97, -3.43)
Pain on motion (VAS 0-100) at 6 months	25.5	19.7	45	40.8	18.2	45	-15.30 (-23.14, -7.46)
Adverse events	Zero events in both groups						

Table 7. LLLT as add-on to other physical therapy (*Continued*)

Study ID: Otadi 2012
Participants: Shoulder tendinitis
Intervention: Low-level laser therapy plus therapeutic ultrasound plus exercises
Control: Therapeutic ultrasound plus exercises

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Function (Constant-Murley score 0-100, higher = better function) change from baseline to 4 weeks	19.4	19.95	21	29.95	13.05	21	-10.55 (-20.74, -0.36)
	Events	Total		Events	Total		Risk ratio (95% CI)
Overall pain (> 3 point reduction on 0-10 VAS) at 4 weeks	15	21		15	21		1.00 (0.68, 1.47)
Overall pain (> 3 point reduction on 0-10 VAS) at 12 weeks	8	21		3	21		2.67 (0.82, 8.69)

Study ID: Vecchio 1993
Participants: Rotator cuff tendinitis
Intervention: Low-level laser therapy (LLLT) plus exercise
Control: Placebo LLLT plus exercise

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Rest pain (VAS 0-10, 0 = no pain) change	2.2	2.62	19	1.4	2.40	16	0.80 (-0.86, 2.46)

Table 7. LLLT as add-on to other physical therapy (*Continued*)

from baseline to 4 weeks							
Rest pain (VAS 0-10, 0 = no pain) change from baseline to 8 weeks	3.9	3.05	19	2.2	4.00	16	1.70 (-0.69, 4.09)
Function (VAS 0-10, higher = worse function) change from baseline to 4 weeks	2.9	2.62	19	2	3.20	16	0.90 (-1.06, 2.86)
Function (VAS 0-10, higher = worse function) change from baseline to 8 weeks	3.6	3.92	19	2.9	4.40	16	0.70 (-2.09, 3.49)
Pain on motion (VAS 0-10, 0 = no pain) change from baseline to 4 weeks	2.7	3.49	19	1.2	4.00	16	1.50 (-1.01, 4.01)
Pain on motion (VAS 0-10, 0 = no pain) change from baseline to 8 weeks	3.6	3.92	19	1.8	4.80	16	1.80 (-1.14, 4.74)
Night pain (VAS 0-10, 0 = no pain) change from baseline to 4 weeks	3.4	3.49	19	2.1	3.60	16	1.30 (-1.06, 3.66)
Night pain (VAS 0-10, 0 = no	4.4	3.92	19	3.2	4.80	16	1.20 (-1.74, 4.14)

Table 7. LLLT as add-on to other physical therapy (*Continued*)

pain) change from baseline to 8 weeks							
Pain on resisted abduction (0-3 scale, 0 = no pain) change from baseline to 4 weeks	0.64	0.78	19	0.29	1.76	16	0.35 (-0.58, 1.28)
Pain on resisted abduction (0-3 scale, 0 = no pain) change from baseline to 8 weeks	0.71	1.05	19	0.18	1.20	16	0.53 (-0.22, 1.28)
Total range of motion (unclear units, unclear if active or passive) change from baseline to 4 weeks	-0.8	1.31	19	-0.5	1.20	16	-0.30 (-1.13, 0.53)
Total range of motion (unclear units, unclear if active or passive) change from baseline to 8 weeks	-1.5	1.31	19	-0.8	2.00	16	-0.70 (-1.84, 0.44)
Total adverse events during 8-week trial period	Zero events in both groups						
Study ID: Yeldan 2009 **Participants: Subacromial impingement syndrome** **Intervention: Low-level laser therapy (LLLT) plus exercise plus cold pack** **Control: Placebo LLLT plus exercise plus cold pack**							

Table 7. LLLT as add-on to other physical therapy (*Continued*)

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Rest pain (VAS 0-10, 0 = no pain) at 3 weeks	1.61	1.96	34	1.92	1.89	26	-0.31 (-1.29, 0.67)
Function (Constant-Murley total score 0-100, higher = better function) at 3 weeks	76.67	12.73	34	74.73	15.5	26	1.94 (-5.40, 9.28)
Pain on motion (VAS 0-10, 0 = no pain) at 3 weeks	3.7	1.69	34	4.11	2.19	26	-0.41 (-1.43, 0.61)
Night pain (VAS 0-10, 0 = no pain) at 3 weeks	2.29	2.06	34	2.53	2.38	26	-0.24 (-1.39, 0.91)
Shoulder flexion (degrees, unclear if active or passive) at 3 weeks	139.52	9.89	34	140.53	10.33	26	-1.01 (-6.19, 4.17)
Shoulder abduction (degrees, unclear if active or passive) at 3 weeks	110.67	8.79	34	106.57	9.92	26	4.10 (-0.72, 8.92)
Shoulder external rotation (degrees, unclear if active or passive) at 3 weeks	63.91	5.81	34	62.5	4.66	26	1.41 (-1.24, 4.06)

Table 7. LLLT as add-on to other physical therapy (*Continued*)

Shoulder internal rotation (degrees, unclear if active or passive) at 3 weeks	71.5	4.35	34	73	3.96	26	-1.50 (-3.61, 0.61)
Shoulder extension (degrees, unclear if active or passive) at 3 weeks	41.88	6.29	34	44.3	5.04	26	-2.42 (-5.29, 0.45)
Strength - shoulder abduction force (kg) at 3 weeks	18.28	2.96	34	17.88	3.43	26	0.40 (-1.25, 2.05)
Strength - shoulder flexion force (kg) at 3 weeks	19.54	3.21	34	18.79	3.92	26	0.75 (-1.10, 2.60)
Strength - shoulder external rotation force (kg) at 3 weeks	20.63	3.38	34	20.74	3.21	26	-0.11 (-1.79, 1.57)
Strength - shoulder internal rotation force (kg) at 3 weeks	21.55	3.22	34	20.4	4.12	26	1.15 (-0.77, 3.07)
Strength - shoulder extension force (kg) at 3 weeks	18.8	3.13	34	17.76	2.69	26	1.04 (-0.44, 2.52)
Total adverse events during 3-week trial period	Zero events in both groups						

Table 8. LLLT versus another active intervention

Study ID: England 1989 **Participants: Supraspinatus or bicipital tendinitis** **Intervention: Low-level laser therapy (LLLT)** **Control: NSAID**							
Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Median difference (95% CI)**
Overall pain (VAS 0-10, higher score = more pain) at 2 weeks	NR	NR	< = 10	NR	NR	< = 10	2 (1, 3.5)
Function (VAS 0-10, higher score = worse function) at 2 weeks	NR	NR	< = 10	NR	NR	< = 10	"No significant difference"
Active shoulder abduction (degrees) at 2 weeks	NR	NR	< = 10	NR	NR	< = 10	20 (10, 40)
Active shoulder flexion (degrees) at 2 weeks	NR	NR	< = 10	NR	NR	< = 10	14.99 (5, 30)
Active shoulder extension (degrees) at 2 weeks	NR	NR	< = 10	NR	NR	< = 10	10 (0, 20)
Study ID: Kelle 2014 **Participants: Subacromial impingement syndrome** **Intervention: Low-level laser therapy (LLLT) plus home exercises** **Control: Glucocorticoid injection plus home exercises**							
Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**

Table 8. LLLT versus another active intervention (*Continued*)

Rest pain (VAS 0-100) at 3 weeks	11.1	11.6	45	10.0	11.3	45	1.10 (-3.63, 5.83)
Rest pain (VAS 0-100) at 6 months	11.5	13.8	45	8.9	10.4	45	2.60 (-2.45, 7.65)
Function (UCLA 2-35, higher = better function) at 3 weeks	25.9	4.6	45	27.4	4.1	45	-1.50 (-3.30, 0.30)
Function (UCLA 2-35, higher = better function) at 6 months	26.1	5.6	45	26.8	5.4	45	-0.70 (-2.97, 1.57)
Pain on motion (VAS 0-100) at 3 weeks	32.6	17.6	45	23.6	15.6	45	9.00 (2.13, 15.87)
Pain on motion (VAS 0-100) at 6 months	25.5	19.7	45	22.1	17.9	45	3.40 (-4.38, 11.18)
Adverse events	Zero events in both groups						

NR = not reported

Table 9. TENS as add-on to other physical therapy

Study ID: Baskurt 2006
Participants: Shoulder impingement syndrome
Intervention: TENS plus hot pack
Control: Hot pack

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-10, 0 = no	4.67	1.37	31	5.38	1.45	31	-0.71 (-1.41, -0.01)

Table 9. TENS as add-on to other physical therapy *(Continued)*

pain) immediately post 1 treatment session							

Table 10. TENS versus another active intervention

Study ID: Baskurt 2006
Participants: Shoulder impingement syndrome
Intervention: TENS
Control: Hot pack

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-10, 0 = no pain) immediately post 1 treatment session	5.36	1.35	30	5.38	1.45	31	-0.02 (-0.72, 0.68)

Study ID: Eyigor 2010
Participants: Rotator cuff tendinitis
Intervention: TENS plus home exercises
Control: Glucocorticoid injection plus home exercises

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Rest pain (VAS 0-10, 0 = no pain) at 1 week	2.3	1.2	20	1.5	1	20	0.80 (0.12, 1.48)
Rest pain (VAS 0-10, 0 = no pain) at 4 weeks	1.8	1.5	20	0.6	0.4	20	1.20 (0.52, 1.88)
Rest pain (VAS 0-10, 0 = no pain) at 12 weeks	1	0.7	20	0.2	0.4	20	0.80 (0.45, 1.15)

Table 10. TENS versus another active intervention (*Continued*)

Function (SDQ 0-100, 0 = no disability) at 1 week	67.6	15.9	20	37.9	22.6	20	29.70 (17.59, 41.81)
Function (SDQ 0-100, 0 = no disability) at 4 weeks	42.5	14.7	20	22.1	15.9	20	20.40 (10.91, 29.89)
Function (SDQ 0-100, 0 = no disability) at 12 weeks	28.5	13.5	20	13.7	11.5	20	14.80 (7.03, 22.57)
Pain on motion (VAS 0-10, 0 = no pain) at 1 week	4.5	1	20	3.5	1.4	20	1.00 (0.25, 1.75)
Pain on motion (VAS 0-10, 0 = no pain) at 4 weeks	2.6	1.6	20	1.9	1.2	20	0.70 (-0.18, 1.58)
Pain on motion (VAS 0-10, 0 = no pain) at 12 weeks	2.1	1.3	20	1.2	0.7	20	0.90 (0.25, 1.55)
Night pain (VAS 0-10, 0 = no pain) at 1 week	4.2	1.8	20	2.1	2	20	2.10 (0.92, 3.28)
Night pain (VAS 0-10, 0 = no pain) at 4 weeks	2.7	1.6	20	1.7	1.2	20	1.00 (0.12, 1.88)
Night pain (VAS 0-10, 0 = no pain) at 12 weeks	2	0.9	20	1.2	0.9	20	0.80 (0.24, 1.36)

Table 10. TENS versus another active intervention (*Continued*)

Active shoulder flexion (degrees) at 1 week	144.9	17.6	20	152.5	21.6	20	-7.60 (-19.81, 4.61)
Active shoulder flexion (degrees) at 4 weeks	160	11.9	20	162.7	14.7	20	-2.70 (-10.99, 5.59)
Active shoulder flexion (degrees) at 12 weeks	165.3	8.8	20	170.5	9.1	20	-5.20 (-10.75, 0.35)
Active shoulder abduction (degrees) at 1 week	124.3	23.2	20	143.5	22.9	20	-19.20 (-33.49, -4.91)
Active shoulder abduction (degrees) at 4 weeks	149.8	14.6	20	163.7	16.1	20	-13.90 (-23.43, -4.37)
Active shoulder abduction (degrees) at 12 weeks	159.3	11.8	20	170	13.3	20	-10.70 (-18.49, -2.91)
Active shoulder external rotation (degrees) at 1 week	56.8	15.7	20	59.3	20.9	20	-2.50 (-13.96, 8.96)
Active shoulder external rotation (degrees) at 4 weeks	64.5	9.9	20	68.3	10.8	20	-3.80 (-10.22, 2.62)
Active shoulder external rotation (degrees) at 12 weeks	70.3	8.7	20	69.9	8.9	20	0.40 (-5.05, 5.85)

Table 10. TENS versus another active intervention (*Continued*)

Active shoulder internal rotation (degrees) at 1 week	48.3	13.3	20	59	14.8	20	-10.70 (-19.42, -1.98)
Active shoulder internal rotation (degrees) at 4 weeks	63	11.3	20	66.7	14.2	20	-3.70 (-11.65, 4.25)
Active shoulder internal rotation (degrees) at 12 weeks	68.4	11.8	20	68.6	7.9	20	-0.20 (-6.42, 6.02)
Quality of life (SF-36 physical function 0-100, higher = better) at 12 weeks	74.4	16.9	20	68.5	17.4	20	5.90 (-4.73, 16.53)
Quality of life (SF-36 physical role 0-100, higher = better) at 12 weeks	63.8	15.1	20	51.2	36.7	20	12.60 (-4.79, 29.99)
Quality of life (SF-36 bodily pain 0-100, higher = better) at 12 weeks	61.3	18	20	68.6	16.6	20	-7.30 (-18.03, 3.43)
Quality of life (SF-36 general health 0-100, higher = better) at 12 weeks	58.6	17.1	20	50	19.2	20	8.60 (-2.67, 19.87)
Quality of life (SF-36 vitality 0-100, higher = better) at 12	54.3	12.6	20	51.5	12.1	20	2.80 (-4.86, 10.46)

Table 10. TENS versus another active intervention (*Continued*)

weeks							
Quality of life (SF-36 social functioning 0-100, higher = better) at 12 weeks	73.3	14	20	68.1	25.8	20	5.20 (-7.66, 18.06)
Quality of life (SF-36 emotion role 0-100, higher = better) at 12 weeks	53.8	18.5	20	58.2	21.2	20	-4.40 (-16.73, 7.93)
Quality of life (SF-36 mental health 0-100, higher = better) at 12 weeks	55.1	16.3	20	56.1	13.9	20	-1.00 (-10.39, 8.39)
	Events	**Total**		**Events**	**Total**		**Risk ratio (95% CI)**
Global assessment of treatment success (participant reported "good results" or "very good results") at 1 week	4	20		14	20		0.29 (0.11, 0.72)
Global assessment of treatment success (participant reported "good results" or "very good results") at 4 weeks	12	20		15	20		0.80 (0.52, 1.24)
Global assessment of treatment success (participant reported	13	20		17	20		0.76 (0.53, 1.11)

Table 10. TENS versus another active intervention (*Continued*)

"good results" or "very good results") at 12 weeks						
Total adverse events during 12-week treatment and follow-up period	Zero events in both groups					

Study ID: Pan 2003
Participants: Calcific tendinitis
Intervention: TENS
Control: Extracorporeal shockwave therapy

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n*	Mean	SD	n*	Mean difference (95% CI)
Overall pain (VAS 0-10, 0 = no pain) change from baseline to 4 weeks	-1.1	1.94	29	-3	2.41	33	1.90 (0.82, 2.98)
Overall pain (VAS 0-10, 0 = no pain) change from baseline to 12 weeks	-1.74	2.2	29	-4.08	2.59	33	2.34 (1.15, 3.53)
Function (Constant-Murley score 0-100, higher = better function) change from baseline to 4 weeks	9.59	9.62	29	24.21	13.68	33	-14.62 (-20.45, -8.79)
Function (Constant-Murley score 0-100, higher = better func-	11.86	13.32	29	28.31	13.1	33	-16.45 (-23.04, -9.86)

Table 10. TENS versus another active intervention (*Continued*)

tion) change from baseline to 12 weeks							
	Events*	**Total***		**Events***	**Total***		**Risk ratio (95% CI)**
Strength (improvement on Manual Muscle Testing) at 4 weeks	15	29		21	33		0.81 (0.53, 1.26)
Strength (improvement on Manual Muscle Testing) at 12 weeks	18	29		23	33		0.89 (0.62, 1.28)
Total adverse events during 12-week trial period (soreness in the upper arm after treatment)	0	27		5	32		0.11 (0.01, 1.85)

*Unit of analysis is shoulders, not participants

Table 11. PEMF versus placebo

Study ID: Binder 1984 **Participants: Rotator cuff tendinitis** **Intervention: PEMF for 4 weeks** **Control: Placebo PEMF for 4 weeks**							
Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Overall pain (VAS 0-10, 0 = no pain) change from baseline to 2 weeks	-5	NR	15	-1.14	NR	14	-3.86 (95% CI not estimable)
Overall pain (VAS 0-10, 0 = no	-8.2	NR	15	-2.97	NR	14	-5.23 (95% CI not estimable)

Table 11. PEMF versus placebo (*Continued*)

pain) change from baseline to 4 weeks							
Total active range of motion (degrees) change from baseline to 2 weeks	59.08	NR	15	13.23	NR	14	45.85 (95% CI not estimable)
Total active range of motion (degrees) change from baseline to 4 weeks	75.89	NR	15	17.15	NR	14	58.74 (95% CI not estimable)

Study ID: Galace de Freitas 2014
Participants: Shoulder impingement syndrome
Intervention: PEMF for 3 weeks
Control: Placebo PEMF for 3 weeks

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Overall pain (VAS 0-10 where higher score = worse pain) at 3 weeks	4.8	2.4	22	6	2.1	24	-1.20 (-2.51, 0.11)
Function (Constant-Murley total score 0-100 where higher score = better function) at 3 weeks	40.7	12.6	22	35.6	11.7	24	5.10 (-1.95, 12.15)
Strength (kg): external rotation at 3 weeks	26.8	12.9	22	21.6	10.3	24	5.20 (-1.59, 11.99)

Table 11. PEMF versus placebo (*Continued*)

Strength (kg) : internal rotation at 3 weeks	38.1	17	22	33.7	12	24	4.40 (-4.17, 12.97)

Table 12. PEMF as add-on to other physical therapy

Study ID: Aktas 2007
Participants: Subacromial impingement syndrome
Intervention: Pulsed electromagnetic field (PEMF) plus exercise plus cold pack
Control: Placebo PEMF plus exercise plus cold pack

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-10, 10 = intolerable pain) at 3 weeks	0.9	1.55	20	0.85	1.56	20	0.05 (-0.91, 1.01)
Function (Constant total score 0-100 where higher = better function) at 3 weeks	72.65	17.99	20	72	12.78	20	0.65 (-9.02, 10.32)
Pain on motion (VAS 0-10, 10 = intolerable pain) at 3 weeks	2.7	2.51	20	2.75	2.22	20	-0.05 (-1.52, 1.42)
Night pain (VAS 0-10, 10 = intolerable pain) at 3 weeks	0.8	1.59	20	2.25	3.27	20	-1.45 (-3.04, 0.14)
Active range of motion (Constant subscore 0-40, higher = better ROM) at 3 weeks	35.9	6.91	20	36.7	3.13	20	-0.80 (-4.12, 2.52)

Table 12. PEMF as add-on to other physical therapy (*Continued*)

Strength (Constant sub-score 0-25, higher = better strength) at 3 weeks	12.25	7.33	20	11.5	7.17	20	0.75 (-3.74, 5.24)

Study ID: Galace de Freitas 2014
Participants: Shoulder impingement syndrome
Intervention: PEMF plus exercises for 9 weeks
Control: Placebo PEMF plus exercises for 9 weeks

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-10 where higher score = worse pain) at 3 months	2.7	3	22	3.4	3.1	24	-0.70 (-2.46, 1.06)
Function (Constant-Murley total score 0-100 where higher score = better function) at 3 months	52.7	11.7	22	50.4	12	24	2.30 (-4.55, 9.15)
Strength (kg): external rotation at 3 months	32.7	14.5	22	24.9	10.2	24	7.80 (0.49, 15.11)
Strength (kg): internal rotation at 3 months	43.8	4	22	36.6	13.2	24	7.20 (1.66, 12.74)
Strength (kg): elevation at 3 months	28.5	11.4	22	22.2	8.8	24	6.30 (0.38, 12.22)

Table 13. Microcurrent electrical stimulation (MENS) versus placebo

Study ID: Atya 2012
Participants: Subacromial impingement syndrome
Intervention: Microcurrent electrical stimulation (MENS)
Control: Placebo MENS

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-10, 0 = no pain) at 6 weeks	6	1.07	19	6.8	1.08	21	-0.80 (-1.47, -0.13)
Function (Dutch SDQ total score 0-100 where higher = worse function) at 6 weeks	60.65	7.7	19	67.6	6.88	21	-6.95 (-11.49, -2.41)

Table 14. Multiple electrotherapy modalities versus no treatment

Study ID: Perron 1997
Participants: Calcific tendinitis
Intervention: Acetic acid iontophoresis plus therapeutic ultrasound
Control: No treatment

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Pain on motion (passive abduction) (0-5 scale, 0 = no pain) at 3 weeks	1.38	0.81	11	1.59	0.91	10	-0.21 (-0.95, 0.53)
Passive shoulder abduction (degrees) at 3 weeks	113.18	38.94	11	93.75	26.23	10	19.43 (-8.75, 47.61)

Table 15. Microwave diathermy as add-on to other physical therapy

Study ID: Akyol 2012
Participants: Subacromial impingement syndrome
Intervention: Microwave diathermy plus exercise plus superficial heat
Control: Placebo microwave diathermy plus exercise plus superficial heat

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (10-point scale, 0 = no pain) change from baseline to 3 weeks	-2.65	1.98	20	-2.95	2.74	20	0.30 (-1.18, 1.78)
Overall pain (10-point scale, 0 = no pain) change from baseline to 7 weeks	-2.8	2.23	20	-2.8	3.33	20	0.00 (-1.76, 1.76)
Function (SPADI total score 0-100 where higher = worse function) change from baseline to 3 weeks	-48.2	2.96	20	-48.85	2.74	20	0.65 (-1.12, 2.42)
Function (SPADI total score 0-100 where higher = worse function) change from baseline to 7 weeks	-49.75	3	20	-54.2	2.82	20	4.45 (2.65, 6.25)
Pain on motion (10-point scale, 0 = no pain) change from baseline to 3 weeks	-4.05	2.35	20	-3.45	3.2	20	-0.60 (-2.34, 1.14)

Table 15. Microwave diathermy as add-on to other physical therapy (*Continued*)

Pain on motion (10-point scale, 0 = no pain) change from baseline to 7 weeks	-5.1	2.65	20	-4.1	2.77	20	-1.00 (-2.68, 0.68)
Night pain (10-point scale, 0 = no pain) change from baseline to 3 weeks	-3.85	2.64	20	-4.1	2.31	20	0.25 (-1.29, 1.79)
Night pain (10-point scale, 0 = no pain) change from baseline to 7 weeks	-4.1	2.9	20	-4.5	3.2	20	0.40 (-1.49, 2.29)
Active shoulder abduction (degrees) change from baseline to 3 weeks	29.5	3.23	20	23.75	2.34	20	5.75 (4.00, 7.50)
Active shoulder abduction (degrees) change from baseline to 7 weeks	33.5	3.75	20	27	11.96	20	6.50 (1.01, 11.99)
Active shoulder flexion (degrees) change from baseline to 3 weeks	26	2.32	20	18.5	1.76	20	7.50 (6.22, 8.78)
Active shoulder flexion (degrees) change from baseline to 7 weeks	28.25	2.31	20	20.5	1.82	20	7.75 (6.46, 9.04)

Table 15. Microwave diathermy as add-on to other physical therapy (*Continued*)

Active shoulder internal rotation (degrees) change from baseline to 3 weeks	11.5	1.31	20	19.25	1.71	20	-7.75 (-8.69, -6.81)
Active shoulder internal rotation (degrees) change from baseline to 7 weeks	17.25	1.78	20	22.5	1.88	20	-5.25 (-6.38, -4.12)
Active shoulder external rotation (degrees) change from baseline to 3 weeks	12.5	1.8	20	21.5	1.37	20	-9.00 (-9.99, -8.01)
Active shoulder external rotation (degrees) change from baseline to 7 weeks	15.25	1.9	20	22.75	1.44	20	-7.50 (-8.54, -6.46)
Quality of life (SF-36 physical function 0-100, higher = better) change from baseline to 3 weeks	0.08	0.89	20	0.14	0.19	20	-0.06 (-0.46, 0.34)
Quality of life (SF-36 physical function 0-100, higher = better) change from baseline to 7 weeks	0.11	0.1	20	0.19	0.18	20	-0.08 (-0.17, 0.01)
Quality of life (SF-36 social function 0-100, higher = better) change	0.19	0.15	20	0.12	0.12	20	0.07 (-0.01, 0.15)

Table 15. Microwave diathermy as add-on to other physical therapy (*Continued*)

from baseline to 3 weeks							
Quality of life (SF-36 social function 0-100, higher = better) change from baseline to 7 weeks	0.25	0.21	20	0.17	0.18	20	0.08 (-0.04, 0.20)
Quality of life (SF-36 physical role limitation 0-100, higher = better) change from baseline to 3 weeks	0.31	0.47	20	0.46	0.44	20	-0.15 (-0.43, 0.13)
Quality of life (SF-36 physical role limitation 0-100, higher = better) change from baseline to 7 weeks	0.43	0.57	20	0.56	0.47	20	-0.13 (-0.45, 0.19)
Quality of life (SF-36 emotional role limitation 0-100, higher = better) change from baseline to 3 weeks	0.26	0.44	20	0.06	0.23	20	0.20 (-0.02, 0.42)
Quality of life (SF-36 emotional role limitation 0-100, higher = better) change from baseline to 7 weeks	0.35	0.45	20	0.05	0.3	20	0.30 (0.06, 0.54)
Quality of life (SF-36 mental health 0-	0.04	0.04	20	0.03	0.05	20	0.01 (-0.02, 0.04)

Table 15. Microwave diathermy as add-on to other physical therapy (*Continued*)

100, higher = better) change from baseline to 3 weeks							
Quality of life (SF-36 mental health 0-100, higher = better) change from baseline to 7 weeks	0.04	0.06	20	0.06	0.11	20	-0.02 (-0.07, 0.03)
Quality of life (SF-36 energy 0-100, higher = better) change from baseline to 3 weeks	0.04	0.07	20	0.02	0.07	20	0.02 (-0.02, 0.06)
Quality of life (SF-36 energy 0-100, higher = better) change from baseline to 7 weeks	0.06	0.09	20	0.04	0.09	20	0.02 (-0.04, 0.08)
Quality of life (SF-36 pain 0-100, higher = better) change from baseline to 3 weeks	0.39	0.21	20	0.38	0.17	20	0.01 (-0.11, 0.13)
Quality of life (SF-36 pain 0-100, higher = better) change from baseline to 7 weeks	0.43	0.24	20	0.46	0.26	20	-0.03 (-0.19, 0.13)
Quality of life (SF-36 general health 0-100, higher = better) change from baseline to 3 weeks	0.1	0.11	20	0.11	0.14	20	-0.01 (-0.09, 0.07)

Table 15. Microwave diathermy as add-on to other physical therapy (*Continued*)

Quality of life (SF-36 general health 0-100, higher = better) change from baseline to 7 weeks	0.13	0.15	20	0.18	0.16	20	-0.05 (-0.15, 0.05)
Isokinetic strength (60º/s internal rotation) change from baseline to 3 weeks	2.6	5.66	20	5.15	6.37	20	-2.55 (-6.28, 1.18)
Isokinetic strength (60º/s internal rotation) change from baseline to 7 weeks	0.75	5.01	20	-1.6	3.36	20	2.35 (-0.29, 4.99)
Isokinetic strength (60º/s external rotation) change from baseline to 3 weeks	0.7	4.34	20	3.5	3.7	20	-2.80 (-5.30, -0.30)
Isokinetic strength (60º/s external rotation) change from baseline to 7 weeks	1.4	5.25	20	2.45	4.32	20	-1.05 (-4.03, 1.93)
Isokinetic strength (180º/s internal rotation) change from baseline to 3 weeks	1.6	2.89	20	2.8	4.56	20	-1.20 (-3.57, 1.17)
Isokinetic strength (180º/s internal rotation) change	2.4	5.09	20	3.15	4.78	20	-0.75 (-3.81, 2.31)

Table 15. Microwave diathermy as add-on to other physical therapy (*Continued*)

from baseline to 7 weeks							
Isokinetic strength (180º/s external rotation) change from baseline to 3 weeks	0.9	3.21	20	1.65	3.6	20	-0.75 (-2.86, 1.36)
Isokinetic strength (180º/s external rotation) change from baseline to 7 weeks	0.2	3.2	20	1.25	2.46	20	-1.05 (-2.82, 0.72)
Total adverse events at 3 weeks	Zero events in both groups						
Total adverse events at 7 weeks	Zero events in both groups						

Table 16. Acetic acid iontophoresis as add-on to other physical therapy

Study ID: Leduc 2003
Participants: Calficic tendinitis
Intervention: Acetic acid iontophoresis plus exercise plus heat pack
Control: Sham iontophoresis plus exercise plus heat pack

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Function (SPADI total score 0-100, higher = worse function) at 6 weeks	23	15	17	40	17	10	-17.00 (-29.72, -4.28)
Active shoulder abduction (degrees) at 6 weeks	133	24	17	130	30	10	3.00 (-18.81, 24.81)

Table 16. Acetic acid iontophoresis as add-on to other physical therapy (*Continued*)

Active shoulder flexion (degrees) at 6 weeks	154	12	17	143	48	10	11.00 (-19.29, 41.29)
Active shoulder external rotation (degrees) at 6 weeks	75	11	17	72	16	10	3.00 (-8.21, 14.21)
Active shoulder internal rotation (degrees) at 6 weeks	69	20	17	71	26	10	-2.00 (-20.71, 16.71)

Table 17. Multiple electrotherapy modalities versus another active intervention

Study ID: Grymel-Kulesza 2007
Participants: Chronic rotator cuff injuries
Intervention: Therapeutic ultrasound plus TENS plus exercise plus massage
Control: Cryotherapy plus exercise plus massage

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Active shoulder abduction (degrees) at 2 weeks	129	37.71	15	122.3	22.03	15	6.70 (-15.40, 28.80)
Active shoulder extension (degrees) at 2 weeks	30.67	7.04	15	24.67	6.11	15	6.00 (1.28, 10.72)
Active shoulder external rotation (degrees) at 2 weeks	69.33	14.62	15	55	15.12	15	14.33 (3.69, 24.97)
Active shoulder internal rotation (degrees) at 2	67.67	12.37	15	58.67	13.69	15	9.00 (-0.34, 18.34)

Table 17. Multiple electrotherapy modalities versus another active intervention (*Continued*)

weeks							
Strength (Jobes' 5-point scale) - supraspinatus at 2 weeks	4.37	0.48	15	3.9	0.11	15	0.47 (0.22, 0.72)
Strength (Jobes' 5-point scale) - subscapularis at 2 weeks	4.3	0.49	15	4.03	0.48	15	0.27 (-0.08, 0.62)
Strength (Jobes' 5-point scale) - infraspinatus at 2 weeks	4.2	0.32	15	4	0.38	15	0.20 (-0.05, 0.45)
Strength (Jobes' 5-point scale) - biceps at 2 weeks	4.6	0.39	15	4.37	0.44	15	0.23 (-0.07, 0.53)
	Events	**Total**		**Events**	**Total**		**Risk ratio (95% CI)**
Night pain (number of participants with any night pain) at 2 weeks	0	15		11	15		0.04 (0.00, 0.68)

Study ID: Ozgen 2012
Participants: Supraspinatus tendinitis
Intervention: Therapeutic ultrasound plus TENS plus hot pack plus home exercises
Control: Sodium hyaluronate injection plus home exercises

Outcome	**Intervention**			**Control**			**Effect estimate**
	Median	**IQR**	**N**	**Median**	**IQR**	**N**	**Mean difference (95% CI)**
Rest pain (VAS 0-10, 0 = no pain) at 3 weeks	0	0, 0	12	0	0, 2.5	12	0 (95% CI not estimable)

Table 17. Multiple electrotherapy modalities versus another active intervention (*Continued*)

Rest pain (VAS 0-10, 0 = no pain) at 3 months	0	0, 0	12	0	0, 1.5	12	0 (95% CI not estimable)
Rest pain (VAS 0-10, 0 = no pain) at 4 years	0	0, 0	10	0	0, 0	11	0 (95% CI not estimable)
Function (ASES 0-60, higher score = better function) at 3 weeks	56.5	40, 59	12	56.5	52, 60	12	0 (95% CI not estimable)
Function (ASES 0-60, higher score = better function) at 3 months	56	46, 59	12	60	59.5, 60	12	-4.00 (95% CI not estimable)
Function (ASES 0-60, higher score = better function) at 4 years	60	60, 60	10	60	60, 60	11	0 (95% CI not estimable)
Pain on motion (VAS 0-10, 0 = no pain) at 3 weeks	0	0, 3	12	0.5	0, 4	12	-0.5 (95% CI not estimable)
Pain on motion (VAS 0-10, 0 = no pain) at 3 months	2.5	0, 4	12	0	0, 0	12	2.5 (95% CI not estimable)
Pain on motion (VAS 0-10, 0 = no pain) at 4 years	0	0, 0	10	0	0, 0	11	0 (95% CI not estimable)

Table 17. Multiple electrotherapy modalities versus another active intervention (*Continued*)

Night pain (VAS 0-10, 0 = no pain) at 3 weeks	0	0, 1	12	2	0, 4.5	12	-2 (95% CI not estimable)
Night pain (VAS 0-10, 0 = no pain) at 3 months	1	0, 4	12	0	0, 3	12	1 (95% CI not estimable)
Night pain (VAS 0-10, 0 = no pain) at 4 years	0	0, 0	10	0	0, 0	11	0 (95% CI not estimable)
Active shoulder abduction (degrees) at 3 weeks	180	170, 180	12	180	135, 180	12	0 (95% CI not estimable)
Active shoulder abduction (degrees) at 3 months	180	162.5, 180	12	180	180, 180	12	0 (95% CI not estimable)
Active shoulder abduction (degrees) at 4 years	180	180, 180	10	180	180, 180	11	0 (95% CI not estimable)
Active shoulder flexion (degrees) at 3 weeks	175	147.5, 180	12	177.5	163.5, 180	12	-2.50 (95% CI not estimable)
Active shoulder flexion (degrees) at 3 months	180	150, 180	12	180	177.5, 180	12	0 (95% CI not estimable)
Active shoulder flexion (degrees) at 4 years	180	180, 180	10	180	180, 180	11	0 (95% CI not estimable)
Active shoulder extension (degrees) at 3 weeks	52.5	35, 60	12	60	45, 60	12	-7.50 (95% CI not estimable)

Table 17. Multiple electrotherapy modalities versus another active intervention (*Continued*)

Active shoulder extension (degrees) at 3 months	60	45, 60	12	60	60, 60	12	0 (95% CI not estimable)
Active shoulder extension (degrees) at 4 years	60	60, 60	10	60	60, 60	11	0 (95% CI not estimable)
Active shoulder external rotation (degrees) at 3 weeks	78.5	40, 90	12	90	67.5, 90	12	-11.50 (95% CI not estimable)
Active shoulder external rotation (degrees) at 3 months	90	70, 90	12	90	90, 90	12	0 (95% CI not estimable)
Active shoulder external rotation (degrees) at 4 years	90	90, 90	10	90	90, 90	11	0 (95% CI not estimable)
Active shoulder internal rotation (degrees) at 3 weeks	87.5	70, 90	12	90	76.5, 90	12	-2.50 (95% CI not estimable)
Active shoulder internal rotation (degrees) at 3 months	90	75, 90	12	90	90, 90	12	0 (95% CI not estimable)
Active shoulder internal rotation (degrees) at 4 years	90	90, 90	10	90	90, 90	11	0 (95% CI not estimable)
	Events	**Total**		**Events**	**Total**		**Risk ratio (95% CI)**

Table 17. Multiple electrotherapy modalities versus another active intervention (*Continued*)

Global assessment of treatment success (excellent improvement) at 3 months	7	12	8	12	0.88 (0.47, 1.63)
Global assessment of treatment success (excellent improvement) at 4 years	10	10	11	11	1.00 (0.84, 1.19)
Total adverse events during 4 year trial period	Zero events in both groups				

Table 18. Microwave diathermy versus another active intervention

Study ID: Rabini 2012
Participants: Rotator cuff tendinopathy, with or without partial thickness tendon tears
Intervention: Microwave diathermy
Control: Glucocorticoid injection

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-100, 0 = no pain) at 4 weeks	35.1	24.3	40	29.6	10.3	42	5.50 (-2.65, 13.65)
Overall pain (VAS 0-100, 0 = no pain) at 12 weeks	38.4	22.9	40	28.9	14.3	42	9.50 (1.19, 17.81)
Overall pain (VAS 0-100, 0 = no pain) at 24 weeks	37.6	30	40	29	17.3	42	8.60 (-2.07, 19.27)
Function (Constant-Murley total	90.1	15	40	82.4	17.7	42	7.70 (0.61, 14.79)

Table 18. Microwave diathermy versus another active intervention (*Continued*)

score 0-100, higher = better function) at 4 weeks							
Function (Constant-Murley total score 0-100, higher = better function) at 12 weeks	86.6	12.7	40	83.2	9.9	42	3.40 (-1.55, 8.35)
Function (Constant-Murley total score 0-100, higher = better function) at 24 weeks	88.1	20	40	89.9	12.6	42	-1.80 (-9.08, 5.48)
Total adverse events during 24-week trial period	Zero events in both groups						

Table 19. One electrotherapy modality versus another

Study ID: Binder 1984
Participants: Rotator cuff tendinitis
Intervention: PEMF for 6 weeks
Control: Placebo PEMF for 4 weeks followed by active PEMF for 2 weeks

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Overall pain (VAS 0-10, 0 = no pain) change from baseline to 6 weeks	-8.98	NR	15	-7.75	NR	14	-1.23 (95% CI not estimable)
Total active range of motion (de-	101.4	NR	15	63.45	NR	14	37.95 (95% CI not estimable)

Table 19. One electrotherapy modality versus another (*Continued*)

grees) change from baseline to 6 weeks							

Study ID: Binder 1984
Participants: Rotator cuff tendinitis
Intervention: PEMF for 8 weeks
Control: Placebo PEMF for 4 weeks followed by active PEMF for 4 weeks

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Overall pain (VAS 0-10, 0 = no pain) change from baseline to 4 months	-11.12	NR	15	-10.37	NR	14	-0.75 (95% CI not estimable)
Total active range of motion (degrees) change from baseline to 4 months	122.37	NR	15	115.77	NR	14	6.6 (95% CI not estimable)
	Events	Total		Events	Total		Risk ratio (95% CI)
Global assessment of treatment success (participants symptomless) at 4 months	9	15		10	14		0.84 (0.49, 1.43)
Total adverse events during 4 months	"Although many patients found the coils cumbersome, especially at night, no untoward reactions were reported during the controlled study"						

Study ID: Calis 2011
Participants: Subacromial impingement syndrome
Intervention: Therapeutic ultrasound plus exercise plus hot pack
Control: Low-level laser therapy plus exercise plus hot pack

Table 19. One electrotherapy modality versus another (*Continued*)

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-10, 0 = no pain) at 3 weeks	2.21	2.09	21	2.56	2.28	15	-0.35 (-1.81, 1.11)
Function (Constant-Murley total score: 0-100, higher score = better function) at 3 weeks	62.85	6.85	21	64.6	16.18	15	-1.75 (-10.45, 6.95)
Pain on motion (VAS 0-10, 0 = no pain) at 3 weeks	4.24	2.26	21	3.73	2.37	15	0.51 (-1.03, 2.05)
Night pain (VAS 0-10, 0 = no pain) at 3 weeks	3.74	2.18	21	3.68	2.85	15	0.06 (-1.66, 1.78)
Shoulder abduction (degrees, unclear if active or passive) at 3 weeks	155.95	9.21	21	155.8	7.35	15	0.15 (-5.27, 5.57)
Shoulder flexion (degrees, unclear if active or passive) at 3 weeks	177.04	3.74	21	174.46	6.94	15	2.58 (-1.28, 6.44)
Shoulder internal rotation (degrees, unclear if active or passive) at 3 weeks	74.85	7.29	21	70.93	6.06	15	3.92 (-0.45, 8.29)

Table 19. One electrotherapy modality versus another (*Continued*)

Shoulder external rotation (degrees, unclear if active or passive) at 3 weeks	81.66	5.82	21	83.13	5.23	15	-1.47 (-5.10, 2.16)

Study ID: Chard 1988
Participants: Rotator cuff tendinitis
Intervention: PEMF for 8 hrs per day
Control: PEMF for 2 hrs per day

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Overall pain	"The improvement in pain score over the 8 weeks of treatment consistently favoured Group 2 (8 hrs per day) for pain at night, on movement, at rest, and total pain score, but this failed to reach significance"						
Pain on motion	See above quote						
Night pain	See above quote						
Pain with resisted movement	No statistically significant difference between groups over the 8-week treatment period						
Total active range of motion	"…when considering the range of active movements…there was no significant difference between the groups at 8 weeks"						
	Events	**Total**		**Events**	**Total**		**Risk ratio (95% CI)**
Global assessment of treatment success (had no further significant problems over the following year)	14	24		12	19		0.92 (0.57, 1.50)
Total adverse events during 8 week treatment period	Zero events in both groups						

Table 19. One electrotherapy modality versus another (*Continued*)

Study ID: Giombini 2006
Participants: Supraspinatus tendinopathy
Intervention: Therapeutic ultrasound
Control: Microwave diathermy

Outcome	Intervention			Control			Effect estimate
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Rest pain (VAS 0-10, 0 = no pain) at 4 weeks	5.8	0.96	12	2.4	0.46	14	3.40 (2.81, 3.99)
Rest pain (VAS 0-10, 0 = no pain) at 10 weeks	5.15	0.87	12	1.2	0.63	14	3.95 (3.36, 4.54)
Function (Constant-Murley total score, 0-100, higher = better function) at 4 weeks	60	3.21	12	78.1	4.23	14	-18.10 (-20.96, -15.24)
Function (Constant-Murley total score, 0-100, higher = better function) at 10 weeks	61.75	4.18	12	82	5.73	14	-20.25 (-24.07, -16.43)
	Events	**Total**		**Events**	**Total**		**Risk ratio (95% CI)**
Global assessment of treatment success (ready to return to sport) at 4 weeks	6	12		11	14		0.64 (0.34, 1.19)
Global assessment of treatment success (ready to re-	4	12		12	14		0.39 (0.17, 0.89)

Table 19. One electrotherapy modality versus another (*Continued*)

turn to sport) at 10 weeks						
Adverse events	Zero events in both groups					
Study ID: Korkmaz 2010 **Participants: Supraspinatus tendinopathy or partial tears of the supraspinatus tendon** **Intervention: TENS plus exercise** **Control: Pulsed radiofrequency treatment plus exercise**						
Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Rest pain (VAS 0-10, 0 = no pain) at 1 week	2.2	1.3	20	2.4	1.4	20	-0.20 (-1.04, 0.64)
Rest pain (VAS 0-10, 0 = no pain) at 4 weeks	1.8	1.43	20	1.3	0.9	20	0.50 (-0.24, 1.24)
Rest pain (VAS 0-10, 0 = no pain) at 12 weeks	0.95	0.68	20	0.8	0.7	20	0.15 (-0.28, 0.58)
Function (SPADI total score 0-130, higher = worse function) at 1 week	93.9	31.3	20	81.4	21	20	12.50 (-4.02, 29.02)
Function (SPADI total score 0-130, higher = worse function) at 4 weeks	54.7	26.7	20	45.9	14.5	20	8.80 (-4.52, 22.12)
Function (SPADI total score 0-130, higher = worse function) at	32.4	20.5	20	25.5	10.1	20	6.90 (-3.12, 16.92)

Table 19. One electrotherapy modality versus another (*Continued*)

12 weeks							
Pain on motion (VAS 0-10, 0 = no pain) at 1 week	4.8	2	20	5.2	1.8	20	-0.40 (-1.58, 0.78)
Pain on motion (VAS 0-10, 0 = no pain) at 4 weeks	2.7	1.55	20	2.9	1	20	-0.20 (-1.01, 0.61)
Pain on motion (VAS 0-10, 0 = no pain) at 12 weeks	2.1	1.29	20	2.3	0.8	20	-0.20 (-0.87, 0.47)
Night pain (VAS 0-10, 0 = no pain) at 1 week	4.6	1.8	20	4.4	2	20	0.20 (-0.98, 1.38)
Night pain (VAS 0-10, 0 = no pain) at 4 weeks	3	1.41	20	2.7	1.2	20	0.30 (-0.51, 1.11)
Night pain (VAS 0-10, 0 = no pain) at 12 weeks	2.1	0.96	20	1.8	0.9	20	0.30 (-0.28, 0.88)
Active shoulder abduction (degrees) at 1 week	128.3	23	20	138.5	26.9	20	-10.20 (-25.71, 5.31)
Active shoulder abduction (degrees) at 4 weeks	152.8	15.5	20	157.7	18.1	20	-4.90 (-15.34, 5.54)
Active shoulder abduction (degrees) at 12 weeks	161.3	11.8	20	164	13.1	20	-2.70 (-10.43, 5.03)

Table 19. One electrotherapy modality versus another (*Continued*)

Active shoulder flexion (degrees) at 1 week	145	18.4	20	151.2	23.4	20	-6.20 (-19.25, 6.85)
Active shoulder flexion (degrees) at 4 weeks	161	12.9	20	161.7	16.9	20	-0.70 (-10.02, 8.62)
Active shoulder flexion (degrees) at 12 weeks	166.3	9	20	168.5	10.1	20	-2.20 (-8.13, 3.73)
Active shoulder external rotation (degrees) at 1 week	55.8	14.7	20	57.2	19.9	20	-1.40 (-12.24, 9.44)
Active shoulder external rotation (degrees) at 4 weeks	63.5	10	20	66	11.9	20	-2.50 (-9.31, 4.31)
Active shoulder external rotation (degrees) at 12 weeks	69.3	7.8	20	67.7	9.7	20	1.60 (-3.86, 7.06)
Active shoulder internal rotation (degrees) at 1 week	46.5	14.5	20	58	16	20	-11.50 (-20.96, -2.04)
Active shoulder internal rotation (degrees) at 4 weeks	61	12.3	20	68	11.5	20	-7.00 (-14.38, 0.38)
Active shoulder internal rotation (degrees) at 12 weeks	66.5	10.8	20	70	8.7	20	-3.50 (-9.58, 2.58)

Table 19. One electrotherapy modality versus another (*Continued*)

Quality of life (SF-36 physical function 0-100, higher = better) at 12 weeks	74.25	10.03	20	69.5	16.09	20	4.75 (-3.56, 13.06)
Quality of life (SF-36 physical role 0-100, higher = better) at 12 weeks	60	23.5	20	55.35	14.9	20	4.65 (-7.54, 16.84)
Quality of life (SF-36 bodily pain 0-100, higher = better) at 12 weeks	61.25	17.07	20	67.37	14.83	20	-6.12 (-16.03, 3.79)
Quality of life (SF-36 general health 0-100, higher = better) at 12 weeks	56.73	13.95	20	55.85	18.67	20	0.88 (-9.33, 11.09)
Quality of life (SF-36 vitality 0-100, higher = better) at 12 weeks	56.25	12.65	20	55.95	10.02	20	0.30 (-6.77, 7.37)
Quality of life (SF-36 social functioning 0-100, higher = better) at 12 weeks	74.37	16.95	20	81.24	16.09	20	-6.87 (-17.11, 3.37)
Quality of life (SF-36 emotion role 0-100, higher = better) at 12 weeks	54.93	19.54	20	59.15	20.48	20	-4.22 (-16.63, 8.19)

Table 19. One electrotherapy modality versus another (*Continued*)

Quality of life (SF-36 mental health 0-100, higher = better) at 12 weeks	56.2	16.02	20	54.74	16.67	20	1.46 (-8.67, 11.59)
Global assessment of treatment success	"In all weeks, there was no statistically significant difference between the two groups regarding the...physician-patient satisfaction rate (P > 0.05)"						
Total adverse events during 12 week follow-up period	Zero events in both groups						

Study ID: Montes-Molina 2012a
Participants: Rotator cuff tendinitis (53%), bicipital tendinitis (3%), calcific tendinitis (25%), rotator cuff partial tears (16%) , impingement syndrome (5%), frozen shoulder (5%), dislocations (10%), bursitis (5%)
Intervention: Interferential low-level laser therapy (LLLT)
Control: Continuous LLLT

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Rest pain (VAS 0-10, 0 = no pain) change from baseline to 4 weeks	0.3	1.87	86	0.4	5.95	83	-0.10 (-1.44, 1.24)
Function (SPADI total score 0-100; 0 = no disability) change from baseline to 4 weeks	6.8	26.12	86	7.3	11.45	83	-0.50 (-6.54, 5.54)
Night pain (VAS 0-10, 0 = no pain) change from baseline to 4 weeks	1.3	2.80	86	1.4	2.75	83	-0.10 (-0.94, 0.74)

Table 19. One electrotherapy modality versus another (*Continued*)

Total adverse events during 4-week trial period	Zero events in both groups

Study ID: Montes-Molina 2012b
Participants: Rotator cuff tendinitis, calcific tendinitis or partial rotator cuff tears
Intervention: Interferential light therapy generated by two light probes
Control: Conventional light therapy generated by one light probe

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Rest pain (VAS 0-10, 0 = no pain) at 2 weeks	2.1	2.5	13	1.9	2.3	13	0.20 (-1.65, 2.05)
Function (UCLA shoulder scale 1-35, higher score = better function) at 2 weeks	22.3	6.7	13	23.9	6.8	13	-1.60 (-6.79, 3.59)
Night pain (VAS 0-10, 0 = no pain) at 2 weeks	4	3.8	13	5.8	3.7	13	-1.80 (-4.68, 1.08)
Total adverse events during 2 week trial period	Zero events in both groups						

Study ID: Polimeni 2003
Participants: Supraspinatus tendinitis or biceps tendinitis
Intervention: Therapeutic ultrasound plus mobilisation plus exercises
Control: Radar plus mobilisation plus exercises

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)

Table 19. One electrotherapy modality versus another (*Continued*)

Function (Constant-Murley total score 0-100, higher = better function) at 10 days	No usable outcome data. Difference between groups reported as not statistically significant
Function (Constant-Murley total score 0-100, higher = better function) at 40 days	No usable outcome data. Difference between groups reported as not statistically significant

Study ID: Polimeni 2003
Participants: Supraspinatus tendinitis or biceps tendinitis
Intervention: Therapeutic ultrasound plus mobilisation plus exercises
Control: Diadynamic current plus mobilisation plus exercises

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Function (Constant-Murley total score 0-100, higher = better function) at 10 days	No usable outcome data. Difference between groups reported as not statistically significant						
Function (Constant-Murley total score 0-100, higher = better function) at 40 days	No usable outcome data. Difference between groups reported as not statistically significant						

Table 19. One electrotherapy modality versus another (*Continued*)

Study ID: Santamato 2009
Participants: Subacromial impingement syndrome
Intervention: High intensity laser therapy
Control: Therapeutic ultrasound

Outcome	Intervention			Control			Effect estimate
	Mean	SD	n	Mean	SD	n	Mean difference (95% CI)
Overall pain (VAS 0-10, 0 = no pain) at 2 weeks	2.42	1.42	35	4.44	1.37	35	-2.02 (-2.67, -1.37)
Function (Constant-Murley total score 0-100, higher = better function) at 2 weeks	75.91	7.02	35	72.11	6.95	35	3.80 (0.53, 7.07)

Study ID: Shehab 2000
Participants: Supraspinatus tendinitis, subdeltoid bursitis or bicipital tendinitis
Intervention: TENS plus exercise plus cold pack
Control: Therapeutic ultrasound plus exercise plus cold pack

Outcome	Intervention			Control			Effect estimate
	Median	5th to 95th percentile	n	Median	5th to 95th percentile	n	Mean difference (95% CI)
Overall pain (VAS 0-10, 0 = no pain): at 3 to 5 weeks	0	0, 0.65	26	0.5	0, 2.75	24	-0.5 (95% CI not estimable)
Shoulder flexion (degrees, unclear if active or passive) at 3 to 5 weeks	140	120, 160	26	175	115, 180	24	-35 (95% CI not estimable)
Shoulder abduction (degrees, unclear if active	130	116.7, 156.5	26	180	101.2, 180	24	-50 (95% CI not estimable)

Table 19. One electrotherapy modality versus another (*Continued*)

or passive) at 3 to 5 weeks							

Study ID: Yavuz 2014
Participants: Subacromial impingement syndrome
Intervention: Low-level laser therapy plus hot pack plus exercise
Control: Therapeutic ultrasound plus hot pack plus exercise

Outcome	**Intervention**			**Control**			**Effect estimate**
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**
Overal pain (VAS 0-100, 0 = no pain) at 1 month	39	14.29	16	37.43	15.07	15	1.57 (-8.78, 11.92)
Overal pain (VAS 0-100, 0 = no pain) at 3 months	37	14.37	16	38.04	13.67	15	-1.04 (-10.91, 8.83)
Function (SPADI total score 0-100, higher = worse function) at 1 month	32.6	13.72	16	34.25	14.07	15	-1.65 (-11.44, 8.14)
Function (SPADI total score 0-100, higher = worse function) at 3 months	29.8	13.6	16	30.57	14.47	15	-0.77 (-10.67, 9.13)

Study ID: Yildirim 2013
Participants: Subacromial impingement syndrome
Intervention: Therapeutic ultrasound for 4 minutes plus superficial heat plus TENS plus exercise
Control: Therapeutic ultrasound for 8 minutes plus superficial heat plus TENS plus exercise

Outcome	Intervention			Control			Effect estimate
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**Mean difference (95% CI)**

Table 19. One electrotherapy modality versus another (*Continued*)

Overall pain (VAS 0-10, higher = worse pain) at 5 weeks	5.2	1.26	50	3.38	1.46	50	1.82 (1.29, 2.35)
Function (Constant-Murley total score 0-100, higher = better function) at 5 weeks	59.38	15.32	50	66.8	19.43	50	-7.42 (-14.28, -0.56)
Active shoulder abduction (Constant-Murley sub-score, higher = better ROM) at 5 weeks	6.6	1.62	50	7.52	1.54	50	-0.92 (-1.54, -0.30)
Active shoulder flexion (Constant-Murley sub-score, higher = better ROM) at 5 weeks	7.32	2	50	8.22	2.37	50	-0.90 (-1.76, -0.04)
Active shoulder external rotation (Constant-Murley sub-score, higher = better ROM) at 5 weeks	6.2	3.39	50	7.24	2.58	50	-1.04 (-2.22, 0.14)
Active shoulder internal rotation (Constant-Murley sub-score, higher = bet-	5.72	2.27	50	7.04	2.53	50	-1.32 (-2.26, -0.38)

Table 19. One electrotherapy modality versus another (*Continued*)

ter ROM) at 5 weeks							
Strength (Constant-Murley sub-score, higher = better ROM) at 5 weeks	15.5	12.26	50	16.38	11.36	50	-0.88 (-5.51, 3.75)

APPENDICES

Appendix 1. Search strategies

Search strategy for CENTRAL:

- MeSH descriptor: [Shoulder Pain] explode all trees
- MeSH descriptor: [Shoulder Impingement Syndrome] explode all trees
- MeSH descriptor: [Rotator Cuff] explode all trees
- MeSH descriptor: [Bursitis] explode all trees
- ((shoulder* in All Text or rotator* in All Text) and (bursitis in All Text or frozen in All Text or impinge* in All Text or tendonitis in All Text or tendonitis in All Text or tendinopathy in All Text or pain* in All Text))
- "rotator cuff" in All Text
- "adhesive capsulitis" in All Text
- #1 or #2 or #3 or #4 or #5 or #6 or #7
- MeSH descriptor: [Rehabilitation] explode all trees
- MeSH descriptor: [Physical Therapy Modalities] explode all trees
- MeSH descriptor: [Exercise Movement Techniques] explode all trees
- MeSH descriptor: [Ultrasonography, Interventional] explode all trees
- rehabilitat* in All Text or physiotherapy* in All Text or "physical therap*" in All Text or "manual therap*" in All Text or exercis* in All Text
- (ultrasound in All Text or ultrasonograph* in All Text or tns in All Text or tens in All Text or shockwave in All Text or electrotherap* in All Text or mobili* in All Text)
- #9 or #10 or #11 or #12 or #13 or #14
- #8 and #15

Search strategy for Ovid MEDLINE:

- shoulder pain/
- shoulder impingement syndrome/
- rotator cuff/
- exp bursitis/
- ((shoulder$ or rotator cuff) adj5 (bursitis or frozen or impinge$ or tendinitis or tendonitis or tendinopathy or pain$)).mp.
- rotator cuff.mp.
- adhesive capsulitis.mp.
- or/1-7
- exp rehabilitation/

- exp physical therapy techniques/
- exp musculoskeletal manipulations/
- exp exercise movement techniques/
- exp ultrasonography, interventional/
- (rehabilitat$ or physiotherap$ or physical therap$ or manual therap$ or exercis$ or ultrasound or ultrasonograph$ or TNS or TENS or shockwave or electrotherap$ or mobili$).mp.
- or/9-14
- clinical trial.pt
- random$.mp.
- ((single or double) adj (blind$ or mask$)).mp.
- placebo$.mp.
- or/16-19
- 8 and 15 and 20

Search strategy for Ovid EMBASE:

- 'shoulder pain'/exp
- 'shoulder impingement syndrome'/exp
- 'rotator cuff'/exp
- 'bursitis'/exp
- ((shoulder* OR rotator*) AND ('bursitis'/de OR frozen OR impinge* OR 'tendonitis'/de OR 'tendinitis'/de OR 'tendinopathy'/de OR pain*))
- 'rotator cuff'
- 'adhesive capsulitis'
- #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
- 'rehabilitation'/exp
- 'physiotherapy'/exp
- 'kinesiotherapy'/exp
- 'endoscopic echography'/exp
- rehabilitat* OR physiotherapy* OR 'physical therapy' OR 'manual therapy' OR kinesiotherap* OR exercis*
- 'ultrasound'/de OR ultrasonograph* OR 'transcutaneous nerve stimulation' OR 'transcutaneous electrical nerve stimulation' OR shockwave OR electrotherap* OR mobili*
- #9 OR #10 OR #11 OR #12 OR #13 OR #14
- 'randomized controlled trial'/exp
- #8 AND #15 AND #16

Search strategy for CINAHL Plus (EBSCOhost):

- S1 MH "shoulder pain"
- S2 MH "shoulder impingement syndrome"
- S3 MH "rotator cuff"
- S4 MH bursitis+
- S5 TX (shoulder* N5 bursitis) or TX(shoulder* N5 frozen) or TX(shoulder* N5 impinge*) or TX(shoulder* N5 tend?nitis) or TX(shoulder* N5 tendinopathy) or TX(shoulder* N5 pain*)
- S6 TX (rotator cuff N5 bursitis) or TX(rotator cuff N5 frozen) or TX(rotator cuff N5 impinge*) or TX(rotator cuff N5 tend?nitis) or TX(rotator cuff N5 tendinopathy) or TX(rotator cuff N5 pain*)
- S7 TX rotator cuff
- S8 TX adhesive capsulitis
- S9 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8
- S10 MH Rehabilitation+
- S11 MH physical therapy+
- S12 MH Manual Therapy+
- S13 MH Therapeutic Exercise+
- S14 MH Ultrasonography+
- S15 TX rehabilitat* or physiotherapy* or physical therap* or manual therap* or exercise* or ultrasound or ultrasonograph* or TNS or TENS or shockwave or electrotherapy* or mobili*

- S16 S10 or S11 or S12 or S13 or S14 or S15
- S17 PT clinical trial
- S18 TX random*
- S19 TX(single blind*) or TX(single mask*)
- S20 TX(double blind*) or TX(double mask*)
- S21 placebo*
- S22 S17 or S18 or S19 or S20 or S21
- S23 S9 and S16 and S22

WHAT'S NEW

Date	Event	Description
29 May 2016	New search has been performed	The original review, 'Physiotherapy interventions for shoulder pain' (Green 2003) was split into four reviews upon updating: 'Manual therapy and exercise for rotator cuff disease' (ongoing), this review, 'Electrotherapy modalities for rotator cuff disease', 'Manual therapy and exercise for adhesive capsulitis (frozen shoulder)' (Page 2014a), and 'Electrotherapy modalities for adhesive capsulitis (frozen shoulder)' (Page 2014b). The review has also been broadened by including all randomised and quasi-randomised clinical trials regardless of whether outcome assessment was blinded

HISTORY

Date	Event	Description
1 May 2008	Amended	Converted to RM5. CMSG ID C067-R
24 February 2003	Amended	This review is based on the original review of 'Interventions for shoulder pain'. Please see published notes for further details
24 February 2003	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

MJP was responsible for writing the review, performing the searches, selecting trials, performing risk of bias assessment, data extraction, analysing the data and interpreting the results of the updated review. SG was responsible for performing the searches, selecting trials and performing the data extraction and quality assessment for the original review, defining the review comparisons and outcomes of interest of the original and updated review, analysing and interpreting the results, and contributing to writing both the original and updated review. BM was responsible for selecting trials, performing risk of bias assessment, data extraction and contributing to writing the manuscript for the updated review. MM, SS, JD, and NL were responsible for performing risk of bias assessment, data extraction and contributing to writing the manuscript for the updated review. RB was responsible for performing the data extraction and quality assessment for the original review, defining the review comparisons and outcomes of interest of both the original and updated review, analysing and interpreting the results, and contributing to writing both the original and updated review.

DECLARATIONS OF INTEREST

RB is Joint Co-ordinating Editor of Cochrane Musculoskeletal. To avoid bias, RB was excluded from the editorial and publication process for this review. SG is a practicing physiotherapist in part-time private physiotherapy practice (self employed), and as such receives remuneration for the delivery of physiotherapy interventions. BM is a practicing physiotherapist in private physiotherapy practice and as such receives remuneration for the delivery of physiotherapy interventions.

SOURCES OF SUPPORT

Internal sources

- Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia.
- Australasian Cochrane Centre, Australia.

External sources

- Australian National Health and Medical Research Council (NHMRC) Early Career Fellowship (1088535), Australia.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The original review outcomes were pain, range of motion (active and passive), function/disability and quality of life, strength, return to work, participants' perception of overall effect, global preference, physicians' preference and adverse effects. The outcomes reported in this review have been modified from the original review to make them as consistent as possible with other Cochrane reviews on shoulder disorders and other chronic pain conditions. To improve succinctness of the review, we only included one measurement instrument per outcome domain. We assessed study risk of bias using The Cochrane 'Risk of bias' tool in this update of the review (Higgins 2011b). We have included a 'Summary of findings' table.

NOTES

The original review, 'Physiotherapy interventions for shoulder pain' (Green 2003) was split into four reviews upon updating: 'Manual therapy and exercise for rotator cuff disease' (ongoing), this review, 'Electrotherapy modalities for rotator cuff disease', 'Manual therapy and exercise for adhesive capsulitis (frozen shoulder)' (Page 2014a), and 'Electrotherapy modalities for adhesive capsulitis (frozen shoulder)' (Page 2014b). The review has also been broadened by including all randomised and quasi-randomised clinical trials regardless of whether outcome assessment was blinded.

INDEX TERMS

Medical Subject Headings (MeSH)

*Rotator Cuff; Diathermy [methods]; Electric Stimulation Therapy [*methods]; Magnetic Field Therapy [methods]; Muscular Diseases [*therapy]; Randomized Controlled Trials as Topic; Shoulder Pain [*therapy]; Transcutaneous Electric Nerve Stimulation [methods]; Ultrasonic Therapy [methods]

MeSH check words

Adult; Humans; Middle Aged

Musculoskeletal Conditions

OA Arthritis
Open Access

Systematic review

Evidence on the effectiveness of interferential current therapy in the treatment of knee osteoarthritis: A meta-analysis

ML D Buenavente[1*], CB Gonzalez-Suarez[1], MA B Lee-Ledesma[1], LA S Liao[1]

Abstract

Introduction

This study evaluated available evidence regarding the effectiveness of interferential therapy (IFC) on knee osteoarthritis (OA)in providing pain relief and improving physical function such as doing activities of daily living and its efficacy in reducing intake of analgesics, such as Paracetamol.

Methodology

Online database search was done for randomized controlled trials (RCTs) comparing IFC against control or sham IFC in knee OA. Data from studies were pooled and analyzed using the Review Manager Software 5.2.

Results

There was a significant difference between intervention group and control group in decreasing pain in the osteoarthritic knee using the Visual Analog Scale (VAS) and the Western Ontario and McMaster University (WOMAC) Osteoarthritis Index as objective measures, as well as in decreasing intake of paracetamol. However, there was no significant difference between intervention group and control group in improving function in the osteoarthritic knee with reference to the WOMAC subscale for physical function.

Conclusion

IFC is effective in reducing pain and likewise decreasing paracetamol intake in patients with knee OA. It is best to combine IFC with exercise in managing pain, reducing intake of pain medication and improving function in patients with knee OA.

Introduction

Osteoarthritis (OA) is the most common degenerative joint disease.[1,2,3,4,6,7,8,9] It is highly prevalent in the general population and is increasing in frequency with age. Pain, disability, and deterioration in quality of life are the main consequences of the disease. Although the main pathology is in the cartilage and subchondral bone, it is considered as an organ disease since nearly all of the periarticular tissues are involved.[1,3] It can affect any joint in the body but involvement of the spine or weight-bearing joints such as the hip and knee may result in more disabling conditions than in other parts of the body. Although many predisposing factors, such as genetic, metabolic, and mechanic disturbances could attribute to its development, the exact etiopathogenesis of knee OA has yet to be defined. Thus, an absolute cure for OA is not available. A symptomatic approach is widely used along with a variety of treatment options. Treatment goals include management of painful symptoms and improvement of functional capacity. These goals are achieved by combining nonpharmacologic modalities, such as exercise programs, physiotherapy modalities and pharmacologic interventions including Paracetamol, Opioids, and NSAIDs.[2,4,13,14,23]

Therapeutic exercise plays a major role in the management of OA of the knee, with established evidence on improving both pain and function. It has been recognized as the standard of care in the treatment of osteoarthritis and is a strongly recommended non-pharmacologic intervention with a high level of evidence. The Cochrane review on exercise on osteoarthritis in 2008 showed platinum level of evidence that therapeutic, land-based exercise has a benefit in terms of reduction of knee pain and disability. It was also recommended that any type of exercise program that is done regularly and is closely monitored by health professionals can improve pain and physical function related to knee OA in the short term range. This includes individual physiotherapy-led sessions and exercise classes to home-based programs.[14] The American College of Rheumatology (ACR) published guidelines in 2012 on the non-pharmacologic and pharmacologic management of osteoarthritis. They gave a conditional recommendation regarding the use of physical modalities, including electrophysiologic agents such as Transcutaneus Electrical Nerve Stimulation (TENS) and Interferential Current Therapy (IFC), in knee osteoarthritis and the use of acetaminophen/paracetamol, topical and oral NSAIDs, tramadol and intra-articular steroid injection. This is due to absence of high-quality evidence and/or evidence of only a small gradient of difference between desirable and undesirable effects of the treatment based on the consensus of 75% or more of the technical expert panel.[2]

TENS and IFC are forms of electroanalgesia based on the gate control theory of pain perception by Melzack and Wall. Interferential therapy delivers currents to deep tissues through the use of kilohertz-carrier-frequency pulsed or sinusoidal currents to overcome the impedance offered by the skin. It involves application to the skin of two medium frequency currents (in the range of 2000-4000 Hz) in order to produce an amplitude modulated low frequency effect within the tissues. The basic concept behind IFC is that skin impedance (resistance) is inversely proportional to the frequency of an applied current;

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Table 1: Methodological Quality Assessment of the Studies Included Using the Modified CASP.

Modified CASP	Atamaz, 2012	Adedoyin, 2002	Gundog, 2012	Adedoyin, 2005
Did the trial address a clearly focused issue?	Y	Y	Y	Y
Was the assignment of patients to treatments randomized?	Y	N	Y	Y
Were all of the patients who entered the trial properly accounted for at its conclusion?	Y	Y	Y	Y
Were patients, health workers and study personnel 'blind' to treatment?	Y	Y	Y	Y
Were the groups similar at the start of the trial?	Y	Y	Y	Y
Aside from the experimental intervention, were the group treated equally?	Y	Y	Y	Y
Were all clinically important outcomes considered?	Y	Y	Y	Y
TOTAL	7	6	7	7

therefore there is less skin resistance to a frequency of 2000Hz than to a frequency of 200Hz.[5,12] It has been claimed that IFC can be used to treat deeper tissues because lower pulse amplitude is required to overcome the associated skin resistance. The two medium-frequency currents "interfere" within the tissues and produce an amplitude-modulated beat frequency, which is calculated as the difference between the values of the two currents applied. IFCs have been used clinically since the 1950s, and its main clinical indications include pain management, reduction of swelling, and muscle strengthening.[12,13,18, 20,21,22,27]

There is emerging evidence from placebo-controlled trials suggesting that IFC is effective for pain reduction associated with osteoarthritis, degenerative disc disease, or vertebral fractures, however, there are limited data on its effectiveness.[12] Most of the previous studies on the use of electrophysiologic agents have no effect in the relief of pain since it was used as a standalone intervention compared with another physicalintervention or with sham intervention. The study of Johnson and Tabasam in 2003 investigated the analgesic effect of IFC versus TENS and versus sham electrotherapy in experimentally induced ischemic pain. They concluded that IFC reduced pain intensity to a greater extent than sham electrotherapy. However, there was no difference in the magnitude of analgesia when compared with TENS.[27] With regard to the effect of IFC on pressure pain sensitivity, Fuentes et al found out that active interferential was more efficient than placebo in decreasing muscle pain sensitivity and sham interferential therapy was not significantly different from control.[22] Despite the above mentioned studies, there are still a limited number of studies on the use of IFC in knee osteoarthritis. Recent researches have refined their methods where electrophysiologic agents are used in conjunction with standard of care which is therapeutic exercise.

Materials and Methods

Objectives

The primary objective of this meta-analysis is to evaluate the evidence of the effectiveness of interferential current therapy in the treatment of knee osteoarthritis with respect to pain relief and improvement of physical function, such as performing activities of daily living, as an adjunct treatment to exercise which is the standard of care. The secondary objective of this meta-analysis is to determine whether IFC is effective in reducing intake of analgesics, such as Paracetamol.

Study Selection and Inclusion/Exclusion Criteria

The studies considered eligible for inclusion in the review were randomized controlled trials (RCTs) or clinical controlled trials (CCTs) comparing IFC with a placebo or sham intervention in patients with osteoarthritic knee pain in journals published in the English language. Exclusion criteria for this study were: 1) descriptive studies with low level of evidence, 2) studies based on animal data, 3) studies with healthy subjects in experimental setting.

Population

Studies included in the review were restricted to trials with participants meeting the following criteria: 1) male and female subjects over the age of 18, 2) any nationality or race, and 3) subjects with knee pain diagnosed with knee osteoarthritis clinically based on the American College of Rheumatology Diagnostic Criteria or radiographically based on the Kellgren-Lawrence Classification.

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All authors abide by the Association for Medical Ethics (AME) ethical rules of disclosure.

Intervention
Studies with the use of IFC in the experimental group were included. Sham IFCwas used in the placebo or control group.

Outcome Measures
The primary outcome measures of interest were knee pain and physical function. The Visual Analog Score (VAS) was used to measure knee pain and the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) was used to measure knee pain andphysical function.
The secondary outcome measure includes the number of rescue medication (Paracetamol) in grams per week.

Critical Appraisal and Quality Assessment
The studies included were RCTs and a CCT with a high methodological critical appraisal score using the Critical Appraisal Skills Programme (CASP). The CASP scale consists of 11 items that are scored according to the degree to which the specific criteria are met.[16] It was modified to have a total of 7 items answerable by yes or no (why was this modified), and a score of 6 out of 7 (85%) was considered to be a high quality and valid study. The studies were assessed by two independent reviewers. If there were any difference in the score of the two reviewers, it would have been resolved by an adjudication of a third reviewer. Inter rater reliability of the two reviewers was calculated using Cohen's kappa coefficient with a result of 0.85.

Search Strategy
Keywords related to interferential therapy, IFC, and knee osteoarthritis were used, in searching for RCTs, CCTs and other relevant studies regarding the effectiveness of IFC in knee osteoarthritis. These terminologies were extensively searched in databases namely Science Direct, British Medical Journal, New England Journal of Medicine, Scopus, Pro-Quest, Science Direct, EBSCO, Bandolier, PubMed Central, Cochrane Library, eMedicine, MedScape, Sagepub, Archives of Physical Medicine & Rehabilitation and Google Scholar. The reference lists of all the studies gathered relevant to the study were likewise reviewed for possible inclusion of other studies. For this meta-analysis, readily accessible studies from the year 1950 up to September 2013 were retrieved. A copy of any published article that potentially met the inclusion criteria was obtained.

Data collection and extraction
The data collected were extracted using the data extraction tool developed specifically for use in reviewing included studies, based from the Joanna Briggs Data Extraction Tool.[17] The following were recorded from each study: the author, country of origin, year of publication, sample size, subject age and gender, intervention description and control group description, trial design, randomization, blinding, handling of dropouts, inclusion and exclusion criteria, details of treatment, control procedure, primary and secondary outcome measures and main results.

Data synthesis and statistical analysis
Results from comparable studies were pooled in a statistical analysis using the Review Manager software (RevMan 5.2) from the Cochrane Collaboration. The standardized mean differences (SMD), weighted mean differences (WMD), and their 95% confidence intervals (CI) were calculated from available data and the forest plot of comparison was constructed. The statistic I^2 was also used to determine heterogeneity. I^2 measures the extent of inconsistency among the results of the studies, and is interpreted as approximately the proportion of total variation in study estimates that is due to heterogeneity rather than sampling error. If the I^2 was >75%, indicating the presence of heterogeneity, the random effect model was applied. Otherwise, the fixed effect model was used. [15]

RESULTS

This work conforms to the values laid down in the Declaration of Helsinki (1964). The protocol of this study has been approved by the relevant ethical committee related to our institution in which it was performed. All subjects gave full informed consent to participate in this study.

Study Inclusion
An initial database search identified 247 articles using the keywords 1) Interferential therapy, 2) interferential current therapy, 3) IFC, and 4) knee osteoarthritis. Of these articles, five were screened based on the title and abstract review. There were 242 studies excluded after applying the inclusion and exclusion criteria. Reasons for exclusion from the study were: 1) use of IFC on conditions other than knee osteoarthritis, 2) use of other physical interventions other than IFC in knee osteoarthritis, 3) descriptive studies, and 4) animal studies. A full article review of five published articles found eligible after database search and abstract review was done (Figure 1). Of the five published articles, only four were considered relevant and had comparable outcome measures, i.e. knee pain, knee function and paracetamol intake, which were included in the meta-analysis[6,7,8,9]. The remaining article was excluded[10], since it was published in Serbian, with only the abstract having an English translation. All of the studies were considered to be of high methodological value using the modified CASP (Table 1). The included studies had a score of at least 6 out of 7 (85%). The studies included were RCTs and a CCT, comparing a group of participants receiving the standard of care, which is therapeutic exercise, with the intervention, IFC, or with a placebo or sham group that did not receive the intervention. All of the studies specified eligibility criteria and underwent random allocation and concealment, with the subjects having similar baseline characteristics.

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Table 2: Key Characteristics of the Included Studies.

First Author, Year, Location	Method	Participants	Intervention and Control Groups	Number of treatments	Primary Outcome Measure	Secondary Outcome Measures	Results
Atamaz, 2012, Turkey	RCT, double-blind, multicenter trial	N= 66 IFCs: 31 IFCs sham: 35 Drop-outs: 5 Completed: 61	IFC vs IFC sham	5x a week for 3 weeks	Knee pain: VAS (0-100) Evaluation at baseline, 1month, 3 months, & 6 months	Paracetamol use: in grams/week Knee pain & function: WOMAC, NHP Active ROM of B knees Time to walk a distance of 15m Treatment satisfaction: VAS(0-100)	At 1 month **VAS-pain** Mean Difference (95%CI): IFC 24 (17.6-30.4) Sham IFC 19.8 (13.0-26.6) *P*=1.00 **WOMAC-pain** Mean Difference (95%CI): IFC 2.7 (1.8-3.6) Sham IFC 2.7 (1.8-3.7) *P*=1.00 **WOMAC-function** Mean Difference (95%CI): IFC 6.4 (3.8-9.2) Sham IFC 8.3 (4.9-11.7) *P*=1.00 **Paracetamol intake** IFC Mean ±SD 2.8±5.4 *P<0.05* Sham Mean ±SD10.4±14.7 *P<0.05* *Data for paracetamol intake provided by author
Adedoyin, 2002 Nigeria	Controlled Trial, Single blind	N= 30 IFC: 15 Placebo: 15	IFC vs Placebo	8 20-min treatment sessions in 4 weeks	Pain perception: VAS (0-10) Evaluation at baseline and after 4 weeks		Experimental Group: Mean±SD 1.23±1.16 P<0.05 Control Group: Mean±SD 3.13±1.6 P<0.05 * Provided by author
Gundog (2012) Turkey	RCT Single blind study	N= 30 IFC: 15 Sham: 15	IFC vs Sham	5 times a week for 3 weeks	Visual analog scale (0-100) Evaluation at baseline, after treatment and at first month	Western Ontario and McMaster University Osteoarthritis Index (WOMAC) Paracetamol intake (g/wk) 15-m walking time (in minutes) Range of motion (ROM) Physician and patient judgments regarding treatment effectiveness: VAS(0-100)	**VAS-pain** IFC Mean ±SD 17.0±10.7 *P*<0.05 Sham IFC Mean ±SD 58.8±15.4 *P*<0.05 **WOMAC –pain** IFC Mean ±SD 6.7±1.2 *P*<0.05 Sham IFC Mean ±SD 16.1±1.5 *P*<0.05 **WOMAC-function** IFC Mean ±SD 26.2±3.5 *P*<0.05 Sham IFC Mean ±SD 57.8±6.1 *P*<0.05 **Paracetamol intake (g/wk)** IFC Mean ±SD 5.9 ±9.9 *P<0.05* Sham IFC Mean ±SD 15.4 ±5.6 *P<0.05*
Adedoyin (2005) Nigeria	RCT, Single blind	N= 31 IFC: 16 Exercise: 15 Drop-outs: 5 Completed: 46	IFC+Exercise vs Exercise	Twice a week for 4 weeks	VAS (0-10) Evaluation at baseline and after 4 weeks	WOMAC	**VAS** Experimental Group: Mean±SD 1.60±0.91 *P<0.001* Control Group Mean±SD 1.67±0.72 *P<0.001* **WOMAC** Experimental Group: Mean±SD 16.67±4.34 *P<0.001* Control Group Mean±SD 18.67±4.70 *P<0*

Study description and Subjects

All included studies were published from 2002 to 2012. Two studies were done in multiple centers in Turkey while the other two were done in a teaching hospital in Nigeria. A total of 157 patients were included in the studies with similar inclusion criteria, i.e. ages 40-80 years old, meeting the clinical criteria of the American College of Rheumatology for knee osteoarthritis and/or a radiologic evidence (Kellgren-Lawrence grade 2 or 3) of knee osteoarthritis, with knee pain for at least 6 months. Females (73%) were the more predominant gender in all studies. Exclusion criteria were also indicated in the studies, which included participants with previous use of electrical stimulation or with contraindication to electrotherapy, those who underwent intra-articular injection within six months prior to the study or had previous surgery, had ongoing infection, or was pregnant or lactating at the time of study. There were reported drop-outs in two studies. In the study done by Atamaz (2012), there were five drop outs with reasons includingworsening of symptoms or not enough time to attend. In the study of Adedoyin (2005) five were also excluded from the study due to non-completion of treatment. No adverse effects were reported in both studies during the research period. The key characteristics of the included studies are shown in Table 2.

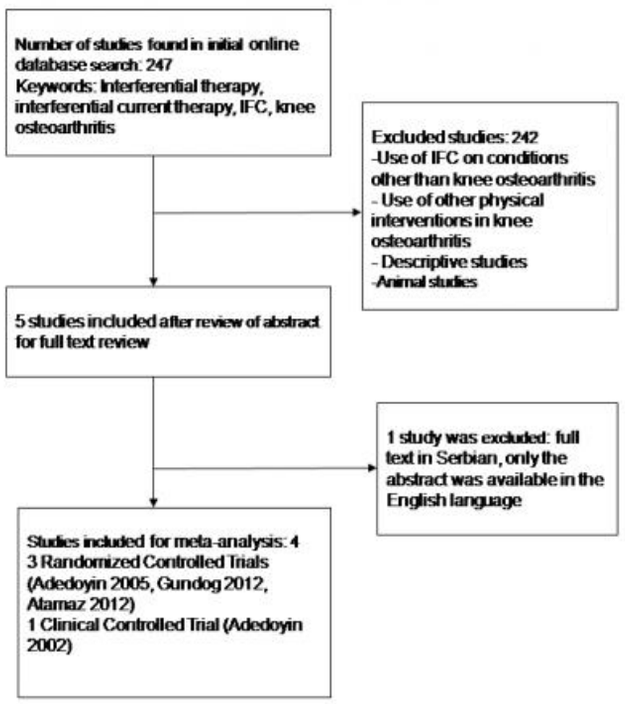

Figure 1: Study Screening Process.

Intervention

All studies were RCTs and a CCT comparing IFC with sham IFC or with a control group.In the studies by Atamaz (2012) and Gundog (2012), IFC was applied using two electrodes at the knee region, with an amplitude modulated frequency setting of 100Hz for 20 minutes by the same physiotherapistwhich was done 5 times a week for three weeks. Atamaz (2012), also used other physical modalities, such as TENS and short wave diathermy (SWD), aside from IFC, and compared its effectiveness in knee osteoarthritis. Only the data from the IFC group was included in the data analysis.In the study of Adedoyin (2002), IFC of the same amplitude modulated frequency was applied using two pairs of electrodes for 15 minutes, and was reduced to 80Hz for 5 minutes, for 8 sessions in 4 weeks, while IFC of 80Hz beat frequency applied using two electrodes for 20 minutes was used twice a week for a total of 8 sessions in the study he did in 2005. All studies used IFC with two 8cmx6cm electrodes applied at the knee region.

The program for the control or sham group and intervention group in the studies of Adedoyin (2002), Adedoyin (2005), and Atamaz (2012) included an exercise program which were either jogging, riding a bicycle ergometer, performing stretching exercises and isometric exercises of the quadriceps. However, in the study by Gundog (2012), only sham IFC was used and no exercise program was given. In all of the studies, evaluation of the participants were done at baseline and after one month of treatment. Only the study of Atamaz included evaluation after three months and after six months of treatment. In this regard, the researchers were not able to include the assessment of the long term effect of IFC, since only the article of Atamaz evaluated its chronic effect on knee pain.

Outcome Measures

The following outcome measures were evaluated in all studies: VAS and WOMAC Osteoarthritis Index. The studies of Atamaz (2012) and Gundog (2012) included intake of paracetamol in grams per week as an outcome measure.

Other outcome measures in the studies of Atamaz (2012) and Gundog (2012) were 15-m walking time in minutes, range of motion (ROM) of the knee. Physician and patient judgments regarding treatment effectiveness were also used as outcome measures in the study by Gundog (2012) while treatment satisfaction and Nottingham Health Profile (NHP) were also used in the study of Atamaz (2012).

Meta-analysis

The mean and standard deviation were available in tabulated form in the studiesof Gundog and Atamaz. However, Adedoyin presented the data in both the 2002 and 2005 studies in graphical form. The paracetamol intake was also presented in graphical form in the study of Atamaz. The raw data, including the mean and standard deviation, were requested by the researchers and were provided for by the authors of the studies. The data were pooled and analyzed using the RevMan 5.2 software.

The Visual Analog Scale

The VAS evaluated the severity of knee pain prior to and one month after treatment with the intervention. There

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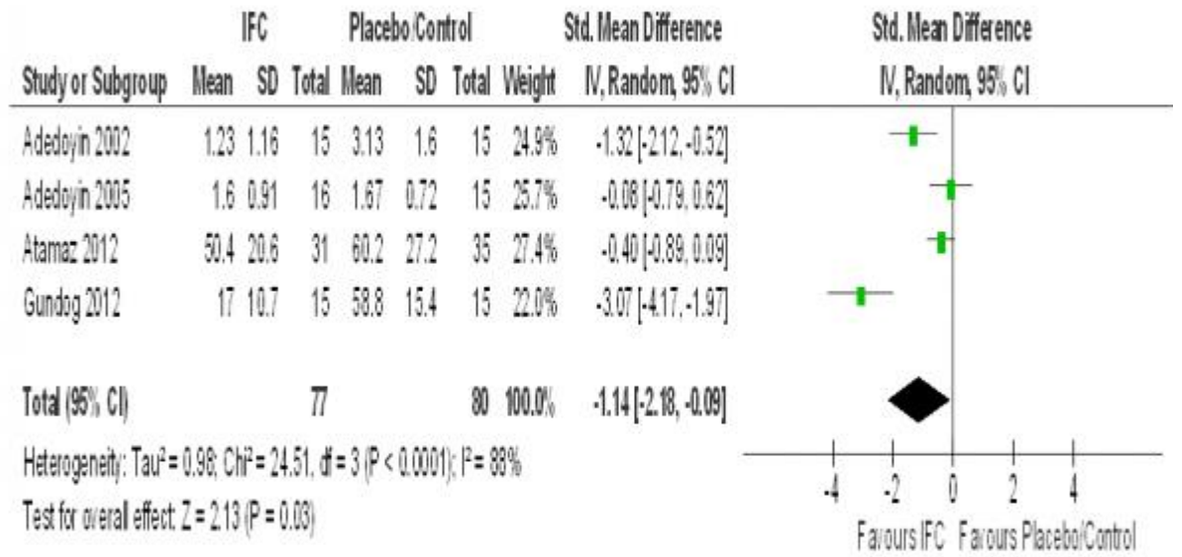

Figure 2: Forest plot of comparison: 1 Interferential Therapy vs Placebo/Control, Outcome: 1.1 Knee Pain –VAS.

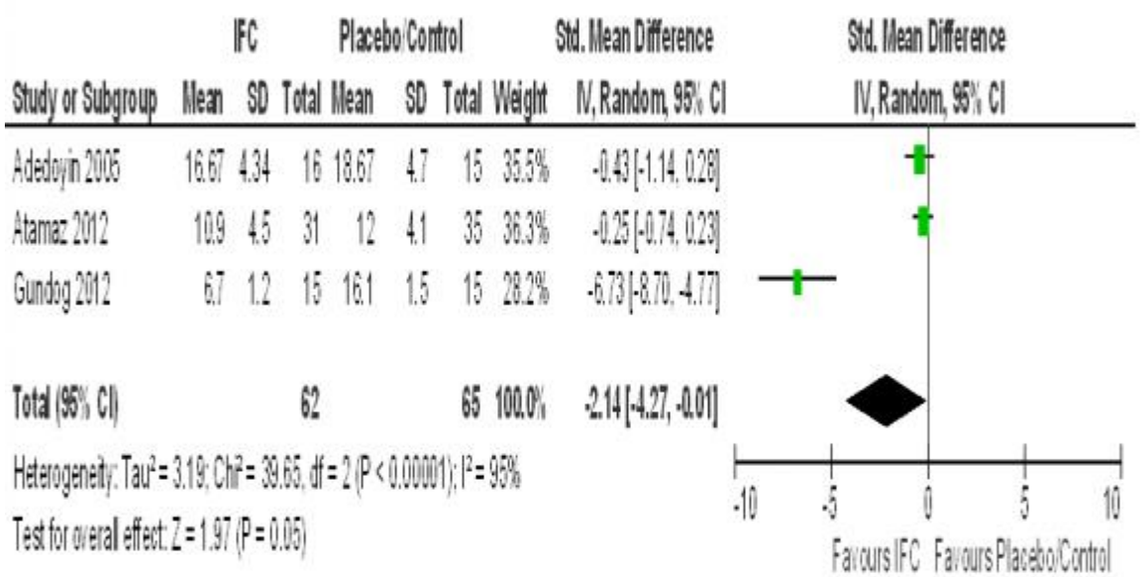

Figure 3: Forest plot of comparison: 1 Interferential Therapy vs Placebo/Control, Outcome: 1.1 Knee Pain –WOMAC.

was a significant difference between intervention group and control group in decreasing pain in the osteoarthritic knee with a standard mean difference of -1.14 (95% CI: -2.18, -0.09) with a p value of 0.03 (Figure 2).

The WOMAC subscale for Pain

The WOMAC subscale for pain also evaluated the severity of knee pain prior to and after one month of treatment with the intervention. There was also a significant difference between intervention group and control group in decreasing pain in the osteoarthritic knee with a standard mean difference of -2.14 (95% CI: -4.27, -0.01) with a p value of 0.05 (Figure 3).

The WOMAC subscale for Physical Function

The WOMAC subscale for function evaluated the physical functional disability of participants with knee osteoarthritis at baseline and at one month after intervention. There was no significant difference between intervention group and control group in improving function in the osteoarthritic knee with a weighted mean

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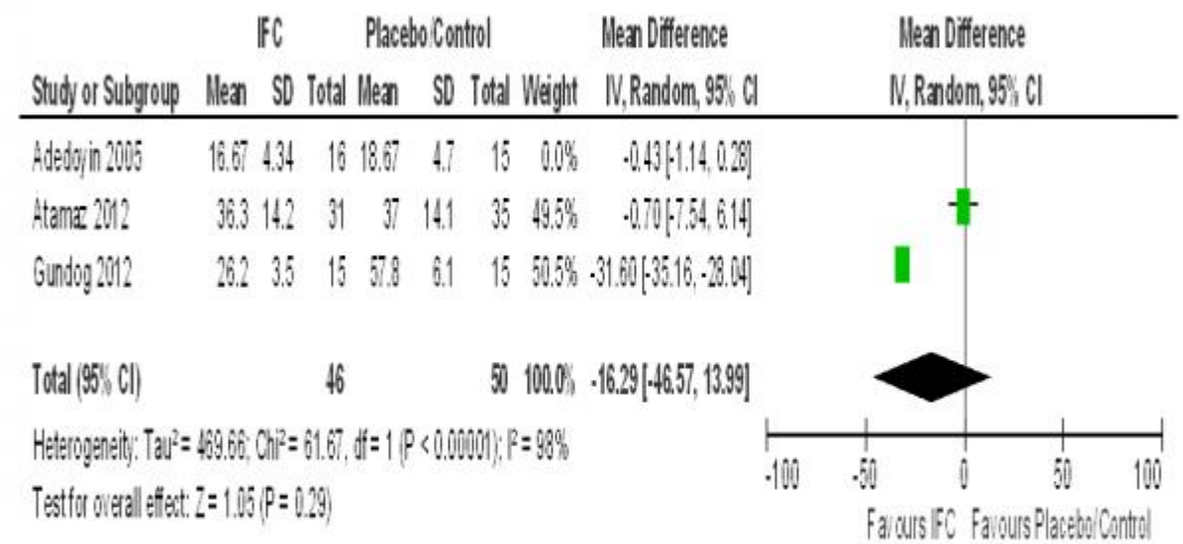

Figure 4: Forest plot of comparison: 1 Interferential Therapy vs Placebo/Control, Outcome: 1.3 Physical Function - WOMAC.

difference of -16.29 (95% CI: -46.57, 13.99) with a p value of 0.29 (Figure 4).

Paracetamol Intake

Intake of paracetamol in grams per week was monitored in both studies of Atamaz 2012 and Gundog 2012. There was a significant difference between intervention group and control group in decreasing the amount of paracetamol intake in the IFC groups with a weighted mean difference of -9.12 (95% CI: -12.66, -5.99) with a p value of 0.00001 (Figure 5).

Discussion

The results of the meta-analysis revealed that the use of IFC can decrease pain in patients with knee osteoarthritis after 4weeks of treatment. Theuse of IFC also led to a decrease in paracetamol intake when compared to sham IFC. Thus it can be recommended that the use of physical therapy agents in knee OA provided additional benefit in alleviating pain. In terms of physical function, IFC showed improvement of the WOMAC scores over a 4-week treatment in the studies of Atamaz (2012) and Gundog (2012). However, upon pooling of data and meta-analysis, it did not show any significant difference with placebo.

A systematic review of the physical interventions used in the treatment of knee osteoarthritis done by Bjordal et al done in 2007 concluded that for patients with X-ray grade 2–4 and pain intensity levels above 50 mm on VAS, an intensive regimen of 2–4 weeks with TENS, electro-acupuncture and low level laser therapy seems to safely induce statistically significant and clinically relevant short-term pain relief. However, only 2 studies using IFC were included in the meta-analysis and were analyzed along with studies using TENS.[19]Aside from knee osteoarthritis, IFC has been used to decrease pain in other musculoskeletal conditions. In a meta-analysis done by Fuentes, et. Al, they concluded that IFC included in a multimodal treatment plan produced a pain relieving effect in acute and chronic painfulmusculoskeletal conditions, such as back pain, knee pain and shoulder pain, compared with no treatment or placebo. They found out that combined with other interventions, IFC was shown to be more effective than placebo.[20]

Currently, use of electrophysiologic agents, including IFC, is only given a conditional recommendation by the ACR since the included studies compared IFC to other modalities and exercise, not as an adjunct to the standard of care. Also, the Cochrane reviews on the use of electrotherapy on chronic low back pain (2008) and neck pain (2013) were inconclusive because of the conflicting evidence and the quality of the included trials were poorly conducted studies, thus further research was recommended. [24,25]In the authors' setting, guidelines published by the Philippine Academy of Rehabilitation Medicine on low back pain recommended the use of interferential therapy.[26]

This is the first meta-analysis, to the authors' knowledge, on the use of IFC as a co-intervention with exercise, specifically on the treatment of osteoarthritic knee pain, which showed its effectiveness in the pain alleviation and reduction on pain medication intake. This meta-analysis showed that IFC, in conjunction with exercise, is effective in decreasing pain and in taking of rescue medications in patients with knee osteoarthritis. This study concurred with the result of the meta-analysis of Fuentes in 2010 where the efficacy of IFC on musculoskeletal pain showed that when included in a multimodal treatment, IFC has a pain relieving effect compared with a control condition and with the meta-analysis of Bjordal in 2007, where different

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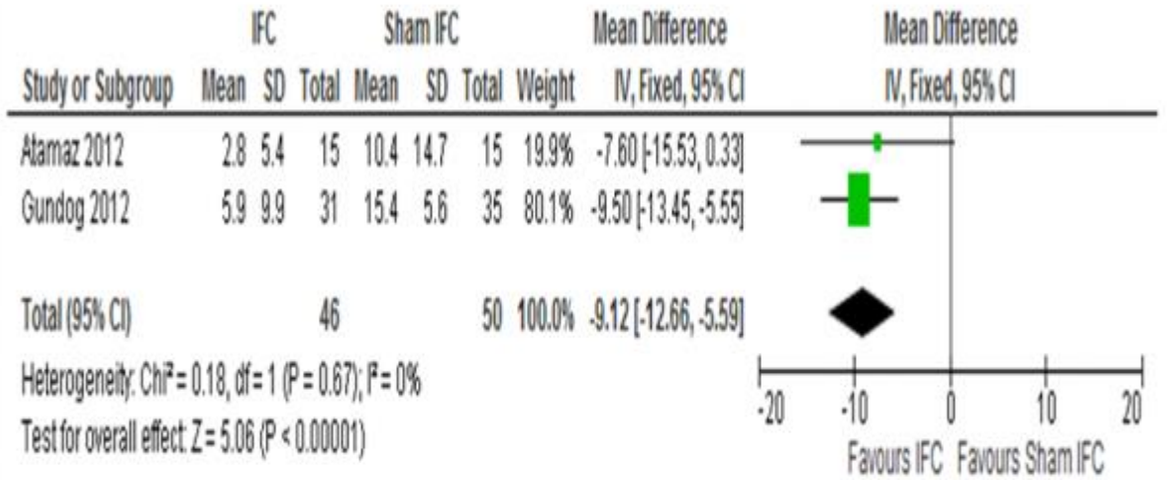

Figure 5: Forest plot of comparison: 1 Interferential Therapy vs Placebo/Control, Outcome: 1.4 Paracetamol Intake.

physical modalities which included IFC used for treatment of osteoarthric knee pain showed clinically relevant short-term pain relief.[19,20] Exercise therapy, education and weight loss still remain to be the cornerstones of long-term management of knee osteoarthritis, but there is evidence that IFC is a useful co-intervention in pain management. The results of this meta-analysis will help the field of Physical Medicine and Rehabilitation in establishing the effectiveness of modalities being used in musculoskeletal pain. There is scientific soundness in using electrophysiologic agents as one of the treatment armamentarium. With the results of this meta-analysis, there is evidence in the effectiveness in decreasing pain in OA when multimodal treatment approach is utilized.

Conclusion

IFC, in conjunction with standard of care, which is therapeutic exercise,is effective in reducing pain and decreasing paracetamol intake in patients with knee osteoarthritis after a month of treatment. The therapeutic regimen of IFC with beat frequency of 80-100Hz for 20 minutes for two to five times a week can also be recommended. It is best to combine physical agents, such as IFC, with exercise in managing pain and improving function in patients with knee osteoarthritis. More studies with a larger sample size, longer treatment and follow up periods may be beneficial for future randomized controlled studies on the effect of IFC on knee pain and function in patients with osteoarthritis.

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Effectiveness of Interferential Current Therapy in the Management of Musculoskeletal Pain: A Systematic Review and Meta-Analysis

Jorge P. Fuentes, Susan Armijo Olivo, David J. Magee, Douglas P. Gross

Background. Interferential current (IFC) is a common electrotherapeutic modality used to treat pain. Although IFC is widely used, the available information regarding its clinical efficacy is debatable.

Purpose. The aim of this systematic review and meta-analysis was to analyze the available information regarding the efficacy of IFC in the management of musculoskeletal pain.

Data Sources. Randomized controlled trials were obtained through a computerized search of bibliographic databases (ie, CINAHL, Cochrane Library, EMBASE, MEDLINE, PEDro, Scopus, and Web of Science) from 1950 to February 8, 2010.

Data Extraction. Two independent reviewers screened the abstracts found in the databases. Methodological quality was assessed using a compilation of items included in different scales related to rehabilitation research. The mean difference, with 95% confidence interval, was used to quantify the pooled effect. A chi-square test for heterogeneity was performed.

Data Synthesis. A total of 2,235 articles were found. Twenty studies fulfilled the inclusion criteria. Seven articles assessed the use of IFC on joint pain; 9 articles evaluated the use of IFC on muscle pain; 3 articles evaluated its use on soft tissue shoulder pain; and 1 article examined its use on postoperative pain. Three of the 20 studies were considered to be of high methodological quality, 14 studies were considered to be of moderate methodological quality, and 3 studies were considered to be of poor methodological quality. Fourteen studies were included in the meta-analysis.

Conclusion. Interferential current as a supplement to another intervention seems to be more effective for reducing pain than a control treatment at discharge and more effective than a placebo treatment at the 3-month follow-up. However, it is unknown whether the analgesic effect of IFC is superior to that of the concomitant interventions. Interferential current alone was not significantly better than placebo or other therapy at discharge or follow-up. Results must be considered with caution due to the low number of studies that used IFC alone. In addition, the heterogeneity across studies and methodological limitations prevent conclusive statements regarding analgesic efficacy.

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Successful management of musculoskeletal pain is a major challenge in clinical practice. One of the electrotherapeutic techniques used for managing musculoskeletal pain is interferential current therapy (IFC). The results of questionnaire surveys in England,[1] Canada,[2] and Australia[3,4] have shown that IFC is widely used by diverse clinicians throughout the world.

Interferential current therapy is the application of alternating medium-frequency current (4,000 Hz) amplitude modulated at low frequency (0–250 Hz).[5–7] A claimed advantage of IFC over low-frequency currents is its capacity to diminish the impedance offered by the skin.[6] Another advantage speculated for IFC is its ability to generate an amplitude-modulated frequency (AMF) parameter, which is a low-frequency current generated deep within the treatment area.[6,8–10] Several theoretical physiological mechanisms such as the "gate control" theory,[11] increased circulation, descending pain suppression, block of nerve conduction, and placebo have been proposed in the literature to support the analgesic effects of IFC.[5,8,12]

Despite IFC's widespread use, information about it is limited. A review of the literature reveals incomplete and controversial documentation regarding the scientific support of IFC in the management of musculoskeletal pain. For example, a systematic review about the use of electrotherapy for neck disorders[13] excluded the analysis of IFC. Moreover, much of the IFC information is not written in English,[10,14–22] and most articles appear to be based on case reports,[23–25] clinical studies not including a randomization process,[26,27] letters to the editor,[28,29] clinical notes,[30] experimental settings,[31–37] descriptive studies,[8,12,38,39] or experience in the field[40,41] instead of methodologically qualified studies.

Thus, the objective of this systematic review and meta-analysis was to determine the analgesic effectiveness of IFC compared with control, placebo, or other treatment modalities for decreasing pain in patients with painful musculoskeletal conditions.

Method

Search Strategy

Relevant studies of IFC in musculoskeletal pain management from 1950 to February 8, 2010, were obtained through an extensive computerized search of the following bibliographic databases: MEDLINE (1950 through week 4 of 2010), EMBASE (1988 through week 5 of 2010), CINAHL (1970 through February 8, 2010), Scopus (1970 through February 8, 2010), Cochrane Library (1991 through the first quarter of 2010), ISI Web of Science (1970 through February 8, 2010), and PEDro (Physiotherapy Evidence Database) (1970 through February 8, 2010). The key words "interferential," "interferential therapy," "interferential current," "musculoskeletal pain," "electrotherapy," "electroanalgesia," "muscle pain," "low back pain," "shoulder pain," "hip pain," "knee pain," "neck pain," "osteoarthritis pain," and "joint pain" were used in the search, including combinations of these words. For details regarding the search terms and combinations, see eAppendix 1 (available at ptjournal.apta.org). The literature search procedure was complemented by manually searching the bibliographies of the identified articles for key authors and journals.

Study Selection and Inclusion/Exclusion Criteria

Studies that met the following criteria were considered for inclusion: (1) randomized controlled trials (RCTs) from journal publications in the English language (because the clinical application of IFC often is based on its coadjutant effect, studies in which IFC was used as a cointervention also were included); (2) studies of male and female humans between 18 and 80 years of age; (3) studies of subjects clinically diagnosed with a painful musculoskeletal condition, such as muscle (eg, low back pain, neck pain), soft tissue (eg, tendinosis/tendinitis), or joint (eg, osteoarthritis) disorders; (4) regarding the type of interventions, all randomized comparisons of isolated or coadjutant IFC applications versus placebo, control, another physical therapy intervention, or another type of intervention; and (5) studies in which the outcome of interest was pain, as measured by the use of a visual analog scale (VAS) or numeric pain rating scale (NRS). Exclusion criteria for this study were: (1) studies based on animal data, (2) studies published in languages other than English, and (3) studies including subjects who were healthy in experimental settings.

Data Extraction and Quality Assessment

Two independent reviewers screened the abstracts of the publications found in the databases. The reviewers analyzed all articles initially selected by the abstract or title for the inclusion and exclusion criteria. Each criterion was graded on a yes/no basis. In case of discrepancies between reviewers regarding whether a particular article met a criterion, the ratings were compared and the

criterion forms were discussed until a consensus was reached.

A critical appraisal was conducted to determine the methodological quality of the final selected studies. We used 7 scales (ie, Delphi List, PEDro, Maastricht, Maastricht-Amsterdam List, Bizzini, van Tulder, and Jadad) commonly used in the physical therapy field to evaluate the methodological quality of the included studies, compiled in a set of 39 items.[42] These items were grouped into 5 categories: patient selection, blinding, intervention, outcomes, and statistics. Based on a recent systematic review,[42] no one scale effectively determines the overall methodological quality of individual studies. For this reason, we used all of them in a compiled fashion.

The articles were evaluated on the basis of only the information available in the articles using the critical appraisal sheet (eAppendix 2; available at ptjournal.apta.org). For each item listed on the critical appraisal sheet, a score of 1 was given when the item was included in the article, and a score of 0 was given when the item was not included or the information provided by the authors was not sufficient to make a clear statement. In cases where the study did not consider a particular item, the item was marked as not applicable on the critical appraisal sheet. The scoring for each study was calculated by dividing the number of items included by the number of applicable items. Finally, each study was graded as having low, moderate, or high methodological quality based on how many items from the critical appraisal were met. The cutoff was determined as follows: 0–0.40=low methodological quality, 0.41–0.70=moderate methodological quality, and 0.71–1.00=high methodological quality. This criterion was determined *a priori* to the quality assessment. Similar criteria for cutoffs have been used in correlational studies to determine reference values for quality of association or agreement.[43,44]

The critical appraisal was independently completed by the 2 reviewers, and the results were compared. At this stage, the intraclass correlation coefficient (ICC) was calculated using SPSS version 17 software* in order to determine the agreement between the reviewers for article grading. Any discrepancies were settled through discussion.

Data Synthesis and Analysis

Studies investigating similar outcomes and interventions and those providing clear quantitative data were grouped, evaluated for heterogeneity, and pooled, if possible. When combining outcome data was not possible, narrative, descriptive, and qualitative summaries were completed. In the present study, a meta-analysis was performed to quantify the pooled effect of IFC alone or as an adjunct treatment on pain intensity when compared with placebo, control group, or comparison intervention. Because the pooled effect was based on the results of the VAS or NRS, the mean difference was used to quantify the pooled effect. RevMan 5.0 software† was used to summarize the effects (ie, pooled mean differences) and construct the

* SPSS Inc, 233 S Wacker Dr, Chicago, IL 60606.

† Copenhagen, Denmark: The Nordic Cochrane Centre, The Cochrane Collaboration, 2008.

The Bottom Line

What do we already know about this topic?

Despite the widespread use of interferential current (IFC), information about its clinical effectiveness is limited and controversial. The pain-reducing effect of IFC, when applied alone or as part of a multimodal treatment plan to treat musculoskeletal pain, has not been determined.

What new information does this study offer?

The application of IFC as part of a multimodal treatment plan appears to produce a modest pain-relieving effect in a broad spectrum of acute and chronic musculoskeletal conditions when compared with no treatment or placebo. In addition, the potential long-term effects of IFC versus placebo observed at 3-month follow-up are of interest.

Interferential current alone was not significantly better than placebo and other interventions (ie, manual therapy, traction, or massage). However, heterogeneity across the included studies, along with methodological limitations identified in these studies, prevents conclusive statements regarding the analgesic efficacy of IFC.

If you're a patient, what might these findings mean for you?

If you are seeking pain treatment, IFC could be potentially effective in reducing musculoskeletal pain; however, its application should be included as part of a multimodal treatment plan.

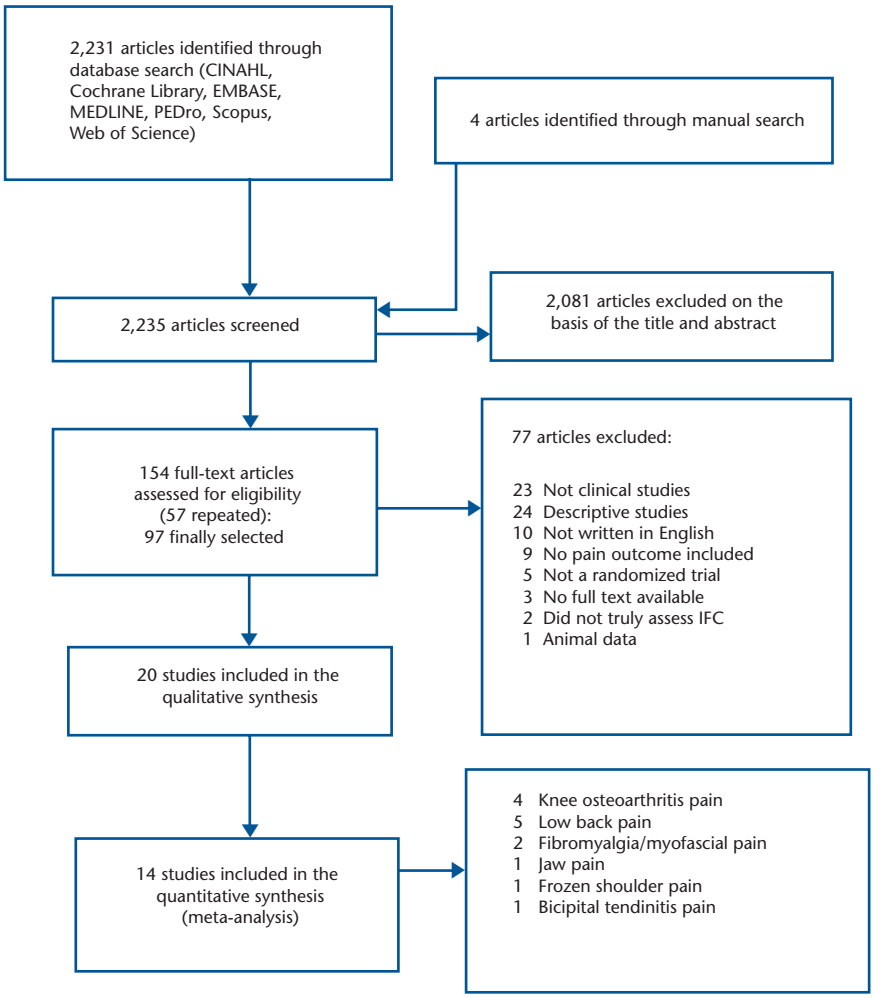

Figure 1.
Study screening process. IFC=interferential current therapy.

forest plots for all comparisons. For this analysis, the 95% confidence interval (CI) was used. A chi-square test for heterogeneity was performed ($P<.10$).[45] In the presence of clinical heterogeneity in the study population or intervention, the DerSimonian and Laird random-effects model of pooling was used based on the assumption of the presence of interstudy variability to provide a more conservative estimate of the true effect.[45,46] If there was relative homogeneity, a fixed-effects model was used to pool data.[45]

Results

A total of 2,235 articles were found in the database search. Of these, 154 were selected as potential studies of interest based on abstract review (Fig. 1). After full article review, only 20 studies were deemed to fulfill the initial selection criteria.[47–66] The kappa agreement between the reviewers in selecting articles after applying the inclusion and exclusion criteria was perfect at $\kappa=1.0$.

Seventy-seven studies were rejected after applying the inclusion and exclusion criteria. The primary reasons for exclusion from the study were: (1) the use of subjects who were healthy in an experimental setting[31–37,67–82]; (2) descriptive studies in the form of case reports, dissertations, or clinical notes,[8,12,23–25,30,38–41,69,83–96]; (3) studies not published in the English language[10,14–22]; (4) the absence of pain outcomes[97–105]; (5) randomized trial not used[26,27,106–108]; (6) use of a current other than IFC[109,110]; (7) use of animal data[111]; and (8) unavailability of the full text of the article.[112–114] At the end of the critical appraisal stage, there was an agreement of $\kappa=.83$ between the 2 raters. This ICC value is considered as "excellent" agreement according to the approach described by McDowell.[115]

Characteristics of the Studies

All 20 studies reviewed in detail were RCTs that examined the pain-reducing effectiveness of IFC. These studies analyzed the effects of IFC for several diagnoses considered to be either acute or chronic painful conditions. Only 6 articles (30%)[48,54,56,57,61,63] examined the clinical analgesic effectiveness of IFC as a single therapeutic modality. The rest of the articles included the application of IFC as a cointervention along with other therapeutic alternatives such as exercise,[47,49,53,58–60,62,64–66] shortwave diathermy,[51,59] hot packs,[55,60] ice,[58] myofascial release,[55] neuromuscular electrical stimulation,[52] infrared radiation,[51] and ultrasound.[50,60,62] Details of the studies' characteristics are shown in Table 1.

Methodological Quality of the Studies

The results of the critical appraisal for the selected studies are presented in Table 2. Three of the 20 studies were considered to be of high methodological quality, 14 studies were considered to be of moderate quality, and 3 studies were considered to be of poor quality. Even though the quality of most of the studies was rated as acceptable (17 studies were rated as being of moderate or high quality), there are some points regarding quality that need to be highlighted. Study flaws regarding patient selection were mainly related to description and appropriateness

Table 1.
Characteristics of the Studies[a]

Study	Country	Condition	Sample	Study Arms	Outcomes	Cointerventions	Follow-up	Treatment	Results	Strengths/Weaknesses
Quirk et al,[59] 1985	England	Knee OA	38	1. Active IFC + exercises 2. Active SWD + exercises 3. Exercises	ROM, pain (VAS), exercise endurance, maximum knee girth	Exercises	3 and 6 mo	• 12 patients in the IFC + exercise group, 12 patients in the SWD + exercise group, and 14 patients in the exercise group • Frequency of 0–100 Hz for 10 min and 130 Hz for 5 min, 3 times a week for 4 wk	• Significant improvement in groups 1, 2 and 3 ($P<.02$, $P<.05$, $P<.03$, respectively) • No significant difference among groups	• Randomized • Confounders not controlled • Reliability and validity of outcomes not reported • Small sample size • No control/placebo group included • Poor description of intervention
Adedoyin et al,[47] 2002	Nigeria	Knee OA	30	1. Active IFC 2. Placebo IFC	Pain (VAS)	Exercises	None	• 15 patients in IFC group and 15 patients in the placebo group • IFC: 4 electrodes (2 placed lateromedially and 2 placed anteroposteriorly), frequency of 100 Hz for the first 15 min and 80 Hz for the next 5 min, intensity (appreciable sensation) • Both groups had treatments and mobilization exercise twice a week for 4 wk	• Significant difference between initial and final pain rating in both groups ($P<.01$) • Significance difference between 2 groups after treatment ($P<.01$). Pain rating was found to be significantly better in the active IFC group than in the placebo group.	• Randomized • Clinicians blinded • Good control of confounders • Good description of intervention • Small sample size • Validity of outcomes not reported
Adedoyin et al,[49] 2005	Nigeria	Knee OA	51, 5 were excluded from the analysis	1. IFC + exercise 2. TENS + exercise 3. Exercise alone	Functional disability (WOMAC), pain (10-point pain rating scale)	Exercises	None	• 15 patients in the TENS + exercise group, 16 patients in the IFC + exercise group, and 15 patients in the exercise only group • IFC: 2 electrodes (either side of the knee longitudinally), frequency of 80 Hz continuous, intensity (strong tingling sensation), 20-min session, 2 sessions a week for 4 wk	• Significant time effect in WOMAC and pain scores ($P<.001$) • No significant difference between groups in WOMAC and pain scores ($P=.241$, $P=.813$) • All treatment protocols led to significant reductions in pain and improvement in function	• Randomized • Clinicians blinded • Sample size calculated *a priori* and adequate • Good description of intervention • Confounders not controlled • No control/placebo group included • Reliability of outcomes not reported
Defrin et al,[54] 2005	Israel	Knee OA	62	1. Active IFC noxious stimulus unadjusted 2. Active IFC noxious stimulus adjusted 3. Active IFC innocuous stimulus unadjusted 4. Active IFC innocuous stimulus adjusted 5. Placebo IFC 6. Control	Pain intensity (VAS), pain relief (0–100%), morning stiffness (10-cm line scale), active ROM (goniometer), electrically induced pain threshold (interferential current equipment)	None	None	• 11 patients in group 1, 11 patients in group 2, 12 patients in group 3, 11 patients in group 4, 9 patients in the placebo group, 8 patients in the control group • 2 electrodes (medial and lateral aspects of the knee); carrier current of 4,000 Hz, frequency between 30 and 60 Hz, intensity 30% above (noxious) or 30% below (innocuous) pain threshold, raise intensity (maintain sensation) for adjusted groups, 12 sessions every other day for 4 wk	• Significant improvement in groups 1 to 4 compared with the control group ($P<.001$) • Significantly larger decrease in noxious groups (1 and 2) for pain intensity ($P<.05$) and pain thresholds ($P<.01$) when compared with innocuous groups (3 and 4) • No significant difference between adjusted and unadjusted groups ($P=.47$)	• Randomized • Good description of intervention • Small sample size • Confounders not controlled • Reliability and validity of outcomes not reported • Control and placebo groups included

(Continued)

Table 1.
Continued

Study	Country	Condition	Sample	Study Arms	Outcomes	Cointerventions	Follow-up	Treatment	Results	Strengths/Weaknesses
Atamaz et al,[51] 2006	Turkey	Knee OA	85, 2 dropped out at discharge	1. Active IFC + IR + SWD 2. Intra-articular hyaluronan	Movement (ROM), pain (VAS), and function (SF-36, WOMAC, 15 min walking time)	IR and SWD	1, 3, 6, 9, and 12 mo	• 40 patients in the hyaluronan group (20 NaHA, 20 hylan) and 42 patients in the physical therapy group • Treatment applied 5 times a week for 3 wk with a series of IR, SWD, and interferential therapy	• Significant improvement in WOMAC, SF-36, and pain scores in both groups ($P<.05$) • Significant difference for pain at rest, pain on touch, and SF-36 in favor of physical therapy group at 1, 3, and 6 mo ($P<.05$) • Significant difference in WOMAC scores in favor of hyaluronan group ($P<.05$)	• Randomized • Clinicians blinded • Small sample size • No description of physical therapy interventions • Confounders not controlled • Reliability and validity of outcomes not reported • No control/placebo group included
Burch et al,[52] 2008	United States	Knee OA	116, 15 dropped out at discharge	1. IFC + NMES 2. Low-current intensity TENS	Pain and knee function (WOMAC), pain intensity (VAS), quality of life (VAS)	NMES	None	• 57 patients in the IFC + NMES group, 59 patients in the low-current TENS group • 15 min of true IFC (5 KHz with a beat sweep frequency of 1–150 Hz) followed by 20 min of NMES • 5 times a week for 8 wk	• IFC + NMES group reduced pain and increased function compared with low-current intensity TENS • The IFC + NMES group group had a significantly greater decrease in overall pain VAS ($P=.038$)	• Multicenter RCT • Clinicians blinded • Adherence tested • Sample size calculated *a priori* and appropriate • No true control/placebo group included • Confounders well controlled • Adverse effects reported • Reliability of outcomes not reported
Werners et al,[63] 1999	Germany	Chronic LBP	152, 20 were lost at 3-month follow-up	1. Active IFC 2. Lumbar traction + massage	Disability (Oswestry Disability Index), pain (VAS)	None	3 mo	• 74 patients in the IFC group and 73 patients in the traction group • 2 electrodes (placed paravertebrally in pain area), frequency of 30–60 Hz, six 10-min sessions over 14–21 d	• Significant improvement in both groups ($P<.05$) • No significant difference between groups	• Randomized • Sample size calculated *a priori* and appropriate • Confounders not controlled • Reliability and validity of outcomes not reported • No control/placebo group included
Hurley et al,[57] 2001	Northern Ireland	Acute LBP	60, 12 dropped out at 3-mo follow-up	1. Active IFC painful area + The Back Book 2. Active IFC spinal nerve + The Back Book 3. Control (The Back Book)	Pain (PRI), disability (RMDQ), generic health status (EQ-5D)	None	3 mo	• 18 patients in the painful area group, 22 patients in the spinal nerve group, and 20 patients in the control group • 2 electrodes, carrier frequency of 3,850 Hz, frequency of 140 Hz, 30 min • 2–3 treatment sessions weekly until discharge	• Significant improvement in pain severity, disability and health status for all groups at discharge ($P<.05$) and at follow-up ($P<.01$) • Significantly greater RMDQ score in spinal nerve group ($P=.042$)	• Randomized • Good description of treatment • Small sample size • Confounders not controlled • Clinical significance reported • Reliability and validity of outcomes not reported
Hurley et al,[56] 2004	Northern Ireland	Acute LBP	240, 82 lost at 12-mo follow-up	1. Active IFC 2. Manipulative therapy 3. IFC + manipulative therapy	Functional disability (RMDQ), pain (VAS, MPQ), quality of life (EQ-5D, SF-36), LBP (recurrence, work absenteeism, analgesic consumption, additional health care)	None	6 and 12 mo	• 52 patients in the MT group, 55 patients in the IFC group, and 51 patients in the MT + IFC group • 2 electrodes on spinal nerve root placement, carrier frequency of 3,850 Hz, frequency of 140 Hz, 30 min • 4 to 10 sessions over a period of 8 wk	• Significant improvement in all groups at discharge, 6 mo, and 12 mo ($P<.05$) • No significant difference between groups ($P>.05$)	• Randomized • Assessors blinded • Good description of treatment • Sample size calculated *a priori* and appropriate • Adverse effects reported • Clinical significance reported • No control/placebo group included • Reliability and validity of outcomes reported

(Continued)

Table 1.
Continued

Study	Country	Condition	Sample	Study Arms	Outcomes	Cointerventions	Follow-up	Treatment	Results	Strengths/Weaknesses
Lau et al,[66] 2008	Hong Kong	Acute LBP	110, 6 lost at 6-mo follow-up	1. IFC + medication + education + mobility and walking training 2. Walking training (control group)	Pain (NRS), satisfaction (Numeric Global Rating of Change Scale), disability (RMDQ)	Education, medication, mobility, and walking training	1, 3, and 6 mo	• 55 patients in the physical therapy group and 55 patients in the control group • 4 suction-type electrodes applied around the painful area, sweep frequency 70–130 Hz, intensity just below the pain threshold, 15 min • 1 or 2 sessions over a 24-hr period	• Significant decrease in pain (α=.025) and increase in satisfaction at discharge from the accident and emergency department • No significant difference between groups (α=.025) at 1, 3, and 6 mo follow-ups	• Randomized • Allocation adequate • Assessors blinded • Sample size calculated *a priori* • Intention-to-treat analysis included • High follow-up adherence • No placebo group included • Homogeneity of subjects uncertain
Adedoyin et al,[48] 2005	Nigeria	Chronic LBP	39	1. Active IFC swing pattern 1 integral 1 2. Active IFC swing pattern 6 integral 6 3. Active IFC swing pattern 6 wedge 6	Pain intensity (Verbal Semantic Differential Scale)	None	None	• 13 patients in the 1∫1 group, 13 patients in the 6∫6 group, 13 patients in the 6 wedge 6 groups • 2 electrodes (spinal nerve root correspondence to painful area), frequency of 100 Hz for burst group, sweep set between 50 and 100 Hz for the 6∫6 and the 6 wedge 6 groups, carrier frequency of 4,000 Hz in the channel, channel 2 set to fluctuate between 4,050 and 4,100 Hz • 2 treatment sessions daily for 2 times a week for 3 wk	• Significant decrease in pain over time (P<.001) • No significant effect between groups (P=.063)	• Randomized • Patients blinded • Good description of treatments • Small sample size • No control group • Confounders not controlled • Validity and reliability of outcomes not reported
Zambito et al,[65] 2006	Italy	Chronic LBP	120	1. Active IFC 2. Active horizontal therapy 3. Sham horizontal therapy	Functional questionnaire (Backill), pain (VAS), analgesic consumption	Exercise, analgesic medication	1 and 3 mo	• 45 patients in the active IFC group, 45 patients in the active horizontal therapy group, and 30 patients in the sham horizontal therapy group • 4 electrodes on a standard dermatomal pattern; frequency of 200 Hz, 10 min • 5 sessions weekly for 2 wk	• At discharge, significant and similar improvement in both the VAS and Backill score was reported in all 3 groups (P<.05) • The function and VAS scores continued to improve at 3 mo in the active groups compared with control (placebo) group (P<.01)	• Randomized • Sample size calculated *a priori* and adequate • Double blind approach • Validity and reliability of outcomes not reported • Moderate description of treatment
Zambito et al,[64] 2007	Italy	Chronic LBP	115	1. Active IFC 2. Active horizontal therapy 3. Sham horizontal therapy	Functional questionnaire (Backill), pain (VAS), analgesic consumption	Exercise, analgesic medication	1 and 3 mo	• 35 patients in the active IFC group, 35 patients in the active horizontal therapy group, and 35 patients in the sham horizontal therapy group • 4 electrodes on a standard dermatomal pattern, frequency of 200 Hz, 30 min • 5 sessions weekly for 2 wk	• At discharge, significant and similar improvement in both the VAS and Backill score was reported in the 3 groups (P<.01) • The function and pain scores continued to improve in the 2 active groups at weeks 6 and 14 compared with the control (placebo) group (P<.01)	• Randomized • Sample size calculated *a priori* and adequate • Double blind approach • Validity and reliability of outcomes not reported • Moderate description of treatment

(Continued)

Table 1.
Continued

Study	Country	Condition	Sample	Study Arms	Outcomes	Cointerventions	Follow-up	Treatment	Results	Strengths/Weaknesses
van der Heijden et al,[62] 1999	The Netherlands	Unspecified shoulder soft tissue condition	180, 1 dropped out at 12-mo follow-up	1. Active IFC + active US 2. No IFC + No US 3. Sham IFC + Sham US	Recovery, functional status (SDQ), chief complaint, pain (VAS), clinical status, ROM (goniometer)	Education and exercises	3, 6, 9, and 12 mo	• 34 patients in the active ET + active US group, 39 patients in the active ET + dummy US group, 39 patients in the dummy ET + active US group, 33 patients in the dummy ET + dummy US group, 35 patients in the no adjuvant group • 2 electrodes (1 in deltoid muscle region, 1 over homolateral erector trunci muscles), carrier frequency of 4,000 Hz, frequency of 60–100 Hz, intensity of electric paresthesia, 15 min, 12 sessions over 12 wk	• No significant difference between groups up to 12 mo follow-up (95% CI)	• Randomized • Patients and assessors blinded • Clinical significance reported • Sample size calculated *a priori* and adequate • Good description of treatment method
Taskaynatan et al,[60] 2007	Turkey	Bicipital tendinitis	47	1. IFC + US + hot packs + exercises 2. Steroid iophoresis + US + hot packs + exercises	Pain (VAS), ROM (goniometer), patient satisfaction (NRS), disability (function section of the Pennsylvania Shoulder Scale)	US+ hot packs + exercises	1 mo	• 21 patients in the IFC + US + hot packs + exercises group, 26 patients in the steroid iontophoresis + US + hot packs + exercises group • AMF frequency 0–100 Hz, 15 min, 15 sessions	• Statistical significant improvement at discharge and 1-mo follow-ups in the steroid iontophoresis group ($P<.05$) • Less dramatic improvement was reported for the IFC group at discharge and 1-mo follow-up ($P<.05$)	• Randomized • Assessors blinded • Poor description of interventions • Validity and reliability of outcomes not reported • Adverse effects reported • No dropouts reported
Cheing et al,[53] 2008	Hong Kong	Frozen shoulder	74, 4 dropped out at 8-mo follow-up	1. Active IFC 2. Active electro-acupuncture 3. Control	Shoulder function (Constant Murley Assessment Score), pain (VAS)	Exercise	1, 3, and 6 mo	• 24 patients in the IFC group, 25 patients in the electroacupuncture group, 25 patients in the control group • 4 suction-type electrodes around the shoulder in a coplanar arrangement, intensity just below the pain threshold, AMF swept frequency 80–120 Hz, 20 min • 10 sessions over 4 wk	• Both active groups showed a significant improvement at discharge and 6-mo follow-up for function and pain scores ($P<.001$) • No significant change was found in the control group, and no significant difference was found between the 2 active groups ($P>.05$)	• Randomized • Patients and assessors blinded • Reliability and validity of outcomes moderately reported • Good description of treatment protocols

(Continued)

Table 1.
Continued

Study	Country	Condition	Sample	Study Arms	Outcomes	Cointerventions	Follow-up	Treatment	Results	Strengths/Weaknesses
Hou et al,[55] 2002	Taiwan	Cervical myofascial pain	71	1. Hot pack, active ROM group 2. Hot pack, active ROM, ischemic compression group 3. Hot pack, active ROM, ischemic compression, TENS group 4. Hot pack, active ROM, stretch group 5. Hot pack, active ROM, stretch, TENS group 6. Hot pack, active ROM, IFC, myofascial release group	Index of change in pain threshold (algometer), pain tolerance (algometer), pain (VAS), and cervical ROM (goniometer)	Hot pack, active ROM, myofascial release	None	• 21 patients in the hot pack, active ROM group (B1); 13 patients in the hot pack, active ROM, ischemic compression group (B2); 9 patients in the hot pack, active ROM, ischemic compression, TENS group (B3); 10 patients in the hot pack, active ROM, stretch group (B4); 9 patients in the hot pack, active ROM, stretch, TENS group (B5); 9 patients in the hot pack, active ROM, IFC, myofascial release group (B6) • 4 electrodes; frequency of 100 Hz, carrier frequencies of 4,000 Hz and 4,100 Hz, 20 min	• Significant improvement in all groups ($P<.05$) • Groups B2, B3, B4, B5, and B6 had significantly larger improvement than group B1 ($P<.05$) • Groups B3, B5, and B6 had significantly larger improvement than group B2 ($P<.05$) • Group B6 had significantly larger improvement than group B4 ($P<.05$) • No significant difference among groups B3, B5, and B6	• Randomized • Good description of treatment • Sample size calculated *a priori* • No control/placebo group included • Reliability and validity of outcomes not reported
Almeida et al,[50] 2003	Brazil	Fibromyalgia	40, 23 dropped out	1. Active IFC + US 2. Placebo IFC + US	Pain (body map, VAS), tender points, (tender point threshold), polysomnography, sleep questionnaire	US	None	• 9 patients in the US + IFC group and 8 patients in the sham treatment group • Carrier frequency of 4,000 Hz, frequency of 100 Hz, intensity in the tactile sensation, 12 sessions for 4 wk	• Significant reduction in pain intensity and painful areas in the combined therapy group ($P<.001$) • No significant difference in sham treatment group	• Randomized • Investigator blinded • Small sample size • Very low adherence (missing data 57.5%) • Reliability and validity of measurement not reported
Taylor et al,[61] 1987	United States	Chronic jaw pain	40	1. Active IFC 2. Placebo IFC	Jaw pain (VAS), function (maximum vertical jaw opening)	None	None	• 20 patients in the IFC group and 20 patients in the placebo group • 4 electrodes (extraorally 1–1.5 cm in front of the tragus of ear), frequency of 90–100 Hz for 15 min and 40–90 Hz for 5 min, intensity (comfortable but not too strong), 3 treatments (24–72 hr between treatments)	• Significant improvement in both groups for pain and maximal vertical jaw opening • No significant difference between groups ($P<.05$)	• Randomization used • Patients blinded • Confounders not controlled • Reliability and validity of outcomes not reported • Small sample size • Good description of treatment
Jarit et al,[58] 2003	United States	Postoperative knee pain	87	1. Active IFC 2. Placebo IFC	Postoperative edema, pain (VAS), pain medication, ROM (goniometer)	Ice, exercises	None	• 28 patients in the ACL group (14 IFC and 14 placebo IFC), 34 patients in the meniscectomy group (17 IFC and 17 placebo IFC), 25 patients in the chondroplasty group (15 IFC and 10 placebo IFC) • 4 electrodes, frequency of 5–10 Hz in first 14 min, 80–150 Hz in second 14 min, 3 times daily for 7–9 wk	• Significantly less pain and greater ROM for the active IFC in all groups at all time points ($P<.05$)	• Randomized • Assessor blinded • Good description of treatment • Reliability and validity of outcomes not reported

[a] OA=osteoarthritis, IFC=interferential current therapy, SWD=shortwave diathermy, ROM=range of movement, VAS=visual analog scale, TENS=transcutaneous electrical nerve stimulation, WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index, IR=infrared radiation, SF-36=36-Item Short-Form Health Survey questionnaire, NMES=neuromuscular electrical stimulation, PRI=Pain Rating Index, RMDQ=Roland-Morris Disability Questionnaire, EQ-5D=EuroQol EQ-5D questionnaire, MT=manual therapy, MPQ=McGill Pain questionnaire, LBP=low back pain, US=ultrasound, SDQ=Shoulder Disability Questionnaire, ET=electrotherapy, CI=confidence interval, NRS=numeric rating scale, AMF=amplitude-modulated frequency, ACL=anterior cruciate ligament.

of the randomization procedure and concealment of allocation, with only 9 and 5 of the studies meeting these criteria, respectively. Items related to blinding were not achieved by the majority of the studies. Only 3 of the studies used a double-blinded design.

Testing subjects' adherence to intervention or having adequate adherence was another issue that was not accomplished by many studies (only 8 and 6 studies, respectively). Furthermore, adverse effects were reported in only 3 of the studies, and none of the studies provided details of the follow-up period.

Despite the fact that the adequate handling of dropouts is considered an important method used to prevent bias in data analysis, only 11 of the analyzed studies included information regarding the rate of withdrawals/dropouts. The outcome measures were not described well in terms of validity, reliability, or responsiveness.

Regarding statistical issues, it was uncertain whether sample size was adequate in 15 of the studies. Intention-to-treat analysis was used only in 11 of the studies. Finally, it also was unclear whether extraneous factors such as equipment calibration or medications during the study could affect the treatment responsiveness for IFC. For example, only 2 studies (10%) reported that the IFC equipment was calibrated during the study procedure.

IFC and Type of Pain Management

The effect of IFC has been studied predominantly in patients with chronic painful conditions (16 of 20 trials examined). These conditions included knee osteoarthritis,[47,49,51,52,54,59] chronic low back pain,[48,63–65] shoulder soft tissue pain,[53,60,62] fibromyalgia,[50] chronic jaw pain,[61] and myofascial syndrome pain.[55] In contrast, the analysis of IFC in acute pain included just 4 articles, 3 of them related to acute low back pain and 1 to postoperative knee pain.

Meta-analysis Results

Fourteen studies were included in the meta-analysis (Fig. 1),[47,49–56,60,61,63–66] with an overall sample size of 1,114 patients. Six studies were excluded for the following reasons: information regarding data variability (ie, mean and standard deviation) was not present,[58,59] the unit of variability included was different than the standard deviation (ie, interquartile range, median),[57,62] the comparison included in the trial was not relevant for the study's purpose,[48] and the interventions included in the trial were too heterogeneous[51] (ie, IFC, infrared radiation, shortwave diathermy, and 2 drugs [sodium hyaluronate and hylan G-F 20]).

The 14 selected studies were chosen because they provided complete information on the outcomes evaluated and homogeneity regarding outcome measures. Of these studies, 4 studies[54,56,61,63] addressed the analgesic effect of IFC alone and 10 studies[47,49,50,52,53,55,60,64–66] evaluated the effect of IFC applied as adjunct in a multimodal treatment protocol. In addition, of these 14 studies, 3 studies[53,54,66] compared the effectiveness of IFC with a control group, 6 studies[47,50,54,61,64,65] investigated IFC against placebo, and 7 studies[49,52,53,55,56,60,63] compared IFC with another intervention such as manual therapy or exercise.

Comparison 1: IFC Alone Versus Placebo Group on Pain Intensity at Discharge

Two studies[54,61] were included in this comparison. One study[54] measured outcomes at discharge after 4 weeks of therapy, and the other study[61] measured outcomes after 1 week of therapy. One trial[54] studied the effect of IFC on knee osteoarthritis, and the other trial[61] studied the effect of IFC on temporomandibular joint pain. One study[54] was rated of moderate methodological quality, and the other study[61] was rated of poor quality.[61] In this comparison, both studies had opposite results regarding the effectiveness of IFC when compared with a placebo group (Fig. 2). The pooled mean difference (MD) obtained for this analysis was 1.17 (95% CI=1.70–4.05). These results indicate that IFC alone was not significantly better than placebo at discharge.

Comparison 2: IFC Alone Versus Comparison Group on Pain Intensity at Discharge

Two studies[56,63] were included in this comparison. One study[63] measured outcomes at discharge after 2 to 3 weeks of treatment, and the other study[56] measured outcomes after 8 weeks. One trial[56] studied the effect of IFC on acute low back pain, and the other trial[63] studied the effect of IFC on chronic low back pain. Both studies were of moderate methodological quality. In this comparison, both studies agreed that IFC was not significantly better than manual therapy or traction and massage (Fig. 3). The pooled MD obtained for this analysis was −0.16 (95% CI=−0.62, 0.31). These results indicate that IFC alone was not significantly better than any of the comparisons at discharge from therapy.

Comparison 3: IFC as a Supplement to Another Treatment Versus Control Group on Pain Intensity at Discharge

Three studies[53,54,66] were included in this comparison. Two studies[53,54] used a 4-week discharge period, and one study[66] used a one-day discharge period. One trial[54] studied the effect of IFC on knee osteoarthritis, another trial[53] studied the effect of IFC on frozen shoulder, and the third tri-

Table 2.

Methodological Quality of the Studies[a]

Study	Item Scoring																																								Score/ Rating
	Patient Selection						Blinding						Interventions															Outcomes						Statistics						
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	
Adedoyin et al,[47] 2002	0	0	1	0	0	1	0	0	1	1	0	0	1	1	1	0	0	0	0	n/a	n/a	n/a	0	n/a	n/a	n/a	1	1	1	0	0	1	1	1	1	0	0	1	1	0.48 Moderate
Adedoyin et al,[48] 2005	1	1	1	0	0	1	0	0	0	1	0	0	1	n/a	0	0	0	0	0	0	0	0	0	n/a	n/a	n/a	1	1	1	0	0	0	1	1	1	0	0	1	0	0.37 Poor
Adedoyin et al,[49] 2005	1	1	1	0	0	1	0	0	1	1	0	0	1	0	1	1	1	0	0	1	1	1	0	n/a	n/a	n/a	1	1	1	1	0	0	1	0	1	1	1	1	0	0.61 Moderate
Almeida et al,[50] 2003	1	1	1	0	0	0	0	1	1	1	0	0	1	1	0	0	0	0	0	1	0	0	0	n/a	n/a	n/a	1	1	1	0	0	0	1	1	1	0	0	1	0	0.44 Moderate
Atamaz et al,[51] 2006	1	1	1	0	0	1	0	0	0	0	0	0	0	n/a	1	0	0	0	0	1	1	1	0	0	1	1	1	1	1	0	0	0	1	1	1	0	0	1	0	0.45 Moderate
Burch et al,[52] 2008	1	1	1	1	1	1	0	1	1	1	0	0	1	0	0	0	0	1	0	1	1	1	1	n/a	n/a	n/a	1	1	1	1	0	0	1	1	1	1	0	1	0	0.72 High
Cheing et al,[53] 2008	1	1	1	0	0	1	1	0	1	0	0	0	1	1	0	0	0	1	0	1	1	1	0	0	1	1	1	1	1	1	0	1	1	1	1	0	0	1	1	0.61 Moderate
Defrin et al,[54] 2005	1	1	1	0	0	0	0	0	0	0	0	0	1	1	1	1	1	0	0	0	0	0	0	n/a	n/a	n/a	1	1	1	0	0	0	1	1	1	0	0	1	0	0.42 Moderate
Hou et al,[55] 2002	1	1	1	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1	n/a	n/a	n/a	0	n/a	n/a	n/a	1	0	1	0	0	0	1	1	1	1	0	1	1	0.51 Moderate
Hurley et al,[56] 2004	1	1	1	1	1	1	0	0	0	0	0	0	1	0	1	0	1	1	1	1	0	1	1	0	1	1	1	0	1	1	0	1	1	1	1	1	0	1	1	0.66 Moderate
Hurley et al,[57] 2001	1	1	1	1	1	1	0	0	0	0	1	0	1	1	0	0	0	0	0	1	1	1	0	0	1	1	1	1	1	1	0	1	1	0	1	1	0	1	1	0.61 Moderate
Jarit et al,[58] 2003	1	1	1	0	0	1	0	1	1	1	1	0	1	1	1	0	1	1	0	0	0	0	0	0	1	1	1	1	1	0	0	0	1	0	1	0	0	1	0	0.54 Moderate
Lau et al,[66] 2008	1	1	1	1	1	0	0	1	1	0	0	0	1	0	1	0	1	1	1	1	1	1	0	0	1	1	1	1	1	0	0	1	1	1	1	1	1	1	1	0.72 High
Quirk et al,[59] 1985	1	1	1	0	0	1	0	0	0	0	0	0	0	0	1	0	1	0	1	1	1	0	0	0	1	1	1	0	0	0	0	0	1	0	0	0	0	1	0	0.36 Poor
Taskaynatan et al,[60] 2007	1	1	1	0	0	1	0	0	1	0	0	0	0	n/a	1	1	1	0	0	n/a	n/a	n/a	1	0	0	1	1	1	1	0	0	0	1	1	1	0	0	1	1	0.51 Moderate
Taylor et al,[61] 1987	1	1	1	1	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	n/a	n/a	n/a	0	n/a	n/a	n/a	1	1	1	0	0	0	1	1	1	0	0	1	0	0.39 Poor
van der Heijden et al,[62] 1999	1	1	1	1	0	1	0	1	1	1	0	0	1	n/a	1	1	1	1	1	1	1	1	0	0	1	1	1	1	1	1	1	0	1	1	1	1	0	1	1	0.78 High
Werners et al,[63] 1999	1	1	1	1	1	1	0	0	0	0	0	0	1	n/a	0	0	0	1	1	1	1	0	0	0	0	1	1	0	1	0	0	0	1	1	1	1	1	1	1	0.56 Moderate
Zambito et al,[64] 2007	1	1	1	1	0	0	1	1	1	1	0	0	1	1	1	1	1	0	0	n/a	n/a	n/a	0	0	1	1	1	0	1	0	0	0	1	1	1	1	1	1	1	0.67 Moderate
Zambito et al,[65] 2006	1	1	1	1	0	0	1	1	1	1	0	0	1	1	1	1	1	0	0	n/a	n/a	n/a	0	0	1	1	1	0	1	0	0	0	1	1	1	1	1	1	1	0.67 Moderate
Accomplished items	19	19	20	9	5	13	3	7	11	9	2	0	17	9	13	7	11	8	6	11	9	8	3	0	10	12	20	14	19	6	1	5	20	16	19	10	5	20	11	
Total percentage	95	95	100	45	25	68	15	35	55	45	10	0	85	60	65	35	55	40	30	79	64	57	15	0	83	100	100	70	95	30	5	25	100	80	95	50	25	100	55	

[a] 1=eligibility criteria; 2=described as randomized; 3=randomization performed; 4=randomization described as appropriate; 5=randomization concealed; 6=baseline comparability; 7=described as double blind; 8=blinding described an appropriate; 9=blinding of investigator/assessor; 10=blinding of subject/patient; 11=blinding of therapist; 12=blinding of the outcome (results); 13=treatment protocol adequately described for the treatment and control groups; 14=control and placebo adequate; 15=cointerventions avoided or comparable; 16=cointerventions reported for each group separately; 17=control for cointerventions in design; 18=testing of subject adherence; 19=adherence acceptable in all groups; 20=description of withdrawals and dropouts; 21=withdrawals/dropouts rate described and acceptable; 22=reasons for dropouts; 23=adverse effects described; 24=follow-up details reported; 25=follow-up period adequate; 26=short follow-up performed; 27=timing of outcomes comparable in all groups; 28=description of outcome measures; 29=relevant outcomes included; 30=validity reported for main outcome measure; 31=responsiveness reported for main outcome measure; 32=reliability reported for main outcome measure; 33=use of quantitative outcome measures; 34=descriptive measures reported for the main outcome; 35=appropriate statistical analysis included; 36=sample size calculated *a priori*; 37=adequate sample size; 38=sample size described for each group; 39=intention-to-treat analysis included; n/a=not applicable.

Study or Subgroup	IFC Alone			Placebo			Weight	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Defrin et al,[54] 2005	2.1	0.5	12	−0.5	0.7	9	51.4%	2.60 (2.06, 3.14)
Taylor et al,[61] 1987	1.75	1.96	20	2.08	1.53	20	48.6%	−0.33 (−1.42, 0.76)
Total (95% CI)			32			29	100.0%	1.17 (−1.70, 4.05)
Heterogeneity: tau^2=4.10, χ^2=22.33, *df*=1 (*P*<.00001), I^2=96%								
Test for overall effect: *z*=0.80 (*P*=.42)								

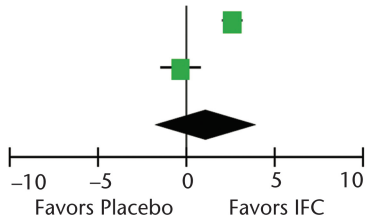

Figure 2.
Forest plot of comparison: interferential current therapy (IFC) alone versus placebo treatment on pain intensity at 1 week and 4 weeks (data presented as change scores). IV=inverse variance, 95% CI=95% confidence interval.

al[66] studied the effect of IFC on acute low back pain. Two studies included in this comparison were of moderate methodological quality,[53,54] and one study was considered to be of high quality.[66] In this comparison, the 3 studies tended to significantly favor IFC applied as a cointervention when compared with the control group (Fig. 4). The pooled MD obtained for this analysis was 2.45 (95% CI=1.69, 3.22). Thus, IFC applied as a cointervention was more than 2 points better, as measured with the VAS, in reducing pain intensity when compared with a control group in these conditions.

Comparison 4: IFC as a Supplement to Another Treatment Versus Placebo on Pain Intensity at Discharge

Five studies[47,50,54,64,65] were included in this comparison. Different times of discharge were used in the studies, ranging from 2 weeks[64,65] to 4 weeks.[47,50,54] Mean difference to pool the data was used. In addition, 95% CI and the random-effects model were chosen. In this comparison, 3 studies[47,50,54] of moderate quality tended to significantly favor IFC as a cointervention when compared with placebo. One study[64] of moderate methodological quality tended to significantly favor the placebo group. One study of moderate quality did not favor either IFC as a cointervention or placebo (Fig. 5, upper part).[65] The pooled MD obtained for this analysis was 1.60 (95% CI=−0.13, 3.34). This finding indicates that although IFC as a cointervention was statistically significantly better than a placebo at decreasing pain intensity at discharge in conditions such as osteoarthritis, chronic low back pain, and fibromyalgia, IFC tended to reduce pain in these conditions when compared with a placebo condition. In addition, the heterogeneity among studies was I^2=96%, which is considered substantial according to Cochrane group guidelines.[45] Therefore, these results should be interpreted with caution.

In this comparison, 2 studies[64,65] provided follow-up data (3 months). Thus, an analysis at the 3-month follow-up was performed (Fig. 5, lower part). The pooled MD obtained for this analysis was 1.85 (95% CI=1.47, 2.23). The 2 studies significantly favored IFC when compared with the placebo. This finding indicates that IFC as a cointervention was better than a placebo at decreasing pain intensity at the 3-month follow-up.

Study or Subgroup	IFC Alone			Comparison			Weight	Mean Difference IV, Random 95% CI
	Mean	SD	Total	Mean	SD	Total		
Hurley et al,[56] 2004	2.13	2.49	65	1.99	2.5	63	29.1%	0.14 (−0.72, 1.00)
Werners et al,[63] 1999	0.42	1.35	50	0.7	1.49	51	70.9%	−0.28 (−0.83, 0.27)
Total (95% CI)			115			114	100.0%	−0.16 (−0.62, 0.31)
Heterogeneity: tau^2=0.00, χ^2=0.64, *df*=1 (*P*=.42), I^2=0%								
Test for overall effect: *z*=0.66 (*P*=.51)								

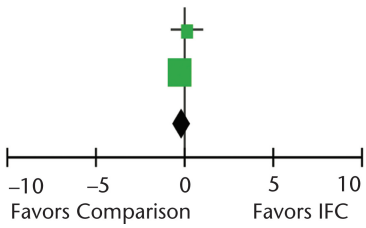

Figure 3.
Forest plot of comparison: interferential current therapy (IFC) alone versus comparison treatment on pain intensity at 3 weeks and 8 weeks (data presented as change scores). IV=inverse variance, 95% CI=95% confidence interval.

Study or Subgroup	IFC Therapy as Supplement Mean	SD	Total	Control Group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Cheing et al,[53] 2008	3.02	1.94	23	0.08	2.13	24	23.0%	2.94 (1.78, 4.10)
Defrin et al,[54] 2005	2.1	0.5	12	−0.7	0.7	8	38.9%	2.80 (2.24, 3.36)
Lau et al,[66] 2008	2.2	1.65	55	0.4	1.5	55	38.1%	1.80 (1.21, 2.39)
Total (95% CI)			90			87	100.0%	2.45 (1.69, 3.22)
Heterogeneity: tau^2=0.31; χ^2=6.76, *df*=2 (*P*=.03), I^2=70%								
Test for overall effect: *z*=6.28 (*P*<.00001)								

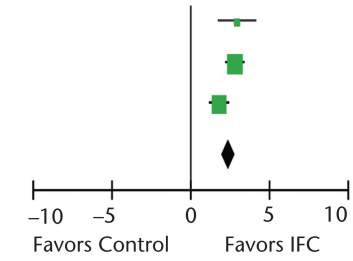

Figure 4.
Forest plot of comparison: interferential current therapy (IFC) as a supplemental treatment versus control treatment on pain intensity at 1 day and 4 weeks (data presented as change scores). IV=inverse variance, 95% CI=95% confidence interval.

Comparison 5: IFC as a Supplement to Another Treatment Versus Comparison on Pain Intensity at Discharge

Five studies[49,52,53,55,60] were included in this comparison (Fig. 6). Different times of discharge were used, ranging from 1 day[55] to 4 weeks[49,53,60] to 2 months.[52] Two studies[49,52] evaluated the effectiveness of IFC as a cointervention for knee osteoarthritis, 2 studies[53,60] evaluated the effectiveness of IFC as a cointervention for shoulder pain, and 1 study[55] evaluated the effectiveness of IFC as a cointervention for myofascial pain.

One study[55] compared IFC plus hot packs, active range of motion, and myofascial release with 5 different treatment modalities; thus, different analyses were run in order to deter-

Study or Subgroup	IFC Therapy as Supplement Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
3.1.1 Pain at discharge (1 week, 2 weeks, 4 weeks)								
Zambito et al,[64] 2007	1.9	0.78	35	2.6	1	35	21.5%	−0.70 (−1.12, −0.28)
Zambito et al,[65] 2006	1.8	1.27	45	1.7	1.65	30	21.0%	0.10 (−0.60, 0.80)
Adedoyin et al,[47] 2002	6.87	1.2	15	4.5	2.79	15	18.6%	2.37 (0.83, 3.91)
Defrin et al,[54] 2005	2.1	0.5	12	−0.5	0.7	9	21.3%	2.60 (2.06, 3.14)
Almeida et al,[50] 2003	4.2	2	9	0	1.82	8	17.6%	4.20 (2.38, 6.02)
Subtotal (95% CI)			116			97	100.0%	1.60 (−0.13, 3.34)
Heterogeneity: tau^2=3.59, χ^2=112.03, *df*=4 (*P*<.00001), I^2=96%								
Test for overall effect: *z*=1.81 (*P*=.07)								
3.1.2 Pain up to 3-month follow-up								
Zambito et al,[64] 2007	3.8	1.1	35	2	0.71	35	76.1%	1.80 (1.37, 2.23)
Zambito et al,[65] 2006	3.2	1.64	45	1.2	1.7	30	23.9%	2.00 (1.23, 2.77)
Subtotal (95% CI)			80			65	100.0%	1.85 (1.47, 2.23)
Heterogeneity: tau^2=0.00, χ^2=0.02, *df*=1 (*P*=.66), I^2=0%								
Test for overall effect: *z*=9.57 (*P*<.00001)								

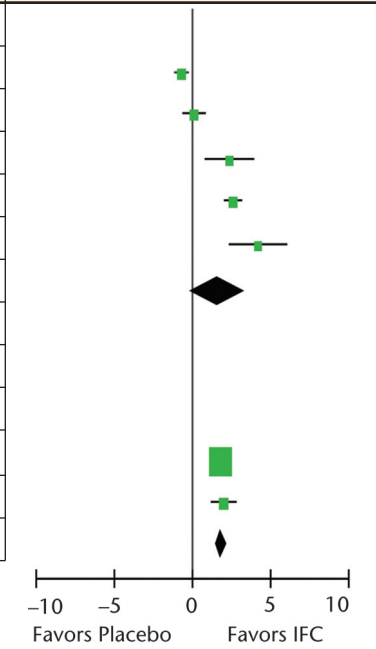

Figure 5.
Forest plot of comparison: interferential current therapy (IFC) as a supplemental treatment versus placebo treatment on pain intensity at 1-week, 2-week, 4-week, and 3-month follow-ups (data presented as change scores). IV=inverse variance, 95% CI=95% confidence interval.

Study or Subgroup	IFC as Supplement			Comparison			Weight	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Adedoyin et al,[49] 2005	5.07	1.39	16	4.74	1.14	15	20.1%	0.33 (−0.56, 1.22)
Burch et al,[52] 2008	2.79	1.32	53	2.32	1.54	53	23.1%	0.47 (−0.08, 1.02)
Cheing et al,[53] 2008	3.17	1.94	23	3.04	1.97	24	18.0%	0.13 (−0.99, 1.25)
Hou et al,[55] 2002 (B1)	3.34	1.14	9	0.77	1.8	21	18.5%	2.57 (1.50, 3.64)
Taskaynatan et al,[60] 2007	0.8	1.49	21	1.4	1.59	26	20.2%	−0.60 (−1.48, 0.28)
Total (95% CI)			122			139	100.0%	0.55 (−0.33, 1.44)

Heterogeneity: tau^2=0.80, χ^2=20.86, *df*=4 (*P*=.0003), I^2=81%

Test for overall effect: *z*=1.22 (*P*=.22)

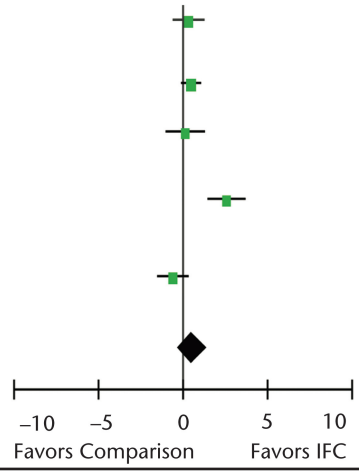

Figure 6.
Forest plot of comparison: interferential current therapy (IFC) as a supplemental treatment versus comparison treatment on pain intensity at 1 day, 2 weeks, 4 weeks, and 2 months (data presented as change scores). IV=inverse variance, 95% CI=95% confidence interval. B1=hot pack + active range of motion.

mine the effect of IFC as a cointervention when compared with all of these modalities (sensitivity analysis). We used the MD to pool the data. In addition, 95% CI and the random-effects model were chosen.

In this comparison, no clear trend favoring either IFC as a cointervention or the comparison treatments was observed for any of the analyses performed (Fig. 6). The pooled MD obtained for the various analyses was 0.55 (95% CI=−0.33, 1.44). The mean difference indicated that IFC as a cointervention was no better than other conventional interventions such as exercise, transcutaneous electrical nerve stimulation, or ultrasound plus hot packs at decreasing pain intensity at discharge.

Discussion

Analysis of the Analgesic Effect of IFC Alone

The results of this meta-analysis indicate that IFC applied alone as an intervention for musculoskeletal pain is not significantly better than placebo or comparison therapy (ie, manual therapy, traction, massage) at discharge from physical therapy treatment. However, few included studies (27%) examined the clinical analgesic effectiveness of IFC as a single therapeutic modality, and most did not focus on a specific musculoskeletal disorder. We also observed differences in length of treatment (ie, 1, 2, 3, and 8 weeks) and type of pain (ie, acute or chronic), indicating no consensus on optimal treatment parameters, which potentially contributed to the nonsignificance of the results.

Analysis of the Analgesic Effect of IFC as Part of a Multimodal Protocol (Cointerventions)

An important factor in this meta-analysis was the inclusion and analysis of studies including the application of IFC as a cointervention in a multimodal treatment protocol. This decision was clinically sound because IFC is used mainly as an adjunct treatment. The results of this study indicate that IFC as a cointervention is significantly better than control and placebo for reducing chronic musculoskeletal pain at discharge and at 3 months posttreatment, respectively. The pooled effect for IFC as a cointervention versus control was 2.45 on the VAS (95% CI=1.69, 3.22). According to some authors, this change is considered a clinically meaningful effect for acute painful conditions.[116–119] However, in chronic pain, a more stringent criterion seems to operate because a relative pain reduction of 50% or at least 3 cm on a VAS has been recommended for detecting a clinically successful pain reduction.[120,121]

In addition, when IFC as a cointervention was compared with placebo at discharge, there was no statistically significant difference between the groups. At 3-month follow-up, IFC as a cointervention obtained a better effect on the VAS, although less pronounced than when compared with a control group (pooled effect=1.85, 95% CI=1.47, 2.23). Thus, it seems that although IFC applied as a cointervention may have a modest analgesic effect, the magni-

tude of the effect is not large enough to be considered clinically relevant when compared with placebo or comparison interventions.

Because this is the first meta-analysis looking at the analgesic effect of IFC, direct comparisons cannot be made. In a previous study, Johnson and Martinson[122] concluded that transcutaneous electrical nerve stimulation, used mainly as an isolated intervention, provided significant pain relief when compared with a placebo intervention in a variety of chronic musculoskeletal conditions. Although methodological differences are present between both meta-analyses, some similarities such as the final sample sizes included, the focus on chronic musculoskeletal conditions, and clinical heterogeneity make the comparison between these 2 meta-analyses worth considering.

Some factors regarding IFC treatment may have accounted for the modest effect size observed. For example, although the stimulation of small-diameter fibers has been demonstrated to produce a more positive effect for chronic pain when compared with the stimulation of large-diameter fibers (Aβ),[54] the included studies, regardless of the type of pain, used stimulation parameters that were related mainly to the stimulation of Aβ fibers and the pain gate mechanism.[11,47–50,52,53,56–58,61,62] Although the stimulation of large-diameter fibers is acknowledged to produce a fast onset of analgesia, an important shortcoming is its brief analgesic effect.[123–125] Thus, it is plausible that in chronic pain, which was the dominant condition in this review, the effectiveness of IFC under these stimulation parameters may have been attenuated, resulting in a small effect in reported pain reduction. Further research is needed to evaluate the effect of noxious stimulation (eg, small-diameter fibers) on IFC effectiveness, especially in chronic pain.

Additionally, IFC has not been applied using a consistent treatment protocol. For example, similar AMF settings (≥80 Hz) were considered for treating either acute[56,57] or chronic[47,50,53,55,64,65] conditions. Moreover, under the same condition (eg, osteoarthritis), the authors inconsistently applied fixed AMF frequencies (ie, 80 Hz)[49] or sweep AMF frequencies (ie, 1–150 Hz, 30–60 Hz, 0–100 Hz).[52,54,59] Although experimental evidence has challenged the role of AMF as the main analgesic component of IFC,[36,37,85,126] inconsistency in the use of this parameter in clinical settings warrants consideration. Based on the current evidence, recommendations for optimal dosage when using IFC are not clear. It seems, however, that clinical evidence supports the fact that AMF should not be the most important parameter for clinical decision making. This fact has been corroborated by recent experimental evidence as well.[80] Instead, the use of a sensory level of intensity appears to be a consistent factor for the majority of the studies. Although some variations in the number of treatments and the treatment time exist, it seems that 10 to 20 minutes of application for 2 to 4 weeks with a total of 12 sessions is the most common treatment protocol for IFC.[47–51,53,54,59,60,62,64,65]

In this systematic review, 16 out of 20 studies evaluated the role of IFC in chronic rather than acute pain. Based on this fact, it seems that IFC has been applied more often in the management of chronic painful conditions. Interestingly, and apparently in contrast to current clinical practice in which IFC is used mostly for short-term pain relief, this meta-analysis provided information regarding potential positive long-term benefits from IFC.[64,65]

Adverse Effects

An important safety feature when applying electrotherapy modalities is the report of adverse effects. Although IFC is considered a safe modality, its application has been associated with local adverse effects such as blisters, burns, bruising, and swelling.[127,128] Interestingly, only 3 studies[52,56,60] included reports of adverse effects as a result of IFC treatment. Two studies[56,60] reported no complications, and one study[52] reported the presence of muscle soreness in one subject. Reporting adverse effects must be mandatory, not only for the safety of patients, but also for the professional integrity of therapists.

Methodological Elements Affecting Observed Effect

Even though the quality of the trials appraised generally was moderate, there are some methodological biases common to these studies that could have had an impact on the results. Selection bias could have existed, as only 9 trials reported appropriate randomization and only 5 trials reported concealment of allocation. Another potentially important bias was the lack of blinding, especially of the patients (9 studies) and assessors (11 studies). The outcome measure for this meta-analysis was pain, which is a subjective outcome and dependent on the subject's report. Trials without appropriate randomization, concealment of allocation, and blinding tend to report an inaccurate treatment effect compared with trials that include these features.[129–131]

Other potential biases that could have affected the observed effects were the lack of an appropriate sample size (only 5 of the trials reported adequate sample size) and the inappropriate handling of withdrawals and dropouts (only 11 trials used intention-to-treat analysis). Reporting clinical significance of results has become a relevant issue to dem-

onstrate the effectiveness of an intervention. Clinical significance provides the clinician with adequate information regarding the clinical impact of an intervention because it can identify when a meaningful change is produced.[132] Despite this message, the report of clinically meaningful changes in the present study was largely neglected, with only 3 studies including this component.[56,57,62]

The present study used a compilation of items from all of the scales used in the studies in the physical therapy literature. Although some of the scales used in physical therapy (ie, PEDro, Jadad) have been validated in some way, our recent analysis of health scales used to evaluate methodological quality determined that none of these scales are adequate for that use alone.[42] Therefore, it was decided that all of these scales would be used to assess methodological quality, and we used a compilation of items to provide a comprehensive and sensitive evaluation of the quality of individual trials. However, further research investigating methodological predictors for determining trial quality in physical therapy is needed.

Summary of Evidence

As an isolated treatment, IFC was not significantly better than placebo or other interventions. Conversely, when included in a multimodal treatment plan, IFC displayed a pain-relieving effect (VAS reduction of over 2 points) compared with a control condition.

Strengths

This meta-analysis is the first systematic investigation regarding the pain-reducing effectiveness of IFC on musculoskeletal pain. A comprehensive search was made of all the published research in this area over a wide range of years (1950–2010). In addition, authors were contacted in an attempt to have complete information about the selected studies. The 20 RCT articles included in this review covered a broad spectrum of acute and chronic musculoskeletal conditions. Interferential current therapy was analyzed as isolated intervention, as well as part of a multimodal treatment plan. In addition, the study provided multiple analyses, including the comparison between IFC and placebo, the comparison between IFC and control, and IFC contrasted to different types of interventions.

Limitations

Outcome level. A main limitation of this meta-analysis is the presence of clinical heterogeneity in the study population in most of the comparisons, casting some doubt on the validity of our results.

Study and review level. A potential limitation is the omission of non–English-language publications; however, English is considered the primary scientific language. It also has been reported that language-restricted meta-analyses only minimally overestimate treatment effects (~2% on average) compared with language-inclusive meta-analyses.[114] Therefore, language-restricted meta-analyses do not appear to lead to biased estimates of intervention effectiveness.[133,134] Applicability of results about the isolated effect of IFC on musculoskeletal pain also is limited, as only 4 studies addressed this issue. Another important limitation is that this study included only pain as an outcome measure. It would be important to know whether outcomes such as disability or function could have been modified by the application of IFC.

Conclusions

Implications for Practice

Interferential current therapy included in a multimodal treatment plan seems to produce a pain-relieving effect in acute and chronic musculoskeletal painful conditions compared with no treatment or placebo. Interferential current therapy combined with other interventions was shown to be more effective than placebo application at the 3-month follow-up in subjects with chronic low back pain. However, it is evident that under this scenario, the unique effect of IFC is confounded by the impact of other therapeutic interventions. Moreover, it is still unknown whether the analgesic effect of IFC is superior to that of these concomitant interventions.

When IFC is applied alone, its effect does not differ from placebo or other interventions (ie, manual therapy, traction, or massage). However, the small number of trials evaluating the isolated effect of IFC, heterogeneity across studies, and methodological limitations identified in these studies prevent conclusive statements regarding its analgesic efficacy.

Implications for Research

Because only 4 studies that evaluated the isolated effect of IFC were identified, and these studies had mixed results, further research examining this issue is needed, ideally in homogeneous clinical samples. Further research also is needed to study the effect of IFC on acute painful conditions. Also of interest would be the study of the effect of IFC in chronic conditions using a theoretical framework for the selection of parameters associated with suprasegmental analgesic mechanisms (ie, noxious stimulus) instead of sensory stimulation.

Mr Fuentes, Dr Armijo Olivo, and Dr Gross provided concept/idea/research design and writing. Mr Fuentes and Dr Armijo Olivo provided data collection and analysis. Mr Fuentes provided project management. Dr Magee and Dr Gross provided consultation (including review of manuscript before submission).

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INTERFERENTIAL THERAPY (IFT)

INTRODUCTION

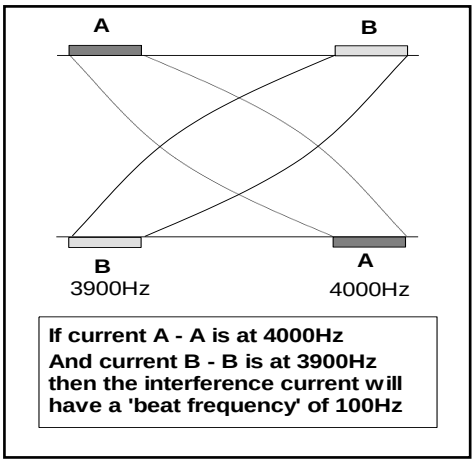
The basic principle of Interferential Therapy (IFT) is to utilise the significant physiological effects of low frequency (≅<250pps) electrical stimulation of nerves without the associated painful and somewhat unpleasant side effects sometimes associated with low frequency stimulation. Recently, numerous 'portable' interferential devices have become easily available. Despite their size, they are perfectly capable of delivering 'proper' interferential therapy, though some have limited functionality and ability for the practitioner to 'set' all parameters. Most multifunction stimulators include all interferential modes, so the practitioner has several machine types to select from (examples below).

		
Dedicated Interferential Therapy Unit (EMS Physio)	Portable Interferential Unit (TENSCare)	Multi function device which includes Interferential (DJO)

Interferential Therapy (IFT / IFC) has been widely used in therapy for many years (usage reviewed in Pope et al, 1995 and more recently Shah and Farrow, 2012; Ladeira et al, 2015; Phadke et al 2015), Its use is probably disproportionate to both the volume and the quality of the published evidence, though it is strongly supported on an anecdotal evidence level, and several reviews are indicating an overall supportive evidence base, especially for pain based management (e.g. Fuentes et al, 2010). There has been a recent increased flow of Interferential research material with additional supportive evidence (2015-17).

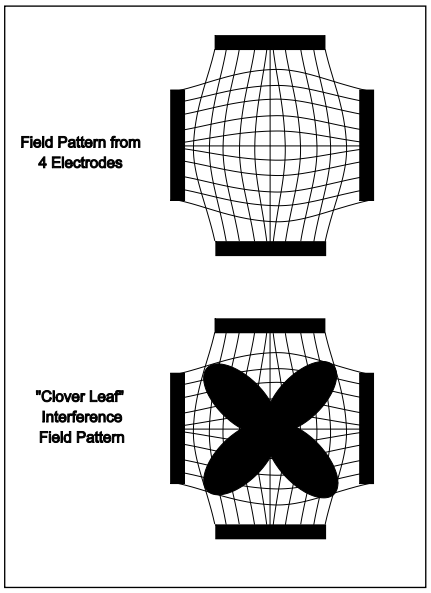
PRINCIPLES

To produce low frequency effects at sufficient intensity and at sufficient depth, patients can experience considerable discomfort in the superficial tissues (i.e. the skin). This is due to the impedance of the skin being inversely proportional to the frequency of the stimulation. [The barrier presented by the skin to the passage of an electric current is more complex than just impedance, or resistance, but will be regarded as such for the purpose of this explanation] In other words, the lower the stimulation frequency, the greater the impedance to the passage of the current & so, more discomfort is experienced as the current is 'pushed' into the tissues against this barrier. The skin impedance at 50Hz is approximately 3200Ω whilst at 4000Hz it is reduced to approximately 40Ω. The result of applying a higher frequency is that it will pass more easily through the skin, requiring less electrical energy input to reach the deeper tissues & giving rise to less discomfort.



The effects of tissue stimulation with these 'medium frequency' currents (medium frequency in electromedical terms is usually considered to be 1KHz-100KHz) has yet to be established. It is unlikely to do nothing at all, but in terms of current practice, little is known of its physiological effects. It is not capable of direct stimulation of nerve in the common context of such stimulation, though some researchers are currently investigating this area.

Interferential therapy utilises two of these medium frequency currents, passed through the tissues simultaneously, where they are set up so that their paths cross & they literally interfere with each other – hence another term that has been used in the past but appears to be out of favour at the moment – Interference Current Therapy. This interaction gives rise to an interference current (or beat frequency) which has the characteristics of low frequency stimulation – in effect ***the interference mimics a low frequency stimulation***.



The exact frequency of the resultant beat frequency can be controlled by the input frequencies. If for example, one current was at 4000Hz and its companion current at 3900Hz, the resultant beat frequency would be at 100Hz, carried on a medium frequency 3950Hz amplitude modulated current.

By careful manipulation of the input currents it is possible to achieve any beat frequency that you might wish to use clinically. Modern machines usually offer frequencies of 1-150Hz, though some offer a choice of up to 250Hz or more. To a greater extent, the therapist does not have to concern themselves with the input frequencies, but simply with the appropriate beat frequency which is selected directly from the machine.

The magnitude of the low frequency interference current is (in theory) approximately equivalent to the sum of the input amplitudes. It is difficult to show categorically that this is the case in the tissues but it is reasonable to suggest that the resultant current will be stronger than either of the 2 input currents.

Numerous researchers have evaluated the effect of varying the medium frequency carrier sine wave current (e.g. Ward et al 2002; Ward, 2009; Venancio et al, 2013; Correa et al, 2013, 2016). There is a general trend in the results that the lower the carrier frequency, the more uncomfortable the resulting stimulation. If there is a choice of carrier frequency on a clinical machine, higher carrier frequencies will be perceived as more comfortable by the patient, and thus it is suggested that they would be able to tolerate a stronger current before discomfort, increasing the effectiveness of the intervention.

The use of 2 pole IFT stimulation is made possible by electronic manipulation of the currents - the interference occurs within the machine rather than in the tissues. There is no known physiological difference between the effects of IFT produced with 2 or 4 electrode systems. The key difference is that with a 4 pole application the interference is generated in the tissues and with a 2 pole treatment, the current is ‘pre modulated’ i.e. the interference is generated within the machine unit (Ozcan et al, 2004). Fiori et al (2014) provide some evidence of a differential effect, in favour of a 4 pole application, but this was lab based work on healthy individuals and thus may not transfer to the clinical environment.

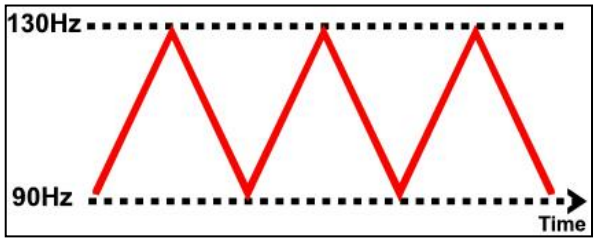
Whichever way it is generated, the treatment effect is generated from low frequency stimulation, primarily involving the peripheral nerves. There may indeed be significant effect on tissue other than nerves, but they have not as yet been unequivocally demonstrated. Low frequency nerve stimulation is physiologically effective (as with TENS and NMES) and this is the key to IFT intervention.

FREQUENCY SWEEP

Nerves will accommodate to a constant signal & a sweep (or gradually changing frequency) is often used to overcome this problem. The principle of using the sweep is that the machine is set to automatically vary the effective stimulation frequency using either pre-set or user set sweep ranges. The sweep range employed should be appropriate to the desired physiological effects (see below). It has been repeatedly demonstrated that 'wide' sweep ranges are ineffective whenever they have been tested or evaluated in the clinical environment

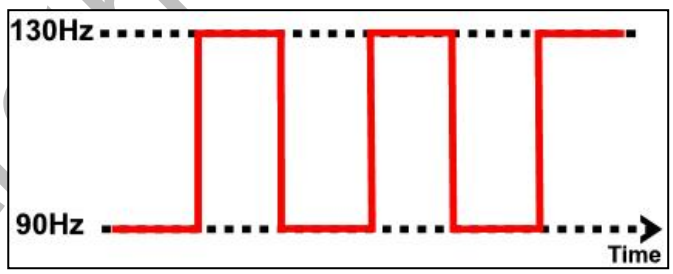
Note : Care needs to be taken when setting the sweep on a machine in that with some devices, the user sets the actual base and top frequencies (e.g. 10 and 25Hz) and with other machines the user sets the base frequency and then how much needs to be added for the sweep (e.g. 10 and 15Hz). Knowing which was round your machine works is critical to effective treatment.

The pattern of the sweep makes a significant difference to the stimulation received by the patient.



Most machines offer several sweep patterns, though there is very limited 'evidence' to justify some of these options. In the classic '***triangular***' sweep pattern, the machine gradually changes from the base to the top frequency, usually over a time period of 6 seconds – though some machines offer 1 or 3 second options. In the example illustrated, the machine is set to sweep from 90 to 130Hz employing a triangular sweep pattern. All frequencies between the base and top frequencies are delivered in equal proportion.

Other patterns of sweep can be produced on many machines, for example a rectangular (or step) sweep. This produces a very different stimulation pattern in that the base and top frequencies are set, but the machine then 'switches' between these two specific frequencies rather than gradually changing from one to the other. The adjacent diagram illustrates the effect of setting a 90 – 130Hz rectangular sweep.



There is a clear difference between these examples – even though the same 'numbers' are set. One will deliver a full range of stimulation frequencies between the set frequency levels and the other will switch from one frequency to the other. There are numerous other variations on this theme, and the 'trapeziodal' sweep is effectively a combination of these two.

The only sweep pattern for which 'evidence' appears to exist is the triangular sweep. The others are perfectly safe to use, but whether they are clinically effective or not remains to be shown.

PHYSIOLOGICAL EFFECTS & CLINICAL APPLICATIONS :

It has been suggested that IFT works in a 'special way' because it is 'interferential' as opposed to 'normal' stimulation. The evidence for this special effect is lacking and it is most likely that IFT is just another means by which peripheral nerves can be stimulated. It is rather a generic means of stimulation – the machine can be set up to act more like a TENS type device or can be set up to behave more like a muscle stimulator – by adjusting the stimulating (beat) frequency. It is often

regarded (by patients) to be more acceptable as it generates less discomfort than some other forms of electrical stimulation.

The clinical application of IFT therapy is based on peripheral nerve stimulation (frequency) data, though it is important to note that much of this information has been generated from research with other modalities, and its transfer to IFT is assumed rather than proven. There is a lack of IFT specific research compared with other modalities (e.g. TENS).

Selection of a wide frequency sweeps has been considered less efficient than a smaller selective range in that by treating with a frequency range of say 1-100Hz, the effective treatment frequencies can be covered, but only for a relatively small percentage of the total treatment time. Additionally, some parts of the range might be counterproductive for the primary aims of the treatment.

CLINICAL APPLICATION

There are 4 main clinical applications for which IFT appears to be used:

- Pain relief
- Muscle stimulation
- Increased local blood flow
- Reduction of oedema

In addition, claims are made for its role in stimulating healing and repair and for various specialised application – e.g. stress incontinence, though for the former examples (healing and repair) there is a dearth of quality research information available.

As IFT acts primarily on the excitable (nerve) tissues, the strongest effects are likely to be those which are a direct result of such stimulation (i.e. pain relief and muscle stimulation). The other effects are more likely to be secondary consequences of these.

PAIN RELIEF:

Electrical stimulation for pain relief has widespread clinical use, thought the direct research evidence for the use of IFT in this role is limited. Logically one could use the higher frequencies (90-130Hz) to stimulate the pain gate mechanisms & thereby mask the pain symptoms. Alternatively, stimulation with lower frequencies (2-5Hz) can be used to activate the opioid mechanisms, again providing a degree of relief. These two different modes of action can be explained physiologically & will have different latent periods & varying duration of effect. It remains possible that relief of pain may be achieved by stimulation of the reticular formation at frequencies of 10-25Hz or by blocking C fibre transmission at >50Hz. Although both of these latter mechanisms have been proposed (theoretically) with IFT, neither have been categorically demonstrated.

A good number of recent studies (e.g. Johnson and Tabasam 2003; Hurley et al 2004; McManus et al 2006; Jorge et al 2006; Walker et al 2006; Fuentes et al, 2011; Atamaz et al 2012; Gundog et al 2012; Rocha 2012; Lara-Palomo et al 2013; Fuentes et al, 2014; Suriya-Amarit et al 2014; Eftekharsadat et al 2015; Samuel and Maiya, 2015; Albornoz-Cabello et al, 2017) provide substantive evidence for a pain relief effect of IFT. Numerous studies have evaluated the capacity of IFT to influence various pain thresholds in healthy subjects. The results are somewhat mixed, and whilst of interest, may not transfer to a clinical environment (e.g. Beatti et al 2012; Venancio et al, 2013; Bae and Lee, 2014; Claro et al, 2014;

MUSCLE STIMULATION:

Stimulation of the motor nerves can be achieved with a wide range of frequencies. Clearly, stimulation at low frequency (e.g. 1Hz) will result in a series of twitches, whist stimulation at 50Hz will result in a tetanic contraction. There is limited evidence at present for the ‘strengthening’ effect

of IFT (though this evidence exists for some other forms of electrical stimulation), though the paper by Bircan et al (2002) suggests that it might be a possibility. On the basis of the current evidence, the contraction brought about by IFT is no 'better' than would be achieved by active exercise, though there are clinical circumstances where assisted contraction is beneficial. For example to assist the patient to appreciate the muscle work required (similar to surged Faradism used previously – but much less uncomfortable). For patients who can not generate useful voluntary contraction, IFT may be beneficial as it would be for those who, for whatever reason, find active exercise difficult. There is no evidence that has demonstrated a significant benefit of IFT over active exercise. Bellew et al (2012) evaluated the stimulatory effects of IFT and various Burst Mode currents in terms of their capacity to generate significant quality muscle contraction, the results were supportive of IFT as a treatment option.

The choice of treatment parameters will depend on the desired effect. The most effective motor nerve stimulation range with IFT appears to lie between approximately 10 and 20, maybe 10 and 25Hz. Stimulation below 10Hz results in a series of coarse twitches which may be of clinical benefit, though it has yet to be unequivocally demonstrated with IFT. Stimulation at higher frequencies than that needed to bring about a partial tetany (usually around 20 or 25Hz) can generate a strong tetanic contraction, which might be considered beneficial to assist patient appreciation of the required muscle work, but again, in terms of IFT intervention, it has yet to be demonstrated that this contraction level is needed over and above a partial tetany.

Youn et al (2016) evaluated the effect of IFT on muscle fatigue, demonstrating some (potential) benefits over a control comparison.

Da Silva et al (2015) reviewed the literature which compared pulsed current and kilohertz frequency stimulation with regards their potential benefits in generating peak muscle torque. There were no significant differences in outcome identified.

Caution should be exercised when employing IFT as a means to generate clinical levels of muscle contraction in that the muscle will continue to work for the duration of the stimulation period (assuming sufficient current strength is applied). It is possible to continue to stimulate the muscle beyond its point of fatigue – the contractions are forced via the motor nerve – and short stimulation periods with adequate rest might be a preferable option. Some IFT devices are capable of generating a 'surged' stimulation mode which might be advantageous in that fatigue would be minimised – this surged intervention would be similar, but more comfortable than Faradism.

BLOOD FLOW

There is very little, if any quality evidence demonstrating a direct effect if IFT on local blood flow changes. Most of the work that has been done involves laboratory experimentation on asymptomatic subjects, and most blood flow measurements are superficial i.e. skin blood flow. Whether IFT is actually capable of generating a change (increase) in blood flow at depth remains questionable. The elegant experimentation by Noble et al (2000) demonstrated vascular changes at 10–20Hz, though was unable to clearly identify the mechanism for this change. The stimulation was applied via suction electrodes, and the outcome could therefore be as a result of the suction rather than the stimulation, though this is largely negated by virtue of the fact that other stimulation frequencies were also delivered with the suction electrodes without the blood flow changes. The most likely mechanism is via muscle stimulation effects (IFT causing muscle contraction which brings about a local metabolic and thus vascular change). The possibility that the IFT is acting as an inhibitor or sympathetic activity remains a theoretical possibility rather than an established mechanism.

Based on current available evidence, the most likely option for IFT use as a means to increase local blood flow remains via the muscle stimulation mode, and thus the 10-20 or 10-25Hz frequency sweep options appears to be the most likely beneficial option.

OEDEMA

IFT has been claimed to be effective as a treatment to promote the reabsorption of oedema in the tissues. Again, the evidence is very limited in this respect and the physiological mechanism by which is could be achieved as a direct effect of the IFT remains to be established. The preferable clinical option in the light of the available evidence is to use the IFT to bring about local muscle contraction(s) which combined with the local vascular changes that will result (see above) could be effective in encouraging the reabsorption of tissue fluid. The use of suction electrodes may be beneficial, but also remains unproven in this respect.

A study by Jarit et al (2003) demonstrated a change in oedema following knee surgery in an IFT group, though the patients did the circumferential knee measures (rather than the therapist) and circumferential knee measurement is not an especially reliable method for identifying oedema as such. The Christie and Willoughby study (1990) failed to demonstrate a significant benefit on ankle oedema following fracture and surgery. The treatment parameters employed are unlikely to be effective given the information now available. If IFT has a capacity to influence oedema, the current evidence and physiological knowledge would suggest that a combination of pain relief (allowing more movement), muscle stimulation (above) and enhanced local blood flow (above) is the most likely combination to be most effective.

OTHER CLINICAL APPLICATIONS

In addition to the 4 key areas identified above, there are several other specialist application for which IFT has been employed. These include stimulation as part of the management of incontinence and pelvic floor training (e.g. Parkkinen et al, 2004; Yazdanpanah et al 2012), Fibromyalgia (e.g. Almedia et al, 2003; Raimundo et al, 2004; Moretti et al 2012), Trigger Point intervention (e.g. Hou, 2002; Jenson et al, 2002) and Psoriasis (Philipp et al 2000). A limited, but potentially interesting development is the employment of IFT in neurology as a means to influence spasticity, gait and function post stroke (Suriya-Amarit et al 2014). Enhancement of fracture healing has also been investigated with mixed results (e.g. Ganne, 1988; Fourie and Bowerbank, 1997)

Acedo et al (2015) compared TENS and IFT for patients with chronic (non specific) neck discomfort. They compared muscle (trapezius) relaxation and reported pain. Whilst both interventions provided pain relief, that associated with the IFT reached a clinically important level whilst the TENS did not (as employed in this study). The IFT additionally provided a significant change in muscle relaxation which was beneficial.

Hasegawa et al (2016) evaluated the benefits of IFT for patients with dry mouth syndrome, demonstrating some benefits with minimal discomfort or pain compared with other options. Elnaggar and Elshafey used IFT with hydrotherapy compared with a standard treatment protocol for patients with juvenile idiopathic arthritis, showing that the IFT contributed to a useful treatment effect.

Wound healing with electrical stimulation is a widely explored intervention. Shahrokhi et al (2014) have extended the normal range of stim modalities to include IFT with interesting preliminary results.

Samhan (2014) reports the effect of IFT on hand function in patients with psoriatic arthritis using an underwater technique (which is valid, but unusual) – demonstrating useful results.

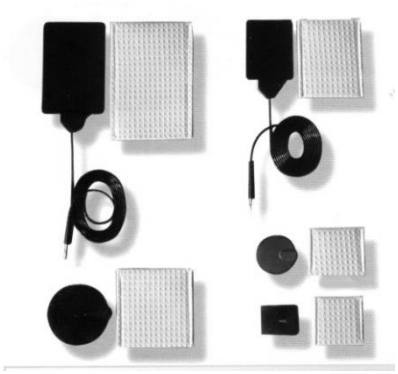
There have been several studies in which the use (home based) of IFT as a means of helping bowel function in children with chronic constipation have been reported (e.g. Chase et al, 2005, Ismail et al, 2009; Leong et al, 2011; Yik et al 2012 a,b; Queratto et al 2013; Southwell, 2013; Kajbafzadeh, et al 2015; Ladi et al 2017). This research is currently being extended in the UK as a multi centered study.

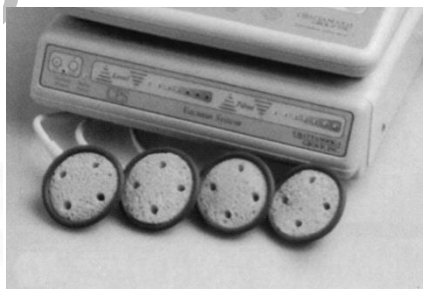
INTERFERENTIAL COMPARED WITH TENS

There have been numerous studies in recent years which have compared the efficacy of iFT and TENS, primarily with regard to pain relief. A significant proportion of these studies have been lab based, though some are more clinically oriented. Overall, these studies indicate that TENS generally provides higher (stronger) levels of pain relief (or some associated outcome), though IFT is generally identified as being more comfortable from the perspective of the recipient. If a patient dislikes the sensation associated with TENS, IFT would constitute a useful fallback stimulation modality on the basis of reported comfort.

TREATMENT PARAMETERS:

Stimulation can be applied using pad electrodes and sponge covers (which when wet provide a reasonable conductive path), though electroconductive gel is an effective alternative. The sponges should be thoroughly wet to ensure even current distribution. Self adhesive pad electrodes are also available (similar to the newer TENS electrodes) and make the IFT application easier in the view of many practitioners. The suction electrode application method has been in use for several years, and whilst it is useful, especially for larger body areas like the shoulder girdle, trunk, hip, knee, it does not appear to provide any therapeutic advantage over pad electrodes (in other words, the suction component of the treatment does not appear to have a measurable therapeutic effect). Care should be taken with regards maintenance of electrodes, electrode covers and associated infection risks (Lambert et al 2000; Koh et al, 2010).





Whichever electrode system is employed, electrode positioning should ensure adequate coverage of the area for stimulation. Using larger electrodes will minimise patient discomfort whilst small, closely spaced electrodes increase the risk of superficial tissue irritation and possible damage / skin burn.

The bipolar (2 pole) application method is perfectly acceptable, and there is no physiological difference in treatment outcome despite several anecdotal stories to the contrary. Recent research evidence supports the benefit of 2 pole application (e.g. Ozcan et al 2004).

Treatment times vary widely according to the usual clinical parameters of acute/chronic conditions & the type of physiological effect desired. In acute conditions, shorter treatment times of 5-10 minutes may be sufficient to achieve the effect. In other circumstances, it may be necessary to stimulate the tissues for 20-30 minutes. It is suggested that short treatment times are initially adopted especially with the acute case in case of symptom exacerbation. These can be progressed if the aim has not been achieved and no untoward side effects have been produced. There is no research evidence to support the continuous progression of a treatment dose in order to increase or maintain its effect.

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INTERFERENTIAL CONTRAINDICATIONS

- Patients who do not comprehend the physiotherapist's instructions or are unable to co-operate should not be treated
- Patients with Pacemakers – some pacemakers are relatively immune to interference from electrical stimulation whilst others can demonstrate serious adverse behaviour. It is suggested that as a general rule, if the patient has a pacemaker, it is best to avoid all electrical stimulation, but like TENS, if it is a treatment that is needed. The stimulation should be tried in a carefully controlled environment where appropriate equipment is available to correct any pacing problems should they arise.
- Patients who are taking anticoagulation therapy or have a history of pulmonary embolism or deep vein thrombosis should not be treated with the vacuum electrode applications
- Similarly, patients whose skin may be easily damaged or bruised
- Application over :
  - The trunk or pelvis during pregnancy (though this MAY be modified in time in line with the TENS advice. At the present time, it is suggested that it is best avoided in these regions)
  - Active or suspected malignancy except in hospice/palliative/terminal care
  - The eyes
  - The anterior aspect of the neck
  - The carotid sinuses
- Dermatological conditions e.g. dermatitis, broken skin
- Danger of haemorrhage or current tissue bleeding (e.g. recent soft tissue injury)
- Avoid active epiphyseal regions in children
- Transthoracic electrode application is considered to be 'risky' by many authorities

INTERFERENTIAL PRECAUTIONS

- Care should be taken to maintain the suction at a level below that which causes damage / discomfort to the patient
- If there is abnormal skin sensation, electrodes should be positioned in a site other than this area to ensure effective stimulation
- Patients who have (marked) abnormal circulation
- For patients who have febrile conditions, the outcome of the first treatment should be monitored
- Patients who have epilepsy, advanced cardiovascular conditions or cardiac arrhythmias should be treated at the discretion of the physiotherapist in consultation with the appropriate medical practitioner
- Treatment which involves placement of electrodes over the anterior chest wall
- Satter (2008) reports an electrical burn following IFT treatment – correct application methods are therefore strongly encouraged
- Keramat and Gaughran (2012) report and unusual range of untoward effects following IFT treatment

INTERFERENTIAL TREATMENT RECORD

- Electrode number (2 pole, 4 pole) and positions
- Frequency applied
- Sweep settings employed (if applicable)
- Current intensity applied (or patient reported sensation)
- Treatment duration

Low Level Laser Therapy for Tendinopathy. Evidence of A Dose–Response Pattern

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Low level laser therapy for tendinopathy. Evidence of a dose - response pattern

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To investigate if low level laser therapy (LLLT) can reduce pain from tendinopathy, we performed a review of randomized placebo-controlled trials with LLLT for tendinopathy.
A literature search for trials published after 1980 using LLLT was conducted on Medline, Embase, Cochrane Library and handsearch of physiotherapy journals in English and Scandinavian languages. Validity assessment of each trial was done according to predefined criteria for location-specific dosage and irradiation of the skin directly overlying the affected tendon..
The literature search identified 78 randomized controlled trials with LLLT, of which 20 included tendinopathy. Seven trials were excluded for not meeting validity criteria on treatment procedure or trial design. Twelve of the remaining thirteen trials investigated the effect of LLLT for patients with subacute and chronic tendinopathy provided a pooled mean effect of 21 % [5.9-36.1, 95%CI]. If only results from the nine trials adhering to assumed optimal treatment parameters were included, the mean effect over placebo increased to 32 % [23.0-41.0, 95% CI].
Low level laser therapy can reduce pain in subacute and chronic tendinopathy if a valid treatment procedure and location-specific dose is used.

Keywords: Low level laser therapy, dose – response pattern, tendinopathy, meta-analysis

BACKGROUND

Low level laser therapy (LLLT) was introduced in a clinical randomised controlled trial (RCT) on musculoskeletal pain as early as in 1980 [1] . In the past two decades a number of clinical RCTs have been performed with LLLT to treat a variety of musculoskeletal and neurogenic pain conditions. Clinical applications of LLLT have been performed either by direct exposure of the skin overlying the injury, exposure of trigger points or acupuncture points, or of nerves inside or outside the painful area. A broad range of doses (0,0001 – 38 J/cm^2) [2] has been reported to produce significant effects on musculoskeletal disorders in about one third of the LLLT trials. Thus the rationale behind the selection of application technique and treatment parameters like power density, size of exposure area, timing or treatment frequency often remains unclear. However, the majority of LLLT-trials have failed to provide successful results while employing doses within the same range as above. Recent review articles [2-4] have concluded that there is little - if any - evidence in favour of LLLT for the treatment of musculoskeletal pain. Several editorials in medical journals have supported the criticism on the clinical use of LLLT [5-7]. Still the amount of RCTs with results in favour of LLLT is by far too large to be explained by random chance alone. There is a missing link between the increasing number of successful results from LLLT in the laboratory and the mediocre results of clinical trials [2]. In an attempt to fill this gap, we decided to investigate if there exists a dose- response pattern for a subgroup of patients from the clinical trials of tendinopathy when the laser treatment procedure was similar to the successful laboratory trials. Three validity criteria for clinical laser treatment procedure may be vital for effectiveness. The first is that the tendinopathy is the target for irradiation. Secondly, power density and dose at the target tendon should be similar to that of the laboratory trials, and thirdly, timing and number of treatment sessions should correspond with laboratory procedures.

RATIONALE FOR TREATMENT OF TENDINOPATH

Acute tendinitis involves an inflammatory response, often induced by repetitive strain, overload or friction of the tendon. One *in vitro*-trial has confirmed that excessive repetitive motion can induce fibroblast inflammation [5]. The nature of persisting symptoms are often periodic [6] and associated with degenerative manifestations in tendon histopathology [7]. In the subacute and chronic cases increased tendon thickness, degeneration of collagen tissue and presence of hyaline foci within the tendon are evident [8]. Both morphological and biomechanical deterioration of tendon properties have been observed, and some authors suggest that the ending "itis" is misleading as degeneration is more apparent at these stages, [7], [12-15].

The gold standard for tendinitis treatment of the upper extremity is considered by several reviewers to be steroid injections, or anti-inflammatory drugs (NSAID)[16-18]. These chemical agents have primarily short-term effects, while longer-lasting effects (> 6 weeks) are less evident and often fail to reach significance. Treatment can also be directed at the degenerative changes within the tendon matrix. An *in vitro*-trial demonstrated that repetitive motion with low load increases fibroblast metabolism and collagen production [11] In subacute and chronic cases results from controlled trials with exercise therapy [12-14] indicate a beneficial effect, and a case report of symptom reduction also found remission of degenerative changes by ultrasonography after exercise therapy [13] . In our opinion, the natural strategy for reducing tendinopathy pain by LLLT is two-fold and directed both at reduction of inflammation, and stimulation of collagen production.

DETERMINATION OF OPTIMAL LLLT DOSE FOR TENDINOPATHY AT TARGET LOCATION

Selection of dose in clinical trials of LLLT seems to be circumstantial, and either picked at random, from the manufacturers` recommendations, or from the author`s own empirical basis. In contrast we assume that there exists an optimal LLLT dose range for the treatment of tendinitis, because laboratory trial reports almost unequivocally have stated that LLLT-effects on collagen tissue are dose-dependent.

We identified ten controlled trials investigating LLLT effect on fibroblast metabolism, and in all except one trial [14] significant increases in collagen production were found.

The results from five *in vitro* trials on fibroblast cell cultures [24-28], suggested that optimal power density and dose for increasing collagen production by 34-37 % were 4.5-7.5mW/cm^2 and 0.45 – 0.6 J/ cm^2 for continuous 632.8 nm HeNe laser and 820 nm GaAlAs laser respectively. Three *in vivo* trials on sutured soft tissue injuries produced similar results on collagen production with slightly higher doses (1-3.6 J/cm^2) of continuous 632,8 nm HeNe laser, and the same power density [29-31]. In the latter trial [39], mechanical properties of the laser-exposed tendon were significantly enhanced due to a more adequate collagen compostion, i.e. with more neutral salt soluble and insoluble collagen. One *in vivo* trial suggested that pulsed 904 nm GaAs laser only needed 0.4 J/ cm^2 to increase fibroblast metabolism [17] .

Interestingly, it appears that it is possible to use a too high power density or dose from LLLT , as these were found to have decreased fibroblast cell metabolism *in vitro* [20-22]. In these trials it was reported that doses lower than 0.1 J/ cm^2 did not produce significant results, while doses in excess of 4.5 J/ cm^2, and power density higher than 10 mW/cm^2, produced an inhibitory effect on the fibroblast metabolism and collagen production. All these trials employed a treatment frequency of 3-5 times per week for 2-4 weeks.

In *in vitro* trials higher energy doses have been reported to suppress inflammation [34-36]. This effect was also reported to be dose-dependent with an optimal range of 1.9 – 6.3 J/cm^2 and

power density of 21.2 mW/cm^2. The upper range limits were not identified. The anti-inflammatory effect was highly significant after 5 days with daily laser treatment.
If these findings are combined, there is an overlap in dose and power density ranges from which the optimal treatment parameters at the target location can be derived:

Dose:	0.1 – 3	J/cm^2
Power density:	5 – 21	mW/cm^2
Treatment frequency:	3 – 5	times per week

BASIC TECHNICAL AND BIOPHYSICAL BACKGROUND

If we confine consideration of laser parameters to caucasian patients, there are five physical factors which may determine if an optimal dose reaches the target in a clinical setting. They can be summarized as:

1) Distance from skin surface to target area;
2) Vascularity of the tissue between skin surface and target;
3) Volume of injured tissue;
4) Laser wavelength; and,
5) Mode of energy delivery (pulse vs continuous).

Only some of the above variables are known, but they provide a basis for extrapolation that can increase the precision in determining what dose reaches the target. *In vivo* trials in animals have shown that the most important absorption zone in the skin was the dermal vascular plexus barrier [20]. As blood haemoglobin is an important absorber of light [21], highly vascularized muscle tissue is harder for laser light to penetrate than the more transparent fatty subcutaneous tissue. Improved regeneration after injury of muscle tissue *in vivo* has also been observed, but LLLT doses were about 10 times higher than doses that have been reported optimal for collagen tissue [22]. For tendon injuries that are covered by muscle, it is important that dose is increased accordingly.
The average distance from the skin to the various tendons have not been definitely established. For the purposes of the current paper, relevant dimensions and distances were estimated by a combination of general anatomical knowledge, diagnostic imaging studies, and a pilot study with ultrasound imaging of some tendons. Typical tendon characteristics are presented in Table 1:

((Table 1))

Red (HeNe/632 nm) or infrared (GaAlAs/820 nm) lasers have been used for LLLT because an optical window of penetration with these wavelengths allows about 1/5 of the laser energy to pass the skin barrier. Another type of infrared laser, the 904 nm GaAs laser has a mode of energy delivery in short strong pulses, but with a low average output. Through *in vitro* trials, it has been shown that infrared light penetrates slightly better (37 % lost at about 2 mm) than visible red laser, which lose the same incident energy at only 0.5 mm [23]. In addition, pulse lasers seem to overcome the skin barrier with lower doses than continuous lasers in *in vivo* trials on animals, i.e. the relative penetration is better [17],[24] .
Given the optimal parameters already indicated above, and the data presented in Table 1, acceptable clinical treatment parameter ranges for three laser types and five common forms of tendinopathies are summarized in Table 2 :

((Table 2))

MATERIALS AND METHODS

Literature search

A literature search was performed on Medline, Embase, Cinahl, PedRo and the Cochrane Controlled Trial Register as advised by Dickersin et al.[25] for both non-clinical controlled trials and randomised controlled clinical trials.
Key words were : Low level laser therapy, low intensity laser therapy, low energy laser therapy, HeNe laser, IR laser, GaAlAs, GaAs, diode laser, tendinitis, collagen, fibroblast, tendon. Handsearching was also performed in national physiotherapy and medical journals from Norway, Denmark, Sweden, Holland, England, Canada and Australia. Additional information was gathered from researchers in the field.

Inclusion criteria

The randomised controlled trials were subjected to the following seven inclusion criteria:

1) Diagnosis: Tendinopathy;
2) Exposure area: Skin overlying site of inflammation or postinflammatory process in tendon;
3) Intensity and dose: According to Table 2;
4) Treatment frequency and numbers: At least twice weekly and no less than six in total;
5) Control group: A control group of at least ten patients that received placebo therapy should be included;
6) Blinding: Patients and outcome assessors should be blinded; and,
7) Specific endpoints within 2 – 6 weeks after inclusion.

Intensity and dose calculations

Data on beam diameter and laser output were collected from the relevant manufacturers` manuals. All doses and power densities were calculated according to the following formulae:
Exposure area: Π (0.5 diameter ^{2}) [cm^2]
Mean output: Pulse intensity x pulse duration x pulses per second/ second [mW]
Power density: Mean output/ exposure area [mW/cm^2]
Dose: Power density x treatment time [J/cm^2]

Outcome measures

We chose pain as an outcome measure, preferrably on a continous scale (VAS etc). In trials where several aspects of pain were measured, measures of pain involving the physical function of the treated tendon (i.e. pain on isometric muscle contraction) were preferred. When possible, 95 % confidence intervals were calculated for differences in change between groups from baseline. Effect size was calculated for all trials as the difference (%) in mean change from baseline to endpoint between the active treatment group and placebo treatment group.

RESULTS

Results of inclusion procedure

The literature search identified 78 clinical RCTs, of which 20 included tendinitis. Among these, two trials had to be excluded for exposing trigger points or acupunture points and not exposing the skin directly overlying the injured tendon [43-44]. One trial [27] had to be excluded for only having three patients with tendinitis in the control group. One comparative trial was excluded for not using placebo-control [28]. Another trial [29] had to be excluded for unwittingly giving the placebo group active HeNe - laser treatment, well within the recommended dose range (2.25 J/ cm^2). Another epicondylitistrial [30] treated in skin contact and violated the recommended treatment distance of 10 cm in the manufacturer`s manual. The optical correction system then left a ”blind” spot of approximately 2.5 -3 cm^2 in the middle of the treatment area which was untreated. In the case of lateral epicondylitis, the injured area of the tendon is smaller than this blind spot and therefore it was judged as unlikely that optimal dose reached the target tendon. Subsequently the trial was excluded from this meta-analysis. One large comparative trial was excluded because it individualised treatment and lacked specific endpoint in time [31]. In addition only a small group received placebo treatment and the results for the placebo group were not presented separately. All excluded trials are presented in Table 3.

<< Table 3>>

Four trials treated the correct spot, but were excluded from analysis for employing treatment parameters outside the acceptable dose and power density range. These four trials and all included trials are presented in Table 4. Three of the listed trials are split in two as they included two locations of tendinopathies and presented the results separately, which gives a total number of 16 listings in the table from 13 publications.

((Table 4))

Results of dose and power density calculations

Complete and correct data on power density and and dose were only reported in three trials [36-38]. But in all sixteen trials that exposed the skin overlying the injured tendon, sufficient information was reported to perform calculations for the missing data.

Outcome measures

All nine trials [32], [38-45]using the suggested optimal treatment was calculated to a weighted mean difference 32 % (23 – 41, 95 % CI) in favour of active LLLT (Figure 1). Trials without optimal treatment dose/power density [34], [46-48], reported either no significant differences or in one trial [36] significantly poorer results from LLLT than placebo. If these four trials were included in the statistical pooling, the effect was reduced to 22.1 % better than placebo (Figure 2). The difference in results between optimal and non-optimal treatment was highly significant ($p<0.001$). The results from all the nine trials that met our inclusion criteria for optimal parametres are shown in an effect size plot (Figure 2).

DISCUSSION

It may be said that previous reviews on LLLT have assumed that an optimal laser dose does not exist. Such an assumption implies that whichever tissue is injured, or whatever pathophysiology, the same dose can be employed for treatment. Even well-known variations in the effct based upon factors such as penetration depths and absorption abilities, distance and type of tissue lying between the laser-exposed skin and the injured tissue, and laser type have been overlooked in many studies. The assumption that there exists a common, universal, LLLT dose in the treatment of musculoskeletal disorders is unreasonable, not only in terms of face validity, but also because of the distinct dose-response patterns that laboratory trials on collagen tissue have revealed.
Another common assumption about LLLT has been that only one therapeutic window of optimal dose exists when living tissue is exposed by laser energy [37]. Recent research findings on dose-response relationships may shed new light on the apparent chaos regarding dose and response in the LLLT literature. This assumption is recently contradicted by a research group that found seven response peaks in a broad dose range for four different cell cultures [38]. These results also imply that there might be ineffective dose intervals within the broad dose range that has been used in clinical trials.

Contrary to previous reviews, we found a dose-response pattern broadly resembling that from the laser laboratory trials. Treatment success was invariably associated with the use of treatment parameters inside our suggested optimal range. In one trial [36] the placebo group improved more than the active LLLT group; the calculated dose and power density at the target tendon was very high in this trial. In fact these parameters were within a range where inhibitory effects on fibroblast metabolism have been reported [20-21]. The clinical outcome may be explained by inhibition of the natural improvement over time for the intervention group. Thus this trial adds further support for the identified dose - response pattern.
However, even if we seem to have identified an optimal dose range there are several unanswered questions. One question is which effect is most important: a reduction of inflammatory mediator activity, or an increase in collagen metabolism? Or maybe further improvement can be achieved through variation of laser dose during the rehabilitation process? Another point is that laser therapy has no known effect on the remodelling phase of the injured tendon. How and when should the physical loading of the tendon be performed in order to restructure and strengthen the tendon after laser therapy? These questions can only be answered through controlled dose-response studies either *in vivo* or in a clinical setting.

One criticism that may arise is that the results of two included trials were reported as not significant by the trial authors [39], [40]. In the first trial, the authors chose to base their conclusion on the data from a 5 category scale for detection of change. We consider that our choice of using data of the continous scale for pain free grip strength is appropriate and more sensitive to detect clinically relevant differences. From the other trial, disagreement was caused by an incomplete statistical calculation that did not include significance testing of change, which also have been commented upon in a previous review [41].
Testing and calibration of laser output was only performed by the authors in one of the clinical trials [32]. Some authors have pointed out existing discrepancies in laser dosimetry and measured deviations in laser output to be on average up to 40 % lower than manufacturers` claims [52-53]. We assume that this problem affects dose and power density similarly in all the trials. With the wide optimal range that we have suggested, this knowledge may only effect one or two borderline trials, and does not alter our conclusion.

Two findings should be of particular interest for clinicians. The first is that the 904 nm GaAs pulse laser seems to overcome the skin barrier more easily, i.e. without needing the same meticulous variation in dose according to tendon location as is needed with the 820 nm GaAlAs lasers. The second finding is that the small beams and high outputs of the 820 nm lasers might give too high power density and dose, which possibly inhibits treatment success in cases of superficially situated tendinopathies.

Our findings contradict those of several previous reviews on LLLT. In a recent review on the 904 nm GaAs lasers, de Bie and colleagues [3] found little evidence of effect from this laser. There are several reasons for this. The research group in Maastricht around Prof. de Bie is probably the group who have contributed most to an understanding of possible dose response patterns for LLLT and musculoskeletal pain. Their review, however did not confine the focus to a single diagnosis, but included a variety of conditions. They did not use dose or power density as inclusion critera, and did not investigate doses for the different sub-groups of diagnoses. Our literature search is also more recent and extensive and includes another three large scale trials [40-42]. These trials were also not included for evaluation of effect in the meta-analysis of Gam et al. [44].

Poor methodological quality in trials may compromise the conclusions of reviews. Although there is room for much improvement, the general picture of methodological quality in LLLT trials is similar to that of medical interventions on the same diagnoses [45]. Four of the nine included trials with optimal treatment have been assessed previously by others and evaluated as being of good or acceptable methodological quality [3],[41], [46].
We decided to present our results in an effect vs size plot-presentation, which is visually informative [47]. From the plot, including all trials regardless of dose, one can deduct a slight tendency towards publication bias in favour of small trials publishing negative results. Our effect size plot resembles that of a ”funnel plot”, which is often thought to strengthen the evidence of effect [47]. In fact all the three largest trials seem to converge towards the calculated mean effect of 32 % better than placebo. As this value complies well with the results of the laboratory trials on collagen tissue, this further strengthens our conclusion.

The patient sample mainly consisted of subacute and long-lasting cases of tendinopathy with a 3-4 month average duration of symptoms and, thus the review conclusion is limited to this stage of the natural history of tendinitis. Two trial reports suggested that the duration of symptoms was inversely related to treatment success, when symptom duration was dichotomized to either more or less than 3 months [43], [48]. Whether LLLT can reduce pain in acute tendinitis/bursitis remains to be evaluated.

CONCLUSION

LLLT has a credible biological action on tendon tissue when used with power density and dose within a suggested optimal range. There is a highly significant correlation between the suggested optimal range and a successful treatment result for subacute tendinitis. An optimal treatment procedure includes laser exposure at the skin directly overlying the injured tendon daily or every second day for at least 2 to 4 weeks. Treatment dose and power density must be differentiated for various tendon locations according to laser type, distance from skin surface and the volume of injured tissue.

Nine randomised controlled clinical LLLT-trials, the majority being of acceptable methodological quality, have shown a significant effect of LLLT in the order of 32 % (23 – 41, CI 95 %) on pain intensity according to our statistical pooling. LLLT appears to be an effective and safe alternative in the treatment of subacute tendinopathy if location-specific dose and a valid treatment procedure is used. However, a number of questions about LLLT remain unanswered. LLLT`s role when used in combination with other interventions, and especially exercises, in the remodelling phase of the tendon repair, may be the most important for future investigations.

Table 1 :

”ESTIMATIONS OF CHARACTERITICS OF TENDONS: DEPTH, CROSS-SECTIONAL DIAMETER AND AREA”

Tendon	**Depth to target tendon (mm)**	**Sagittal cross sectional diameter of normal tendon (mm)**	**Typical sagittal area of tendon defect (mm^2)**
Plantar fascia	8.0 - 12.0	3.0 – 4.0	0.5 - 8
Achilles	1.5 – 3.0	4.0 – 6.0	5 – 20
Patellar	2.5 – 4.0	5.0 – 7.0	10 – 30
Lat. epicondyle	1.5 – 2.5	2.0 – 3.0	0.5 – 10
Rotator cuff	5.0 – 10.0	5.0 - 7.0	5 – 25

Table 2 :

OPTIMAL DOSE-RANGES FOR THE MOST COMMON TENDINOPATHIES

	IR 820 – 830 nm		**IR 904 nm**		**HeNe 632 nm**	
Tendon	Power density	Dose	Power density	Dose	Power density	Dose
Plantar fasciitis	0.010 – 0.200	1.4 - 14	0.004 – 0.200	0.6 - 6	0.030 – 0.600	4.2 - 42
Achilles	0.005 – 0.100	0.7 - 7	0.002 – 0.100	0.3 – 3	0.010 – 0.200	1.4 - 14
Patellar	0.005 – 0.100	0.7 - 7	0.002 – 0.100	0.3 – 3	0.010 – 0.200	1.4 – 14
Epicondylitis	0.005 – 0.100	0.7 - 7	0.002 – 0.100	0.3 - 3	0.010 – 0.200	1.4 - 14
Rotator cuff	0.030 – 0.600	4.2 - 42	0.012 – 0.600	0.4 - 4	0.120 – 0.600	12.6 – 126

Table 2: Suggested optimal range of power density in Watts/ cm^2 and dose in Joules/ cm^2 for the most common tendon injuries when treated by infrared GaAlAs (continuous) lasers with wavelength 820-830 nm, infrared GaAs (pulse) lasers with wavelength 904 nm, and red HeNe (continuous) lasers with wavelength 632 nm respectivel

Table 3: **LIST OF EXCLUDED TRIALS**

Author	**Year**	**Diagnosis**	**Result**	**Reason for exclusion**
Holmich[28]	1999	Adductor tendinopathy	Exercise therapy significantly better than LLLT	Comparative study, lacks placebo control
Simunovic[31]	1998	Lateral and medial epicondylopathy	Significantly better than placebo	Lacked specific endpoint and individualised number of treatments. Only bilateral conditions were given placebo treament, but data for this group were not presented
Mulcahy[27]	1995	Painful musculoskeletal conditions	No significant differences	Lacks credible placebo control as only 3 patients had tendinitis in placebo group
Haker [30]	1991 a	Lateral epicondylopathy	No significant differences	Did not irradiate the tendon due to incorrect application procedure
Haker[49]	1990	Lateral epicondylopathy	No significant differences	Did not irradiate tendon, acupuncture points only
Lundeberg[26]	1987	Lateral epicondylopathy	No significant differences	Did not irradiate tendon, acupuncture points only
Siebert[29]	1987	Epicondylopathy mostly	No significant differences	Gave active laser treatment (2.25J/cm) to placebo group, and consequently lacks placebo control

Table 3 : List of excluded studies. First author, year, diagnoses included, result of study and reason for exclusion are listed

Table 4: **LIST OF INCLUDED TRIALS**

Author	**Year**	**No. of patients**	**Diagnosis**	**Results** * p<0.05 **p<0.01	**Laser-type**	**Power density** W/cm^2	**Dose** J/cm^2
Palmieri[50]	1985	30	Epicondylitis	38 % *	904 nm (P)	0.050	1.8
Gudmundsen[43]	1987	108 (200)	Epicondylitis	39 % *	904 nm (M)	0.030	1.2
Haker[39]	1991b	49	Epicondylitis	34 % **	904 nm (P)	0.090	1.2
Vasseljen[32]	1992	30	Epicondylitis	17 % *	904 nm (M)	0.006	3.5
Løgdberg-Andersson[48]	1997	38 (142)	Epicondylitis	31 % **	904 nm (P)	0.090	0.5-1.0
Papadopuolos[36]	1996	29	Epicondylitis	-35%	820 nm (P)	*0.714*	*30*
Krasheninnikoff[35]	1994	36	Epicondylitis	0 %	830 nm (P)	*0.110*	*13.2*
Gudmundsen[43]	1987	92 (200)	Rotator cuff	27 % *	904 nm (M)	0.030	1.2
England[51]	1989	20 (30)	Rotator cuff./ biceps	25 % **	904 nm (P)	0.050	1.2
Vecchio[40]	1993	36	Rotator cuff	21 %	830 nm (P)	0.428	42.8
Saunders[33]	1995	34	Rotator cuff	40 % *	820 nm (P)	0.572	30
Løgdberg-Andersson[48]	1997	60 (142)	Rotator cuff	31 % *	904 nm (P)	0.090	0.5-1.0
Meier[52]	1988	58 (110)	Patellar	32 % *	904 nm (M)	0.030	1.5
Meier[52]	1988	52 (110)	Achilles	40 % *	904 nm (M)	0.030	1.5
Darre[53]	1994	89	Achilles	10%	830 nm (P)	*0.150*	*20*
Basford[34]	1998	28	Plantar fasciitis	3% (median)	830 nm (P)	*0.955*	*31.5*

Table 4: First author, publication year, number of participants in trial. Figures given in parentheses indicates the total number of participants when the trial included several diagnoses. Diagnosis, percentual difference in effect between laser and placebo groups with asterics indicating level of significance if found, type of laser with abbreviations in parentheses being P which indicates a single point laser and M a multidiode laser, power density calculated as energy delivered per second divided on the skin area exposed by the laser beam, and dose calculated as total energy delivered divided by the area on the skin exposed by the laser beam. Values in italics in the last two columns, indicate that the values are outside the limits for optimal range.

FIGURE 1

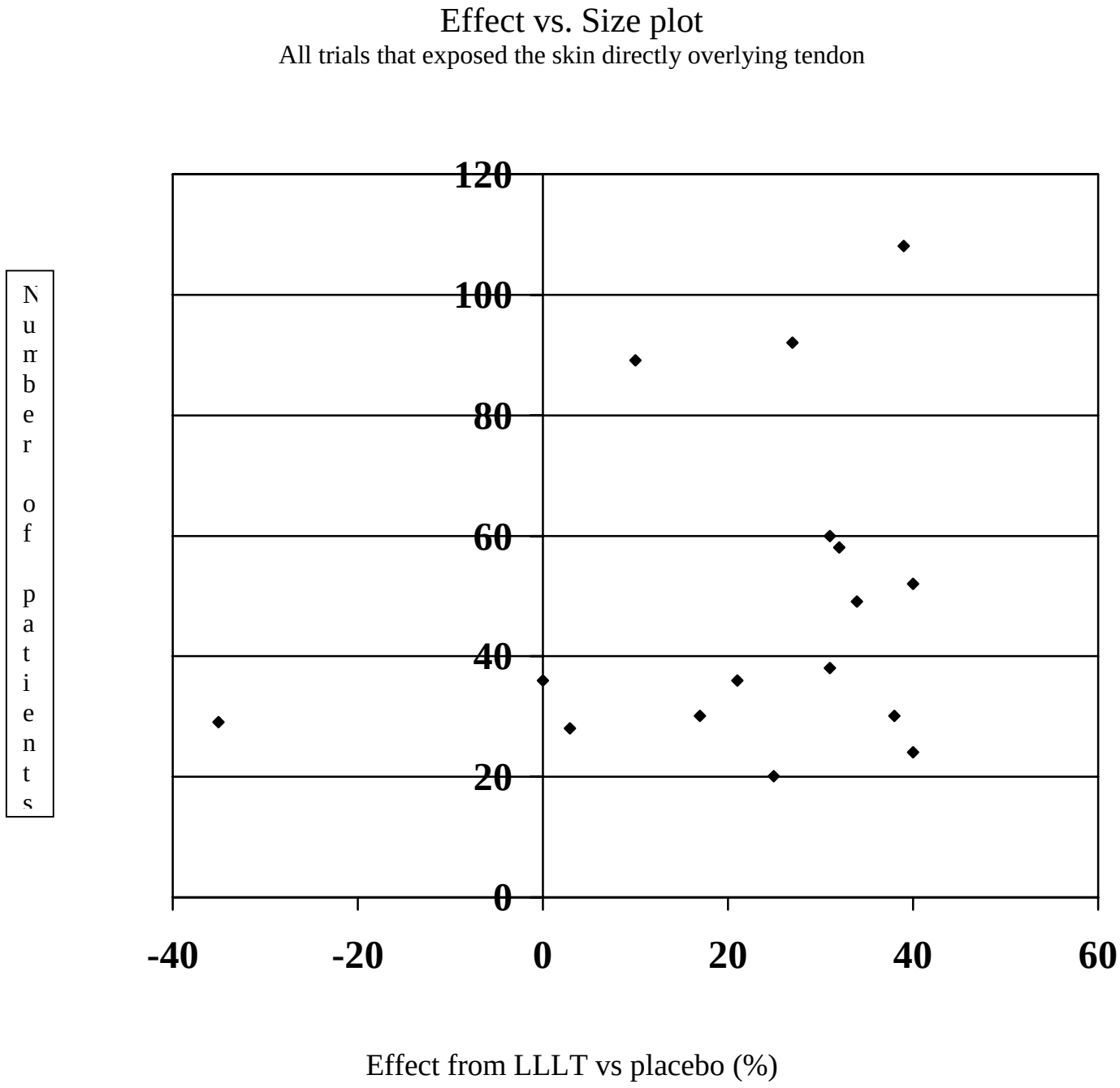

Figure 1: All trials are plotted by their size (number of patients included) (y-axis) and the difference in percentual effect when compared to placebo (x-axis). The trials without optimal treatment dose are found as the four points farthest to the left-hand side of the figure.

Figure 2

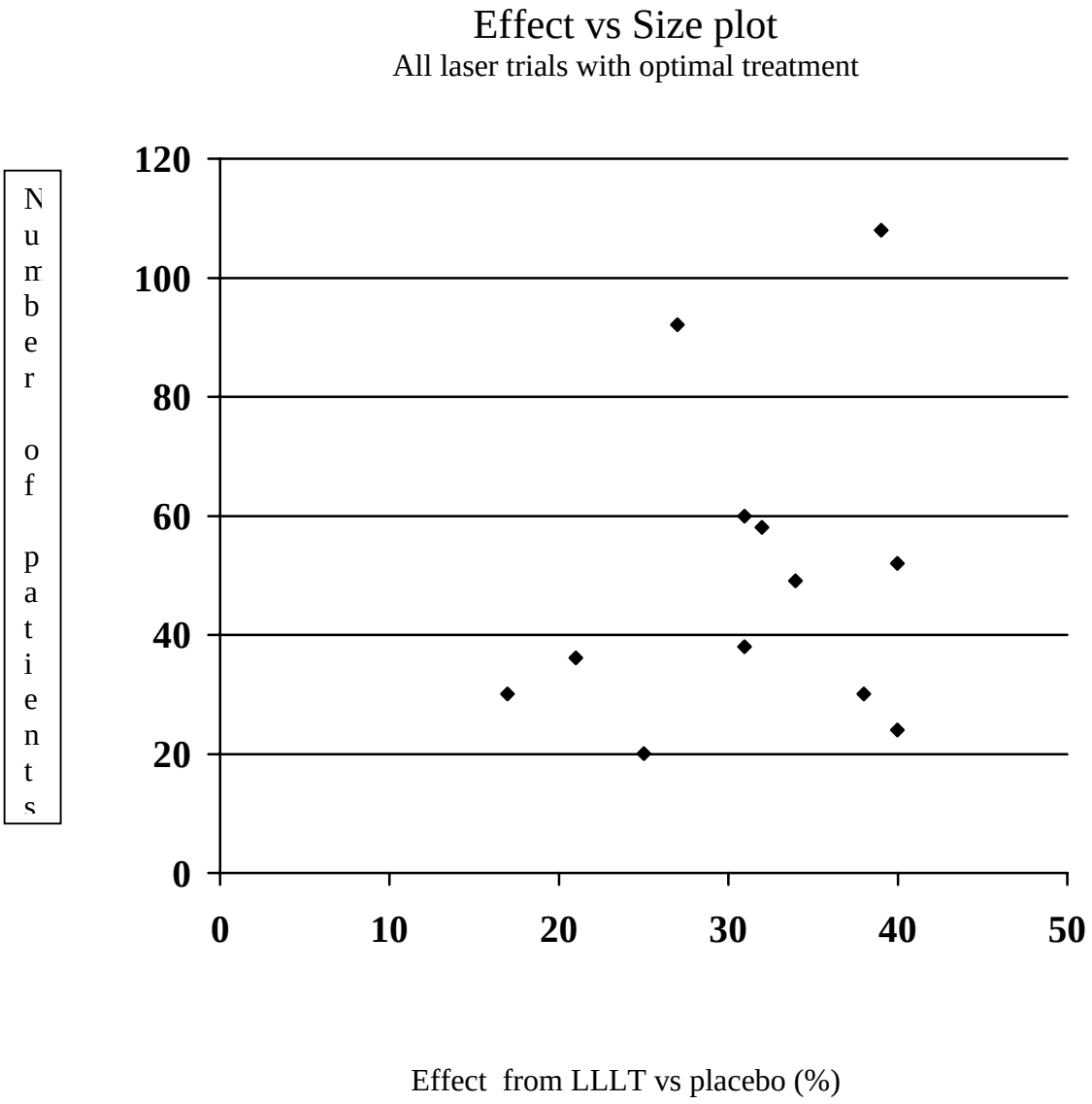

Figure 2: Trials with optimal treatment are plotted by their size (number of patients included) (y-axis) and the difference in percentual effect when compared to placebo (x-axis)

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Overview of Therapeutic Ultrasound Applications and Safety Considerations

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Summary

Applications of ultrasound in medicine for therapeutic purposes have been an accepted and beneficial use of ultrasonic biological effects for many years. Low power ultrasound of about 1 MHz frequency has been widely applied since the 1950s for physical therapy in conditions such as tendinitis or bursitis. In the 1980s, high pressure-amplitude shockwaves came into use for mechanically resolving kidney stones, and “lithotripsy” rapidly replaced surgery as the most frequent treatment choice. The use of ultrasonic energy for therapy continues to expand, and approved applications now include uterine fibroid ablation, cataract removal (phacoemulsification), surgical tissue cutting and hemostasis, transdermal drug delivery, and bone fracture healing, among others. Undesirable bioeffects can occur including burns for thermal-based therapies and significant hemorrhage for mechanical-based therapies (e. g. lithotripsy). In all these therapeutic applications for bioeffects of ultrasound, standardization, ultrasound dosimetry, benefits assurance and side-effects risk minimization must be carefully considered in order to insure an optimal benefit to risk ratio for the patient. Therapeutic ultrasound typically has well-defined benefits and risks, and therefore presents a tractable safety problem to the clinician. However, safety information can be scattered, confusing or subject to commercial conflict of interest. Of paramount importance for managing this problem is the communication of practical safety information by authoritative groups, such as the AIUM, to the medical ultrasound community. In this overview, the Bioeffects Committee outlines the wide range of therapeutic ultrasound methods, which are in clinical use or under study, and provides general guidance for assuring therapeutic ultrasound safety.

Introduction

Ultrasound has seen development not only as a diagnostic imaging modality but as a therapeutic modality in which energy is deposited in tissue to induce various biological effects. Medical uses of ultrasound for therapy began to be explored in the 1930s. Early applications were tried for various conditions using the mechanism of tissue heating (Lehmann, 1953). Over the following decades, scientific advances allowed improved methods for effective treatment of Meniere’s disease by destruction of the vestibular nerve, and of Parkinson’s disease using focused ultrasound for localized tissue destruction in the brain (Fry et al. 1954; Newell, 1963). By the 1970’s, the use of therapeutic ultrasound was established for physiotherapy, and research continued on more difficult applications in

neurosurgery (Wells, 1977), and for cancer treatment (Kremkau, 1979). Subsequently, the development of therapeutic ultrasound has accelerated with a wide range of methods now in use. The potent application of ultrasound for therapeutic efficacy also carries the risk of unintentional adverse bioeffects which can lead to significant, even life threatening patient injury. Therefore, standardization, ultrasound dosimetry, benefits assurance and side-effects risk minimization must be carefully considered in order to insure an optimal outcome for the patient.

The purpose of this review is to briefly outline the recent development of therapeutic ultrasound applications and specialized devices, which have been approved for use, together with associated safety considerations. Therapeutic applications of ultrasound may be used clinically after government approval (e. g. by the Food and Drug Administration (FDA) in the United States) for marketing suitable treatment devices. A list of therapy applications with FDA approved devices in clinical use is provided in Table 1. The fundamental basis behind the ultrasound mediated deposition of energy and mechanisms for biological effects are discussed. This is followed by a discussion of ultrasound treatment methods using heating, which include physical therapy, hyperthermia and high-intensity focused ultrasound. Nonthermal applications are then reviewed, including extracorporeal shock wave lithotripsy, intracorporeal lithotripsy and lower power kilohertz frequency ultrasound devices. Some ultrasound therapy methods have uncertain, possibly multiple mechanisms, including skin permeabilization for drug delivery and low-intensity pulsed ultrasound, which can accelerate the healing of bone fractures. Prospective new methods of therapeutic ultrasound are mentioned at the end, including new microbubble- or cavitation-based treatment methods. Lastly, the reader is reminded about important safety considerations and general guidelines are presented. There is no doubt that continued biophysical discoveries in ultrasound will lead to new treatments and applications. As therapeutic ultrasound's renaissance continues, new treatments already well established in the laboratory will be translated in the near future to the clinic.

The Biophysical Bases for Therapeutic Ultrasound Applications

Ultrasonic energy can be a potent modality for generating biological effects. Given sufficient knowledge of the etiology and exposimetry, bioeffects can be planned for therapeutic purposes or avoided in diagnostic applications. For therapy, ultrasound can induce effects not only through heating, but also through nonthermal mechanisms including ultrasonic cavitation, gas body activation, mechanical stress or other undetermined nonthermal processes (Nyborg et al. 2002).

Starting from the diagnostic reference frame, ultrasound is usually produced from a piezoceramic crystal in very short, i.e., 1- to 5-cycle, pulses. Diagnostic ultrasound is often characterized by the center frequency of the pulses (typically in the 2–12 MHz range), which is usually a frequency inherent to the thickness of the ceramic crystal. As the pressure amplitude, the frequency, or the propagation length is increased, the ultrasound wave can distort, which could ultimately lead to a discontinuity or shock in the waveform. In regard to bioeffects, increasing frequency, nonlinear acoustic distortion, or pulse length can increase heating and enhance some nonthermal mechanisms, e.g., radiation force. Decreasing frequency increases the likelihood of cavitation and gas body activation. Increasing power or intensity tends to increase the likelihood and magnitude of all bioeffects mechanisms. Therapeutic ultrasound devices may use short bursts or continuous waves to deliver effective ultrasonic energy to tissues. Some devices operate at higher amplitude and therefore tend to produce shocked or distorted waves.

Ultrasound-induced heating is the result of the absorption of ultrasonic energy in biological tissue. For diagnostic ultrasound, temperature elevations and the potential for bioeffects are kept relatively low or negligible (Fowlkes et al. 2008) by carefully described indications for use, applying the ALARA (as low as reasonably achievable) principal, limited temporal average intensities, and generally short exposure durations. Therapeutic applications of ultrasonic heating therefore either utilize longer durations of heating with unfocused beams, or utilize higher intensity (than diagnostic) focused ultrasound. The use of unfocused heating, for example in physical therapy to treat highly absorbing tissues such as bone or tendon, can be moderated to produce enhanced healing without injury. Alternatively, the heat can be concentrated by focused beams until tissue is coagulated for the purpose of tissue ablation. Ultrasound heating which can lead to irreversible tissue changes follows an inverse time-temperature relationship. Depending on the temperature gradients, the effects from ultrasound exposure can include mild heating, coagulative necrosis, tissue vaporization, or all three.

Ultrasonic cavitation and gas body activation are closely related mechanisms which depend on the rarefactional pressure amplitude of ultrasound waves. Ultrasound transmitted into a tissue may have rarefactional pressure amplitudes of several megaPascals (MPa). This tensile stress is supported by the medium and, for example, a 2-MPa rarefactional pressure, which is common even for diagnostic ultrasound, represents a negative tension 20 times atmospheric pressure (i. e., 0.1 MPa). This high rarefactional pressure can act to initiate cavitation activity in tissue when suitable cavitation nuclei are present, or directly induce pulsation of pre-existing gas bodies, such as occur in lung, intestine, or with ultrasound contrast agents. Cavitation and gas body activation primarily cause local tissue injury in the immediate vicinity of the cavitational activity, including cell death and hemorrhage of blood vessels.

Other potential mechanisms for biological effects of ultrasound include the direct action of the compressional, tensile, and shear stresses. In addition, second-order phenomena, which depend on transmitted ultrasound energy, include radiation pressure, forces on particles and acoustic streaming. For high-power or high-amplitude ultrasound for therapy, several different mechanisms may be contributing concurrently to the total biological impact of the treatment. In addition to direct physical mechanisms for bioeffects, there are secondary physical, biological, and physiological mechanisms that cause further impact on the organism. Some examples are vasoconstriction, ischemia, extravasation, reperfusion injury, and immune responses (e.g., Alves et al. 2009, Hundt et al. 2007, Silberstein et al. 2008). Sometimes these secondary effects are greater than the direct insult from the ultrasound.

Therapeutic Applications of Ultrasound Based on Heating

Physical Therapy

Unfocused beams of ultrasound for physical therapy were the first clinical application, dating to the 1950s, which often has been referred to simply as “therapeutic ultrasound” (Robertson and Baker, 2001). This modality now typically has a base unit for generating an electrical signal and a hand-held transducer. The hand-held transducer is applied with coupling gel and moved in a circular motion over an injured or painful area of the anatomy to treat conditions such as bursitis of the shoulder or tendonitis, by trained physical therapy technicians. The objective is to warm tendons, muscle and other tissue to improve blood flow and accelerate healing. The coupling medium can also include various compounds for enhancing the treatment. Ultrasound application can also assist by promoting transport of the compound into the skin, a method sometimes called sonophoresis or phonophoresis (as opposed to electrophoresis) (Machet and Boucaud, 2002). Drugs such as lidocaine or cortisol have been used extensively in sports medicine. The level of clinical benefit to the

patient from physical therapy ultrasound treatments remains uncertain (Robertson and Baker, 2001; Baker et al. 2001; Alexander et al. 2010). However, the risk of harm such as burns, appears to be low when the modality is properly applied. Overall, ultrasound for physical therapy has therefore provided a modest level of efficacy and patient benefit, but also a low level of risk.

Hyperthermia

A substantial effort during the 1980s and 1990s sought to develop means to ultrasonically heat relatively large volumes of tissue for the purpose of cancer therapy. This method of hyperthermia involves uniformly heating a tumor to about 42 °C for periods of about 1 hour, which appears to be effective in reducing tumor growth (Sapareto and Dewey, 1984). Multi-element applicators have been used at 1–3.4 MHz (Samulski et al. 1990; Diederich and Hynynen, 1999). In clinical trials, hyperthermia was used with or without radiation therapy and modest efficacy has been reported (Marchal, 1992). Research suggests that hyperthermia may be advantageous for drug delivery treatment using nanoparticles (Kong et al. 2000). However, the moderate-temperature hyperthermia method has not progressed to widespread clinical usage, and the effort in hyperthermia cancer treatment has shifted to the use of high intensity focused ultrasound.

High Intensity Focused Ultrasound

High intensity focused ultrasound (HIFU, or HIFUS) was initially studied clinically for thermal ablation of inoperable brain tissue for Parkinson's disease (Fry et al. 1954; Kennedy et al 2003). In a HIFU system, a signal generator is connected to a focusing transducer, which produces very high local intensities of >1 kW/cm^2 of 0.5–7 MHz ultrasound at the focal spot. The lesion produced in tissue typically may be a few mm in diameter and in length. The position of this spot must be carefully controlled and moved in order to ablate larger volumes of tissue. This method is approved by the FDA in the USA for treating uterine fibroids (Tempany et al. 2003), cardiac ablation (Ninet et al. 2005), visceral soft tissue ablation (Klingler et al. 2008), and aesthetic treatment to lift the eyebrow (Gliklich et al. 2007; Alam et al. 2010). In addition, a method was developed and was approved for treatment of glaucoma using HIFU (Burgess et al. 1986).

In addition to the devices approved by the FDA for clinical use, there are several procedures that are being investigated for clinical application (Evans et al. 2007). HIFU application in therapy and treatment of disease is one of the more active areas of research and development among all the non-ionizing-energy modalities such as radiofrequency, lasers, and microwaves. For example, HIFU is under investigation for therapeutic modulation of nerve conductance (Foley et al. 2008). Among other applications, the oldest and possibly the most investigated area (particularly outside the USA) is the treatment of benign prostatic hyperplasia (BPH) and the treatment of prostate cancer using HIFU. A number of multi-center and systematic studies with several-year follow up has established the use of HIFU as a viable option for the management of prostate cancer (Gelet et al. 2000; Thüroff et al. 2003).

A key element of therapeutic applications with ultrasound energy is the capability to focus energy several millimeters to centimeters away from the transducer plane. It is therefore, very important to accurately determine the location of the treatment zone with ultrasound systems. Further, the tissue changes in the treatment zone must be reliably monitored, in order to confirm that adequate treatment has been achieved. The focused ultrasound beam can then be moved to a different location to complete the treatment of the planned volume. Two methods used for image guidance and treatment monitoring are magnetic resonance imaging (MR) and ultrasound imaging. MR imaging can measure temperature changes

during therapy, within the treatment zone of therapeutic ultrasound procedures (Jolesz, 2009). Specialized clinical systems have ultrasound therapy sub-systems integrated into MR-imagers, which are used for uterine fibroid treatment (Tempany et al. 2003), breast cancer (Gianfelice et al. 2003), and prostate cancer management (Chopra et al. 2009). Ultrasound based guidance and monitoring offers the possibility of systems that incorporate both the treatment and imaging modality in one compact system. The ultrasound image monitoring of tissue changes during ultrasound therapy is based on a combination of speed of sound, attenuation, stiffness, and vapor content changes in the target region (Fedewa et al. 2006, Larrat et al. 2008), including boiling detection and combined measurement and modeling approaches Anand and Kaczkowski, 2009; Canney et al. 2010).

In addition to external focused devices, a number of other devices and systems are being developed for soft tissue coagulation which are primarily used in non-invasive approaches, or through natural orifices such as the transrectal approach for prostate treatments (Makin et al. 2005). For example, transurethral ultrasound has been proposed for heating the prostate (Kinsey et al. 2008; Chopra et al. 2009), and endoscopic treatment using an intraductal ultrasound probe has been used to treat bile duct tumors (Prat et al. 2002).

Significant research and development are being pursued in the area of non-invasive aesthetic applications. Focused ultrasound in these applications is directed within the first 2 – 20 mm of the skin and subcutaneous tissue (dermis – subcutaneous fat). Very small lesions of ~1 mm^3 up to several 10s of cm^3 can be produced. The approach may provide a safer alternative to liposuction for cosmetic applications (Moreno-Morega et al. 2007). Superficial tissue is exposed to HIFU leading either to a contraction of collagen based tissue (dermis) or to destruction of adipose tissue (Gliklich et al. 2007; White et al. 2007). A clinical system has been approved for fat debulking in the European Union and Canada (Fatemi, 2009). Depending on the device, as well as the cosmetic application, both thermal as well as non-thermal mechanisms within an ultrasound field are employed for these procedures. One of these devices is currently approved for clinical use in the USA (Alam et al. 2010), and others are in use worldwide. Long term utilization of this technology, as well as regulatory approval, is still evolving.

HIFU applications involve delivery of substantial ultrasonic energy to localized areas, and undesired tissue injury is always a consideration. Typically, unwanted burns and pain can occur. In addition, HIFU can cause vasospasm and hemorrhage under conditions which generate concomitant cavitation in tissue (Hynynen et al. 1996). Other significant bioeffects and complications can also occur with unique risk-benefit considerations for each application. Treatment of the prostate, such as for prostate cancer, can lead to several urologic complications, including impotence and incontinence (Rove et al. 2010), which can also accompany other types of treatment for prostate cancer. HIFU has been used to treat atrial fibrillation by tissue ablation to produce pulmonary vein isolation. However, severe complications can occur due to creation of an atrial-esophageal fistula (Borchert et al. 2008), a concern which is difficult to eliminate (Neven et al. 2010). Treatment of hepatic and pancreatic cancer can also lead to serious complications, including fistula formation and rib necrosis with delayed rib fracture (Jung et al. 2010). Detailed safety considerations should accompany the introduction of HIFU applications into clinical practice in order to assure benefit, while minimizing risk to the patient.

Therapeutic Applications of Ultrasound Based on Non-Thermal Mechanisms

Extracorporeal Shock Wave Lithotripsy

Extracorporeal shockwave lithotripsy (ESWL) is a widely used ultrasound therapy, which relies on nonthermal mechanisms for its efficacy (McAteer et al. 2005; Weizer et al. 2007). When introduced in the 1980s, lithotripsy gained rapid acceptance and became the dominant treatment method. Shock wave devices similar to lithotripters are approved and marketed for orthopedic indications such as plantar fasciitis and epicondylitis (Haake et al. 2003). The use of shockwaves for treating other problems, such as gall bladder stones, has also been explored, but none have achieved widespread usage. Over 50 lithotripter devices have been on the USA market. Fluoroscopy is used for targeting the acoustic focus on the stone in the USA, although some lithotripters have B-mode ultrasound for targeting. The first lithotripters were electrohydraulic, using an underwater spark source and a reflector. Most lithotripters now are of the electromagnetic design, which deposits a high transient current through a coil that in turn produces a displacement of a plate. Very few lithotripters utilize piezoceramic sources. All produce about the same waveform: a 1-μs shocked spike of about 50 MPa followed by a ~10-MPa, 4-μs negative pressure tail. The center frequency might be estimated to be about 150 kHz although this is not a commonly determined parameter. There was a trend to more focused machines, relative to early spark gap models, but that has fallen out of favor. Evidence has been presented for a reduction in clinical effectiveness and safety for highly focused shockwaves (McAteer et al. 2005), and for the dependence of fragmentation mechanisms on beam width (Eisenmenger, 2001; Sapozhnikov et al. 2007).

For ESWL treatment, the source is coupled to the patient by a water pillow and transmission gel, and in the remaining original lithotripters through a water bath. Coupling has recently been recognized as a significant factor in ESWL treatment efficacy; a point that has implications across therapeutic ultrasound (Pishchalnikov et al. 2006). About 3000 shock waves are triggered at about 2 Hz repetition rate to pulverize the stone so that the pieces (<2mm) can pass naturally in urine. The prominent mechanism is the wave running over the stone creating shear waves to tear the stone apart from within. Cavitation chips away from the outside, adding cracks that grow by dynamic fatigue and further grind down the stone to passable size (Sapozhnikov et al. 2007).

Lithotripsy has several important biological side effects. Lithotripsy causes injury to virtually all patients (Evan and McAteer, 1996). Blood vessel walls break, and there is bleeding into the connective tissue interstitium, which can result in bruising of the parenchyma or the formation of massive subcapsular hematomas. Inflammation ensues (i.e. lithotripsy nephritis), which can lead to scar formation (Koga et al. 1996) and permanent loss of functional renal mass (Evan et al. 1998). In addition to and likely a result of this direct injury cascade, lithotripsy can lead to an accelerated rise in systemic blood pressure, a decrease in renal function, onset of hypertension, an increase in the rate of stone recurrence, and an exacerbation of stone disease (Janetschek et al. 1997; Krambeck et al. 2010). A single retrospective study has linked lithotripsy and diabetes mellitus (Krambeck et al. 2006).

The risks of these adverse bioeffects in lithotripsy have stimulated investigation into mitigation methods with some success (McAteer et al. 2005). For example, a slower repetition rate (1 Hz) is safer and more effective than the common fast rate (2 Hz) (Pace et al. 2005), and a pause early in treatment nearly eliminates injury in animals (Weizer et al. 2007; Handa et al. 2009). Overall, lithotripsy has been a therapeutic ultrasound method with a high level of efficacy and patient benefits, but also some important risks particularly for

patients requiring repeated treatments. The development of safer treatment protocols for lithotripsy is a prime example of the potential value of research on risk mitigation for optimizing the patient risk/benefit profile in therapeutic ultrasound.

Intracorporeal lithotripsy

Lithotripsy is also accomplished by minimally invasive probes which are advanced to the stone. Intracorporeal lithotripsy is the favored treatment for many patients, for example for very large stones, and many different methods and techniques have been reported. The stone may be imaged for guidance by external ultrasound or fluoroscopy, or by ureteroscopic, endoscopic or laparoscopic methods. Rigid probes may be manipulated percutaneously, but some flexible probes can be applied via the ureter. Rigid ultrasonic probes can utilize both pneumatic action at a few Hz to 1,000 Hz, and ultrasonic action at about 25 kHz (Kim et al. 2007; Lowe and Knudsen, 2009). Electrohydraulic probes, which generate a vaporous cavity at the tip (similar to the spark gap external lithotripter but without focusing) (Noor Buchholz, 2002), have been used in the past. Intracorporeal lithotripsy carries risk of hemorrhage, ureteral perforation, urinary tract trauma, and infection due to the invasive nature of the procedures.

Kilohertz-Frequency Ultrasound Devices

Ultrasonic systems operating in the kHz-frequency regime (20 – 90 kHz), similar to “sonicators” used in biological research to break up cells and tissues, are used routinely in general and advanced surgical procedures for tissue cutting and hemostasis as well as for tissue removal. These appear to act primarily though localized biophysical effects close to the probe tip, rather than via radiated ultrasound waves. For example, a kHz-frequency ultrasound probe is used for phacoemulsification to remove the lens of the eye during surgery for cataracts (Packer et al. 2005). The probe appears to mechanically chop up the lens, possibly aided by ultrasonic cavitation, with the lens debris removed by suction through the probe. The procedure is well established in ophthalmology and minimizes the impact on the lens capsule.

Surgical ultrasonic instruments, known as “harmonic scalpels”, have a 40 – 80 kHz vibrating titanium rod with a static clamp member, between which the tissue (and blood vessels) is rapidly coagulated due to localized frictional heating (Koch et al. 2002). Another procedure, ultrasound assisted liposuction, is widely used in cosmetic surgery for the purpose of removing excessive fat tissue (Mann et al. 2008). The mechanism of action apparently involves cavitational fat cell break up with removal of the fat emulsion by suction through the probe. This procedure is invasive, and can lead to complications such as bleeding, scarring and infection.

Therapeutic Applications of Ultrasound with Multiple Mechanisms

Catheter Based Ultrasound

Intravascular catheters have been developed with MHz-frequency ultrasound transducers placed near the tip for enhancing dissolution of thrombi (Parikh et al. 2008). The catheter is placed into a deep vein thrombus and the ultrasound is directed radially into the thrombus. In addition, there are provisions for infusion of thrombolytic drugs, such as tissue plasminogen activator. The ultrasound accelerates the action of the thrombolytic drugs so that the total infusion dose of drugs and treatment times can be reduced significantly. The role of this method, and the full range of its clinical usefulness for thrombolysis is still being evaluated.

Skin Permeabilization

For transdermal drug delivery, the *stratum corneum* (≈ 10–30 μm) forms a barrier to passive drug diffusion for molecules which have a weight greater than 500 Da (Boucaud 2004). One effect of low-frequency ultrasound (<100 kHz) is its ability increase permeability of the *stratum corneum*, which is considered to be a primary barrier to protein diffusion (Pitt et al. 2004; Mitragotri and Kost 2004). The treatment can be monitored by measuring the electrical skin conductance (Farinha et al. 2006). Once a drug has traversed the *stratum corneum*, the next layer is easier to cross and subsequently the drug can reach the capillary vessels to be absorbed (Mitragotri et al. 1995). This skin permeabilization method may be useful for avoiding the multiple use of needles, for example, for delivery of heparin or insulin through the skin (Smith, 2008).

Low Intensity Pulsed Ultrasound

Low intensity pulsed ultrasound has therapeutic application to accelerate the healing of bone fractures including cases of nonunion (Gebauer et al. 2005). The characteristics of the pulsed ultrasound, for example, 1.5-MHz frequency with 30-mW/cm^2 spatial average temporal average intensity, are in the range of diagnostic ultrasound. The biophysical mechanisms for the therapeutic action are uncertain for this application. Therapy involves multiple treatments of 20 min each day by applying the large flat transducer to the site of injury and continuing treatment for periods of months. Although the process appears to be safe and effective, the therapy is slow and its use is predominantly limited to management of non-healing fractures.

Prospective New Methods of Therapeutic Ultrasound

In this era of ultrasonics research, several new means of applying ultrasound for therapy are undergoing intensive research and development. The novel methods utilize low frequency, moderate power ultrasound aided by stabilized microbubbles for gas body activation, or very high power pulsed ultrasound with vigorous cavitation.

Direct sonothrombolysis using external, typically low frequency ultrasound has been tested for treatment of thrombotic disease, such as stroke (Siegal and Luo, 2008). This new strategy shows promise, but also has shown a potential for deleterious side effects. For example, increased brain hemorrhage was found in a clinical trail for treatment with 300 kHz ultrasound plus tissue plasminogen activator relative to treatment with tissue plasminogen activator alone (Daffertshofer et al. 2005). Recent work suggests that microbubbles enhance thrombolysis and may be of value in improving stroke therapy (Hitchcock and Holland, 2010).

Another potential application in brain utilizes transcranial pulsed ultrasound (0.25 – 0.5 MHz), at relatively low levels (I_{SPTA} = 26–163 mW/cm2), to produce cortical and hippocampal stimulation in mice (Tufail et al. 2009). Since measured temperature gradients were <0.01°C, nonthermal mechanisms for the neuronal effects were hypothesized.

Microbubble-based therapeutic strategies are under study for ultrasound directed and targeted therapy. In these strategies, the external ultrasound exposure activates microbubbles in the circulation, which may also act as drug carriers, at a desired site of treatment. Microbubble contrast agents have also found applications in improving the therapeutic efficacy of biologically active molecules (Tinkov et al. 2009). Several possible mechanisms include the enhancement of (1) the concentration of therapeutic biomolecules in the vascular compartment of the target area, (2) increased therapeutic agent delivery by extravasation through blood vessels, and (3) potentially enhanced intracellular delivery. Molecules of the therapeutic agent can be attached to the outer shell of bubbles, incorporated within the

bubble shell or loaded into the interior of microbubbles and released in the vascular compartment through ultrasound-induced microbubble disruption (Unger et al. 2004; Ferrara et al. 2007). The extravasation of a therapeutic agent is achieved through the permeabilization of blood vessels with ultrasound and microbubbles, for example, to cross the blood-brain barrier (Vykhodtseva et al. 2008). The ultrasound-microbubble based delivery of therapeutic agents has one main advantage over other techniques using colloidal drug carriers such as nanoparticles or liposomes: The microbubble-based technique may be targeted through the external control of the ultrasound. This localized approach may then improve the therapeutic efficacy of drugs, such as routinely used chemotherapeutic agents like paclitaxel. The dose of agent to normal tissue is lowered, with a consequent minimization of unwanted drug effects away from the treatment site (Tartis et al. 2006). At the cellular level, ultrasound with microbubbles can be used to transiently permeabilize cell membrane, allowing transfer of large molecules into the cells. DNA transfer has been demonstrated in extensive research on gene therapy applications (Miller, 2006).

The cavitation mechanism is also being exploited to create a new tissue-ablation method known as histotripsy (Kieran et al 2007). In histotripsy (akin to lithotripsy pulses but at a higher frequency), very high amplitude ultrasound pulses typically of less than 50 μs duration at 750 kHz create a cavitation microbubble cloud to homogenize targeted tissue such as tumors with little heating (Xu et al. 2008). Longer HIFU pulses (e. g. >3 ms at 2 MHz) of very high intensity can induce rapid heating and also generate cavitation and boiling with vapor bubbles that expand very rapidly, thus disrupting tissue (Canney et al. 2010).

Because cavitation is a mechanism secondary to the ultrasound exposure, the problems of dosimetry and control are challenging. Determining the energy deposited by ultrasound with cavitation is difficult under the best of circumstances (Apfel 1981; Hamilton and Blackstock, 1998). For cavitating ultrasound, researchers try to follow three rules: (i) understand the medium (including cavitation nuclei), (ii) understand the sound field and (iii) know when a cavitation effect happens (Apfel 1981). The first rule refers to the cavitation threshold while the second rule relates to accurate measurements of the acoustic field. The third relates to observable cavitation events or secondary related information which can be monitored. There are various reliable and scientifically established methods for quantifying an acoustic field (Lewin and Ziskin 1992; Harris 2005; Shaw and ter Haar 2006; Shaw and Hodnett 2008). Passive detection methods, measuring broadband acoustic noise from bubble collapses for monitoring cavitation activity can be deployed and research has indicated useful dosimetric parameters which may be derived for predicting bioeffects (Hwang et al. 2006). As new cavitation-based treatments are developed, new means for cavitation dosimetry and control will be needed to assure optimum patient safety.

General Guidance for Therapeutic Ultrasound Safety

Therapeutic ultrasound methods provide a substantial armamentarium for medical practice. In addition, ultrasound brings fundamentally favorable safety characteristics to the clinic. For example, ionizing radiation with its dose accumulation and cancer risk is absent from ultrasound methods. Low energy exposures, below the threshold for a bioeffect, do not accumulate to produce the effect, even if repeated many times. The ultrasonic waves are dispersed and poorly transmitted in air: no lead gloves, aprons or other protective gear are needed for ultrasound diagnosis or therapy. However, this powerful modality does require attention to several safety factors in order to achieve the optimum benefit to risk ratio.

Operator safety

The operator of the equipment, for the most part, has little risk of harm from the machines, can remain in the treatment room and safely apply the ultrasound with hand held applicators for some applications. However, simple precautions should be followed for complete operator safety; for example, do not test therapeutic ultrasound equipment on oneself or others (as opposed to diagnostic ultrasound imaging which can be used on volunteer models for training purposes under medical supervision).

Patient safety

Ultrasound therapy machines are, of course, capable of causing substantial bioeffects; therefore, deliberate caution must be exercised to minimize injury for each patient. Patients should be fully informed of possible risks, as well as expected benefits.

Quality assurance

Ultrasound therapy machines are typically complex and subject to deterioration or failure. Each machine should be monitored and tested on a regular basis for safe operation and verification of appropriate ultrasound fields to assure efficacious treatment.

Accumulating biological effect

Although no cumulative dose has been defined for any ultrasound therapy, unwanted bioeffects such as scarring from burns or vascular injury which occur during treatment can accumulate with repeated treatments, and this should be anticipated. For example, animal studies show permanent loss of renal functional mass with each lithotripsy and therefore recurrent treatments add injury to already compromised kidneys.

Risk benefit ratios

The benefits and potential risks associated with different therapeutic ultrasound methods vary widely and should be appreciated by the operator. For example, physical therapy ultrasound appears to have a low risk of harm in the hands of skilled physical therapists, but the expectation of therapeutic benefit is also low. Lithotripsy, in contrast, has the tremendous benefit of non-invasively treating a serious disease, which previously required major surgery, but it also has a risk of significant hemorrhage and longer-term kidney injury.

Safety Research

The search for new applications of this powerful tool should be pursued carefully, with thorough testing in appropriate animal models to identify possible human adverse events before clinical trials begin. Accurate and precise evaluation of acoustic fields in water and in situ should follow exposimetry and dosimetry procedures and numerical modeling previously recognized in the ultrasound literature. Means for monitoring heating or secondary mechanisms, such as acoustic cavitation, should be in place. Furthermore, in order to assure optimum patient benefit from therapeutic ultrasound, dedicated research should continually pursue better and safer methods to enhance present therapies and therapy monitoring.

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Table 1

A listing of FDA approved modes for ultrasound therapy.

			Device Characteristics			
Therapy Method	**Therapeutic Outcome**	**Bioeffect Mechanism**	**Applicator**	**Frequency**	**Delivery**	**General Reference**
Unfocused beam	tissue warming	heating	portable hand-held	1–3 MHZ	continuous or repeated bursts	Robertson and Baker 2001
Hyperthermia	cancer therapy	regional heating	multi-element applicator	1–3.4 MHz	1 hour	Samulski et al. 1992
HIFU	uterine fibroid ablation	thermal lesion	computer directed	0.5–2 MHZ	long bursts	Tempany et al. 2003
HIFU	glaucoma relief	permeabilization	fixed probe with waterbath	4.6 MHZ	1–3 s	Burgess et al. 1986
HIFU	laproscopic tissue ablation	thermal lesion	hand-held	4 MHz	long bursts	Klingler et al. 2008
HIFU	laparoscopic or open surgery	thermal lesion	hand-held	3.8–6.4 MHz	long bursts	Ninet et al. 2005
Focused ultrasound	skin tissue tightening	thermal lesion	hand-held, imaging and treatment	4.4–7.5 MHz	20–50 ms bursts	Alam et al. 2010
Extracorporeal Lithotripsy	kidney stone comminution	mechanical stress; cavitation	mainframe with image guidance	~150 kHz	shockwaves	Weizer et al. 2007
Intracorporeal lithotripsy	kidney stone comminution	mechanical stress; cavitation	Percutaneous probes	25 kHz	continuous	Lowe and Knudsen, 2009
Extracorporeal shockwave therapy	plantar fasciitis epicondylitis	unknown	mainframe with applicator head	~150 kHz	shockwaves	Haake et al. 2003
Phacoemulsification	lens removal	vibration ; cavitation	generator with probe	40 kHz	continuous	Packer et al. 2005
US assisted liposuction	adipose tissue removal	fat liquifaction; cavitation	generator with probe	20–30 kHz	continuous	Mann et al. 2008
Tissue cutting and vessel sealing	laparoscopic or open surgery	thermal lesion, vibration	hand-held	55.5 kHz	continuous	Koch et al. 2002
Intravascular US	thrombus dissolution	unknown; gas body activation	intravascular catheter	2.2 MHZ	continuous	Parikh et. al. 2008
Skin permeabilization	transdermal drug delivery	unknown	hand held	55 kHz	continuous	Smith, 2008
Low intensity pulsed US	bone fracture healing	unknown	attached transducer	1.5 MHz	pulsed, long duration	Gebauer et al. 2005

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Transcutaneous electrical nerve stimulation (TENS) for pain management in labour

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Abstract *available in* English | Français | 日本語

Background

Transcutaneous nerve stimulation (TENS) has been proposed as a means of reducing pain in labour. The TENS unit emits low-voltage electrical impulses which vary in frequency and intensity. During labour, TENS electrodes are generally placed on the lower back, although TENS may be used to stimulate acupuncture points or other parts of the body. The physiological mechanisms whereby TENS relieves pain are uncertain. TENS machines are frequently operated by women, which may increase a sense of control in labour.

Objectives

To assess the effects of TENS on pain in labour.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (30 April 2011) and reference lists of retrieved papers.

Selection criteria

Randomised controlled trials comparing women receiving TENS for pain management in labour versus routine care, alternative non-pharmacological methods of pain relief, or placebo devices. We included all types of TENS machines.

Data collection and analysis

Two review authors assessed for inclusion all trials identified by the search strategy, carried out data extraction and assessed risk of bias. We have recorded reasons for excluding studies.

Main results

Seventeen trials with 1466 women contribute data to the review. Thirteen examined TENS applied to the back, two to acupuncture points, and two to the cranium. Overall, there was little difference in pain ratings between TENS and control groups, although women receiving TENS to acupuncture points were less likely to report severe pain (average risk ratio 0.41, 95% confidence interval 0.31 to 0.54; measured in two studies). The majority of women using TENS said they would be willing to use it again in a future labour. Where TENS was used as an adjunct to epidural analgesia there was no evidence that it reduced pain. There was no consistent evidence that TENS had any impact on interventions and outcomes in labour. There was little information on outcomes for mothers and babies. No adverse events were reported.

Authors' conclusions

There is only limited evidence that TENS reduces pain in labour and it does not seem to have any impact (either positive or negative) on other outcomes for mothers or babies. The use of TENS at home in early labour has not been evaluated. TENS is widely available in hospital settings and women should have the choice of using it in labour.

Plain language summary *available in* English | Français | Hrvatski

TENS (transcutaneous nerve stimulation) for pain relief in labour

TENS is a device that emits low-voltage currents and which has been used for pain relief in labour. The way that TENS works is not well understood. The electrical pulses are thought to stimulate nerve pathways in the spinal cord which block the transmission of pain. In labour the electrodes from the TENS machine are usually attached to the lower back (and women themselves control the electrical currents using a hand-held device) but TENS can also be applied to acupuncture points or directly to the head. The purpose of the review was to see whether TENS is effective in relieving pain in labour. The review includes results from 17 studies with a total of 1466 women. Thirteen studies examined TENS applied to the back, two to acupuncture points and two to the cranium (head). Results show that pain scores were similar in women using TENS and in control groups. There was some evidence that women using TENS were less likely to rate their pain as severe but results were not consistent. Many women said they would be willing to use TENS

again in a future labour. TENS did not seem have an effect on the length of labour, interventions in labour, or the well-being of mothers and babies. It is not known whether TENS would help women to manage pain at home in early labour. Although it is not clear that it reduces pain, women should have the choice of using TENS in labour if they think it will be helpful.

Authors' conclusions

Implications for practice

There is some evidence that women using TENS in labour are less likely to rate their pain as severe, but the evidence is neither strong nor consistent. Women using TENS applied to the back (and many using placebo devices) were willing to use TENS in future labours. The relative acceptability of placebo devices may suggest that the device offers a useful distraction, and the fact that women themselves operate the device may enhance a woman's sense of control. The findings regarding the use of TENS to acupuncture points are positive, but only two studies have evaluated this intervention and the fact that the technology is applied by staff trained in acupuncture techniques may limit its implementation. Many obstetric units have self-operated TENS units for application to the back available. TENS does not seem to increase the use of other interventions or cause harm to mothers or babies. Women should be offered the choice of using TENS (with or without other analgesia) at whatever stage of labour they think it might help.

Implications for research

The interpretation of findings in this review was difficult because of the limited information study authors provided on methods, the variability in outcomes measured, and in the instruments used to measure outcomes. There was no information on the costs associated with using TENS or on the use of TENS in very early labour. The side effects of TENS were not generally reported. Overall, there is relatively little background information on the use of TENS. A small number of surveys of obstetric units shed some light on where TENS is available, but this information is limited (McMunn 2009). We do not know how many (or which) women are offered TENS as part of their care in labour, or at what stage in labour it is offered. We do not know whether TENS is routinely discussed as part of childbirth preparation classes or about women's knowledge about TENS in labour. There are various specifications for devices; we do not know whether some devices are more effective than others. TENS units are commercially available and it would be useful for women to have information to evaluate the claims made by manufacturers. There are a number of implications for research. Survey information is needed from obstetric units so that there is a clearer picture

of the current use of TENS. Information is needed on costs and the types of units available. Most of the studies included in the review were small and all were carried out in hospitals. A large-scale trial focusing on the early stages of labour would address some of the unanswered questions.

Background

Transcutaneous electrical nerve stimulation (TENS) is a non-pharmacological method for relieving pain. It has been used to relieve both acute and chronic pain in a variety of settings, and for a range of conditions including dysmenorrhoea (period pain) and back pain (Kaplan 1998; Samanta 1999). TENS has been used in childbirth since the 1970s (Augustinsson 1977).

This review is one in a series of Cochrane reviews examining pain management in labour. These reviews contribute to an overview of systematic reviews of pain management for women in labour (Jones 2011b) and share a generic protocol (Jones 2011a).

Description of the intervention

Pain in labour is a complex phenomenon, and it is known that women's experiences of pain and labour vary enormously (Lowe 2002; Simkin 1989). Physiological, cognitive and psychological factors all seem to be involved in determining individual experience. The precise mechanisms whereby TENS relieves pain are not known. A number of theories have been proposed.

First is the 'gate control theory' of pain (Melzack 1965). According to this theory, the transmission of pain is inhibited by the stimulation of large, afferent nerve fibres which carry impulses towards the central nervous system. When afferent nerves are stimulated, the pathway for other (painful) stimuli is closed by the operation of a 'gate' in the spinal cord that controls transmissions to the brain. When applied to the lower back, the TENS unit emits electrical impulses which excite afferent nerves, and thus inhibits the transmission of painful stimuli arising from the uterus, vagina and perineum during labour (Augustinsson 1977). (According to this theory, the application of heat, cold or massage would be likely to have a similar effect.)

Second, it is suggested that painful stimuli result in chemical changes in the brain, most notably, the release of endorphins which mediate the experience of pain. TENS is thought to complement this chemical process (Lechner 1991). Again, the precise mechanisms are not understood. However, by reducing anxiety, increasing a sense of control, and by providing distraction, TENS is thought to increase women's sense of well-being and thereby reduce pain in labour (Brucker 1984; Findley 1999; Gentz 2001; Simkin 2004). It has

also been proposed that by decreasing maternal anxiety, TENS may reduce the length of labour by suppressing the release of catecholamines which can inhibit the action of the uterus and thereby delay progress (Lowe 2002).

More recent theories suggest that the varied factors influencing the experience of pain are likely to be interactive (Holdcroft 2003; Lowe 2002).

Various models of TENS equipment are available (Kaplan 1997). The TENS unit consists of a hand-held device connected to electrodes which are attached to the skin. During labour the electrodes are usually positioned on the lower back on both sides of the spine at vertebral positions T10 and S2 (Kaplan 1998; Simkin 2004), corresponding to the nerve pathways through which painful impulses from the contracting uterus are thought to enter the spinal cord (Lowe 2002). The TENS unit emits low-voltage impulses, the frequency and intensity of which can be controlled by the woman in labour. When using TENS, women experience a tingling or buzzing feeling at the site of the electrodes. At low voltages these sensations are not painful. TENS has also been used to stimulate acupuncture points, and can also be applied to the cranium by trained therapists.

The availability of TENS has increased over the past two decades. The extent of its use by women in different countries and settings, and at different stages in labour, has not been well documented. A UK study suggested that in 1994 approximately 16% of low-risk primiparous women used TENS in labour; invariably TENS was used alongside other methods of pain relief (Williams 1998). This figure is higher than has been reported in other studies (Carroll 1997; Rajan 1994). A more recent study of maternity units in the UK suggests that the use of TENS was supported by midwives in all units surveyed, although only approximately a fifth had TENS available. The use of TENS by women admitted to these units was reported to be between 1% and 25% although this information was not always routinely recorded; the extent of its use by women at home in early labour remains uncertain (McMunn 2009).

The use of TENS to relieve pain in labour remains controversial. While there is evidence that the technology is well received by women, it is not clear that this is because it is effective in reducing pain. There is evidence that women's satisfaction with the experience of childbirth is affected by their sense of control during labour, and in particular, their sense of control during painful contractions (Green 2003). The fact that women themselves operate the TENS unit may partly explain its popularity. In addition, the units may be used in a variety of settings, and it has been suggested that using the device at home in early labour may delay admission to hospital.

The intervention does not seem to have serious adverse effects on women or their babies, although there has been only limited research in this area (Simkin 1989; Simkin 2004). Serious side effects are rare, but the electrodes may cause some local skin irritation. The use of TENS has cost implications, not only in terms of the purchase or hire of the TENS units but also in terms of staff time setting up the equipment and demonstrating its use to women.

There is some, limited, evidence that TENS can interfere with the operation of other electrical equipment (Bundsen 1981).

Why it is important to do this review

TENS aims to reduce pain in labour. TENS can be used alone or in combination with other non-pharmacological and pharmacological methods of pain relief (Kaplan 1998). Proponents of the therapy argue that it reduces maternal distress and potentially reduces the duration of labour and the need for more invasive co-intervention. On the other hand, if TENS is not effective, it may increase maternal distress by delaying the use of more effective interventions (Gentz 2001).

The review assesses the available evidence from randomised trials examining the effects of TENS in labour on outcomes for women and babies.

Objectives

To assess the effect of TENS on pain in labour.

Methods

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs). We have not included quasi-randomised trials.

Types of participants

Women in labour.

Types of interventions

There are various models and types of TENS equipment available; we have not restricted the inclusion criteria to any particular device specification. We have included studies where women were randomised to receive TENS versus routine care, a placebo TENS device, or non-pharmacological interventions. We are

aware that the use of sham TENS devices may not be an adequate means of blinding women to group allocation, and the use of such devices may influence caregiver behaviour. We have taken this into account in the interpretation of results.

This review is one in a series of Cochrane reviews examining pain management in labour. These reviews contribute to an overview of systematic reviews of interventions for pain management in labour (Jones 2011b), and share a generic protocol (Jones 2011a). To avoid duplication, the different methods of pain management have been listed in a specific order, from one to 15. Individual reviews focusing on particular interventions include comparisons with only the interventions above it on the list. Methods of pain management identified in the future will be added to the end of the list. The current list is as follows.

1. Placebo/no treatment
2. Hypnosis
3. Biofeedback (Barragán 2011)
4. Intracutaneous or subcutaneous sterile water injection (Derry 2011)
5. Immersion in water (Cluett 2009)
6. Aromatherapy (Smith 2011b)
7. Relaxation techniques (yoga, music, audio)
8. Acupuncture or acupressure (Smith 2011a)
9. Manual methods (massage, reflexology)
10. Transcutaneous electrical nerve stimulation (TENS) (this review)
11. Inhaled analgesia
12. Opioids (Ullman 2010)
13. Non-opioid drugs (Othman 2011)
14. Local anaesthetic nerve blocks
15. Epidural (including combined spinal epidural) (Anim-Somuah 2005; Simmons 2007)

Accordingly, where data are available, this review will only include comparisons of TENS with: 1. Placebo/no treatment; 2. Hypnosis; 3. Biofeedback; 4. Intracutaneous or subcutaneous sterile water injection; 5. Immersion in water; 6. Aromatherapy; 7. Relaxation techniques; 8. Acupuncture or acupressure; or 9. Manual methods.

Types of outcome measures

Primary outcomes

1. Pain intensity in labour (measured as a continuous variable using visual analogue scales or by validated questionnaires or as a dichotomous variable has/has not severe pain)
2. Satisfaction with pain relief during labour (as defined by trialists)

Secondary outcomes

Maternal

1. Duration of labour
2. Sense of control in labour (as defined by trialists)
3. Augmentation of labour
4. Induction of labour
5. Use of other methods of pain relief during labour
6. Assisted vaginal birth (instrumental vaginal delivery; forceps or vacuum extraction)
7. Caesarean section
8. Side effects (e.g. local skin irritation)
9. Satisfaction with childbirth experience (as defined by trialists)
10. Cervical dilatation on admission to hospital
11. Breastfeeding
12. Effect (negative) on mother/baby interaction

Fetal/neonate

1. Apgar score less than seven at five minutes
2. Cord blood pH less than 7.1
3. Adverse events (as defined by trialists)
4. Admission to neonatal intensive care unit (NICU) or special care baby unit (SCBU)
5. Infant outcomes at long term follow-up (as defined by trialists)

Other outcomes

1. Cost (as defined by trialists)

Search methods for identification of studies

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (30 April 2011).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. weekly searches of EMBASE;
4. handsearches of 30 journals and the proceedings of major conferences;
5. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL, MEDLINE and EMBASE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

Searching other resources

We searched the reference lists of relevant papers.

We did not apply any language restrictions.

Data collection and analysis

Selection of studies

Two review authors (TD and CB) independently examined abstracts of all potential studies identified by the search to ascertain which met the inclusion criteria. Where we did not have enough information to determine eligibility we sought further information from the study authors. We resolved any disagreement through discussion between all review authors.

The reasons for excluding studies have been set out in the Characteristics of excluded studies tables.

Data extraction and management

All review authors were involved in designing, piloting and revising the data extraction form. Two review authors (TD, CB) independently extracted data using the agreed form. We resolved any disagreement through discussion. After checking (by TD), we entered data into Review Manager (RevMan) software (RevMan 2011) and CB then re-checked the data.

When information regarding study methods and findings were unclear, we attempted to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Assessment of methodological quality of included studies

Two review authors (TD, CB) independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We resolved any disagreement by discussion or by involving a third assessor.

(1) Sequence generation

We have described the methods used for generation of the randomisation sequence for each trial and assessed them as low risk of bias (any truly random process), unclear, or high risk of bias.

We assessed the method as:

- low risk of bias (e.g. random number table; computer random number generator),
- high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number) or,
- unclear.

(2) Allocation concealment

We assessed the quality of each trial, using the following criteria:

- low risk of bias for concealment of allocation: such as telephone randomisation, consecutively numbered sealed opaque envelopes;
- unclear risk of bias for concealment of allocation: e.g. the study does not report any concealment approach;
- high risk of bias for allocation concealment: such as open list of random number tables, use of case record numbers, dates of birth or days of the week.

(3) Attrition (loss of participants, e.g. withdrawals, dropouts, protocol deviations)

We described for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported, the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. We assessed methods as:

- low risk of bias (low levels of sample attrition, reasons for loss explained and balanced across groups);
- high risk of bias (levels of attrition above 20% or loss not balanced across groups);
- unclear.

(4) Blinding of participants, researchers and outcome assessors (checking for performance and detection bias)

We assessed blinding using the following criteria:

- low, high or unclear risk of bias for participants;
- low, high or unclear risk of bias for personnel;
- low, high or unclear risk of bias for outcome assessors

We are aware that blinding women and caregivers where TENS has been compared with sham TENS may not be convincing, but we have recorded where an attempt at blinding has been made.

(5) Selective reporting bias

We described for each included study how we investigated the possibility of selective outcome reporting bias and what we found.

We assessed the methods as:

- low risk of bias (where it is clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review have been reported);
- high risk of bias (where not all the study's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported);
- unclear.

(6) Other sources of bias

We described for each included study any concerns we had about other possible sources of bias.

(7) Overall risk of bias

We made explicit judgements about whether studies were at high risk of bias, according to the criteria given in the Handbook (Higgins 2011). With reference to (1) to (6) above, we assessed the likely magnitude and direction of the bias and whether we considered it likely to impact on the findings.

Measures of treatment effect

We carried out statistical analysis using RevMan software (RevMan 2011). We had anticipated that studies evaluating TENS were likely to include a range of comparison groups and that data on different outcomes (measured in different ways and at different time points) would have been recorded. Where trials were not sufficiently similar, we analysed and presented results separately. However, where possible, and at least for the primary outcome (pain in labour) we have used meta-analysis for combining data to produce a summary statistic.

Dichotomous data

Where, for example, outcome data such as maternal perceptions of pain have been measured as a dichotomous variable (e.g. severe pain versus no severe pain), we have presented results as summary risk ratio (RR) with 95% confidence intervals (CIs).

Continuous data

For continuous data (e.g. pain measured on visual analogue scales), we have used the mean difference (MD) where outcomes have been measured in the same way between trials. We have used the standardised mean difference (SMD) to combine trials that measure the same outcome, but used different methods.

Unit of analysis issues

Cluster-randomised trials

We had intended to include cluster-randomised trials in the analyses along with individually randomised trials. Their sample sizes would have been adjusted using the methods described in Gates 2005 and Higgins 2008 using an estimate of the intracluster correlation co-efficient (ICC) derived from the trial (if possible), or from another source.

If we had used ICCs from other sources, we would have reported this and conducted sensitivity analyses to investigate the effect of variation in the ICC. If we had identified both cluster-randomised trials and individually-randomised trials, we planned to synthesise the relevant information. We would have considered it reasonable to combine the results from both if there was little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit was considered to be unlikely.

We would also have acknowledged heterogeneity in the randomisation unit and performed a subgroup analysis to investigate the effects of the randomisation unit.

We did not identify any cluster-randomised trials for this review, but will include them in updates if such trials are identified in the future.

Cross-over trials

We did not anticipate that there would be any cross-over trials for an intervention carried out during labour, however, one such trial was identified (Chia 1990) but we excluded it for other reasons. In updates of the review, if further cross-over trials are identified which are otherwise eligible for inclusion, we will only include data from the first stage of such studies to avoid the risk of bias associated with treatment order effect.

Dealing with missing data

We have analysed data on all participants with available data in the group to which they were allocated, regardless of whether or not they received the allocated intervention, and irrespective of whether they used additional interventions. If, in the original reports, participants were not analysed in the group to which they were randomised, and there was sufficient information in the trial report, we have attempted to restore them to the correct group.

We noted levels of attrition in included studies.

Where data were not reported for some outcomes or groups, we attempted to contact the study authors to obtain the missing data.

Assessment of heterogeneity

As part of the meta-analyses we examined heterogeneity between trials using the I^2 statistic. We regarded heterogeneity as substantial if I^2 was greater than 30%. Where we identified unexplained heterogeneity among the trials we have made this explicit, so that this can be taken into account in the interpretation of results.

Assessment of reporting biases

If 10 or more studies had contributed data to meta-analysis for any particular outcome, we planned to investigate reporting biases (such as publication bias) using funnel plots. We would have assessed possible asymmetry visually, and used formal tests for funnel plot asymmetry. For continuous outcomes, we would have used the test proposed by Egger 1997, and for dichotomous outcomes, we would have used the test proposed by Harbord 2006. If asymmetry was detected in any of these tests or was suggested by a visual assessment, we planned to perform exploratory analyses to investigate it. In this version of the review insufficient data were available to allow us to carry out this planned analysis.

Data synthesis

We carried out statistical analysis using the RevMan software (RevMan 2011). We used fixed-effect meta-analysis for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect: i.e. where trials examined the same intervention, and where we judged the trials' populations and methods to be sufficiently similar. If we suspected clinical heterogeneity sufficient to expect the underlying treatment effects to differ between trials, or if substantial statistical heterogeneity was detected, we used random-effects meta-analysis to produce an overall summary provided that we considered an average treatment effect across trials was clinically meaningful.

Subgroup analysis and investigation of heterogeneity

We planned subgroup analyses classifying whole trials by interaction tests as described by Deeks 2001.

For the primary outcomes, where data were available, we planned the following subgroup analyses.

- Parity (nulliparous versus multiparous women)
- Stage of labour (first stage latent versus active phase)
- Spontaneous labour versus induced labour
- Term versus preterm birth
- Continuous support in labour versus no continuous support

Sensitivity analysis

We planned to carry out sensitivity analyses to explore the effect of trial quality assessed by concealment of allocation, high attrition rates, or both, with poor quality studies being excluded from the analyses in order to assess whether this made any difference to the overall result.

Results

Description of studies

Results of the search

We identified a total of 28 studies from the search strategy. This review includes 18 studies, with data from 17 studies. One study which was otherwise eligible for inclusion was reported in a brief abstract and did not report any outcome data by randomisation group (Vasegh 2010); we have provided information about this trial in a Characteristics of included studies table but this study does not contribute any outcome data, and is not otherwise discussed in the remaining sections of the review. We excluded nine studies and one study was reported in Portuguese and is awaiting translation and eligibility assessment (Knobel 2005).

Included studies

We have included data from 17 studies with data for a total of 1466 women. Thirteen studies examined TENS applied to the lower back, two the application of TENS to acupuncture points to relieve pain in labour and two the application of Limoge currents to the cranium.

The studies were carried out in a variety of settings and countries. Of the studies examining TENS applied to the back, three were carried out in the USA (Hughes 1988; Tsen 2000; Tsen 2001) and one each in Sweden (Bundsen 1982), Brazil (de Orange 2003), Ireland (Hughes 1988), Canada (Labrecque 1999), Australia (Thomas 1988), Denmark (Steptoe 1984), India (Thakur 2004), Germany (Neumark 1978), Norway (Nesheim 1981), and the Netherlands (van der Ploeg 1996). Two studies focusing on TENS applied to acupuncture points were carried out in Taiwan (Chao 2007) and China (Wang 2007). Both studies examining TENS (Limoge current) to the cranium were carried out in France (Champagne 1984; Wattrisse 1993).

In ten studies TENS was compared with the use of a placebo machine (Champagne 1984; Chao 2007; Harrison 1986; Hughes 1988; Nesheim 1981; Steptoe 1984; Thomas 1988; Tsen 2000; Tsen 2001; van der Ploeg 1996). In the remaining studies, the use of TENS was compared with no intervention (routine care) (Bundsen 1982; de Orange 2003; Labrecque 1999; Neumark 1978; Thakur 2004; Wang 2007; Wattrisse 1993). Three of these studies included three arms: the study by Thakur 2004 compared TENS versus usual care or versus tramadol; a small study by Neumark 1978 examined TENS versus control groups or versus pethidine; and the study by Labrecque 1999 compared TENS versus usual care or versus sterile water injection. For two of these studies we have only included data for those arms comparing TENS with no treatment/placebo (Thakur 2004; Neumark 1978). The data comparing TENs with opioids has been included in another pain management review (Ullman 2010). In the study by Labrecque 1999 we have included the data for TENs versus control and TENS versus sterile water injection in two separate comparisons.

The co-interventions in the various studies varied, and are described more fully in the Characteristics of included studies tables. In two studies by the same author (Tsen 2000; Tsen 2001), women used TENS to the back at the same time as epidural or combined spinal epidural analgesia, and in the trial by Wattrisse 1993, TENS to the cranium was also examined as an adjuvant therapy to epidural analgesia. In the study by de Orange 2003, women used TENS for a short period prior to the insertion of a spinal epidural. In most of the remaining trials, women in both study groups were free to use other analgesia on request. However, in the studies by Neumark 1978 and Wang 2007, women received no analgesics other than the study interventions.

In addition, there was considerable variation amongst the studies in terms of the care women received, and in inclusion and exclusion criteria. In some trials women undergoing induction of labour were excluded, whereas in others, such women were included as part of the sample, and the use of oxytocin was routine in some settings. In some cases women were excluded if they had any analgesia before entry to the trial, whereas for example, in the study by van der Ploeg 1996 all women, in both the intervention and control arms, received patient-controlled pethidine (75 mg) and promethazine (25 mg). These variations in the care received by women in different studies mean that the interpretation of results from the review is not simple.

Information on the characteristics of women included in studies and descriptions of inclusion and exclusion criteria were sometimes limited. It appeared that four studies included *only* women in spontaneous labour (Harrison 1986; Thakur 2004; Tsen 2000; Tsen 2001), one study included *only* women with induced labours (Bundsen 1982), one study included a mix of women in both spontaneous and induced labours, while inclusion criteria relating to labour onset were not specified in the remaining studies. Few of the studies provided a breakdown of findings by parity. Four of the studies included primiparous women only (Champagne 1984; Steptoe 1984; Wang 2007; Wattrisse 1993); the rest included both primiparous and multiparous women. Ten studies included only women at term (Chao 2007; de Orange 2003; Hughes 1988; Labrecque 1999; Nesheim 1981; Thakur 2004; Thomas 1988; Tsen 2000; Tsen 2001; Wattrisse 1993) and in the remaining studies gestational age was not specified. No study reported on whether or not women had continuous support during labour.

Excluded studies

We excluded nine studies from the review. In two cases this was because they did not focus on the use of TENS during labour to relieve pain. Canino 1987 examined the use of TENS for pain relief following caesarean section and Dunn 1989 looked at the effects of TENS on the strength of uterine contractions during labour induction. We excluded the studies by Erkkola 1980, Hulkko 1979, Merry 1983 and Tajali-Awal 1995 for methodological reasons; in the former three studies, group allocation was not random, and in the latter post-randomisation attrition was very high. One study was reported in a brief conference abstract; we made several attempts to contact the study author without success (Anonymous 1995). Finally, two studies which were included in earlier versions of this review (Chia 1990; Tawfik 1982) have been excluded from this update. The reason for these additional exclusions is because this review is one in a series of Cochrane reviews which contribute to an overview of systematic reviews of pain relief for women in labour (Jones 2011b) and share a generic protocol (Jones 2011a). In order to comply with the generic protocol, which has specific inclusion criteria relating to comparison interventions so as to avoid overlap between different reviews, the Tawfik 1982 trial (TENS versus pethidine) has been moved to the parenteral opioids review (Ullman 2010), and the Chia 1990 trial (TENS versus Entonox®) to the inhaled analgesia review (Klomp 2011 in preparation) as neither trial now meets the inclusion criteria for this updated TENS review.

Risk of bias in included studies

Overall, there was little information on methods provided by study authors.

Allocation

Most of the included studies provided very little information on sequence generation or on allocation concealment. In three studies, sequence generation was by computer or by using random number tables (de Orange 2003; Labrecque 1999; Thomas 1988); for the rest, the method of generating the allocation sequence was not clear. In one study exactly the same numbers of primiparous and multiparous women were included in both arms of the trial, as stratification was not mentioned, this balance between groups seems unlikely to have occurred as a result of any truly random method of sequence generation (Thakur 2004).

Little information was provided on steps taken by the investigators to conceal group allocation. One study described using "sealed envelopes" (de Orange 2003); another three, sealed, opaque, sequentially numbered envelopes (Labrecque 1999; Tsen 2000; Tsen 2001). All but one of the remaining studies either did not describe methods to conceal allocation or the method was not clear. In one study allocation was by tossing a coin after recruitment; although it was not clear who was involved in recruiting women to the study; this method is likely to introduce a high risk of bias (Nesheim 1981).

Blinding

As we have described above, in several studies investigators attempted to blind study participants and care providers to group allocation by providing a placebo device (Champagne 1984; Chao 2007; Harrison 1986; Hughes 1988; Nesheim 1981; Neumark 1978; Steptoe 1984; Thomas 1988; Tsen 2000; Tsen 2001; van der Ploeg 1996). Assessing the success of blinding and risk of bias where sham TENS devices were provided was extremely difficult. Authors described identical machines, with lights and noises, or machines hidden in pouches, but it was not clear whether or not women, or those providing care, really had no idea of whether or not they were using an active device. None of the authors provided qualitative data regarding the success of blinding. The issue of blinding is likely to be important, as lack of blinding or inadequate blinding may affect both outcome assessment and the behaviour of care providers (for example, a midwife who was aware, or suspected, that a woman had received an inoperative machine may have encouraged a woman to accept other analgesia, and this may have affected the results of a trial).

In studies comparing TENS with no intervention, blinding was not attempted.

The lack of blinding, and the lack of information on whether successful blinding was achieved by the use of sham devices, are potential sources of bias in these studies and should be kept in mind when interpreting results.

Incomplete outcome data

In most of the studies, levels of attrition were relatively low, although even where there was modest attrition, women may have been excluded for reasons associated with outcomes. For example, in the study described by Bundsen 1982, four of the original sample of 28 were excluded from the analyses as they went on to request an epidural (two women) or to have a caesarean section (two women). In the studies by Harrison 1986 and Thomas 1988 there were high levels of missing data for some outcomes.

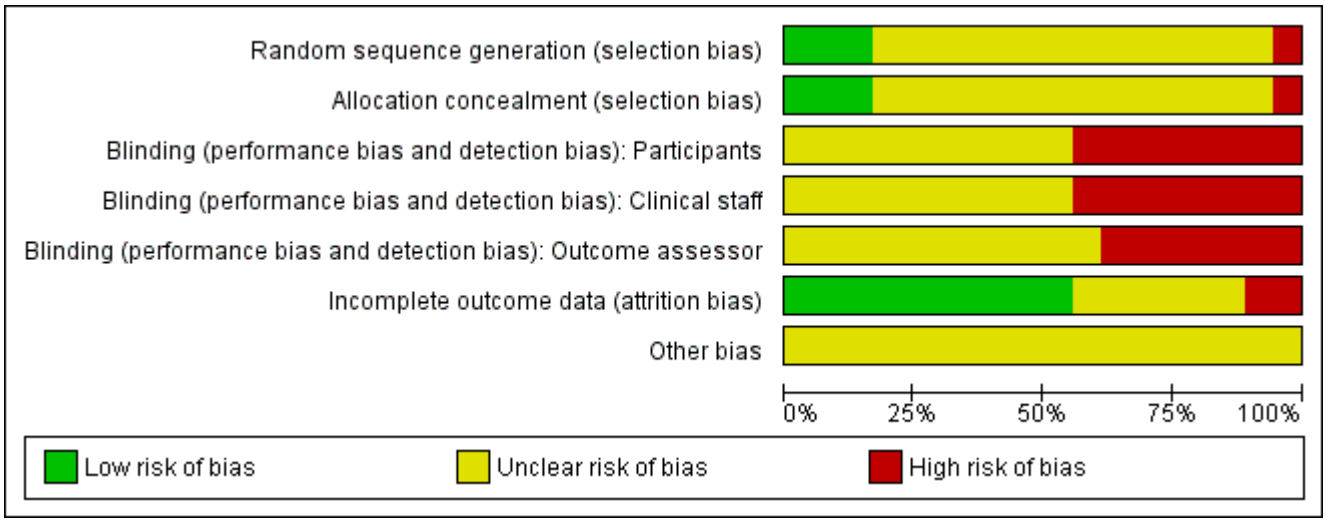
Other potential sources of bias

Several of the studies had unbalanced study groups. The trial by Bundsen 1982 included nine women in the control group compared with fifteen in the intervention group. This difference may have occurred by chance, but nevertheless it means that results are difficult to interpret. In some studies there were unequal numbers of primiparous and multiparous women in the two study groups (Nesheim 1981; Thomas 1988; Tsen 2000). In the Tsen 2000 trial, 30% of the women in the intervention group were nulliparous compared with 80% in the control group. Again, these differences may have occurred by chance, but the way that primi- and multiparous women experience pain in labour may be different, so this imbalance in groups affects the interpretation of results. Several of the studies included only small samples, and while this may not be a source of bias, it does have an impact on whether or not the results can be generalised. Most study authors did not report the numbers of women approached compared with those women actually recruited to studies and randomised.

We have summarised overall results for risk of bias in Figure 1 and Figure 2.

Figure 1

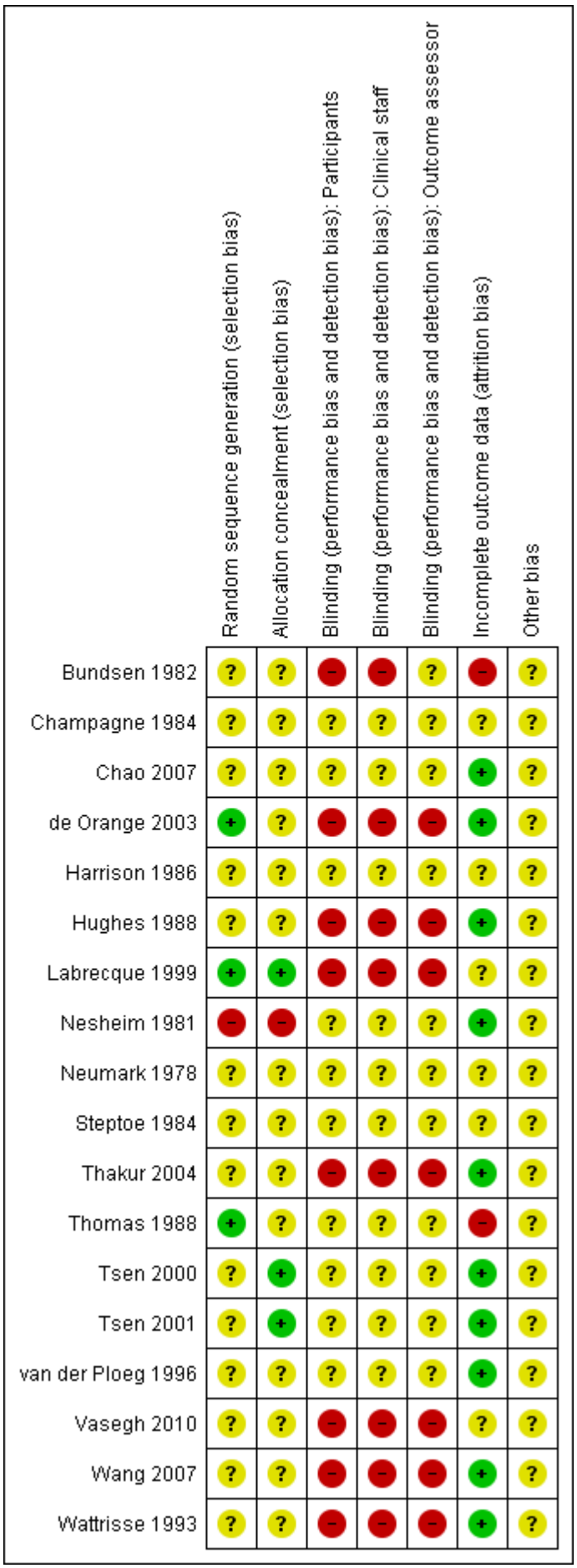
Open in figure viewer | **Download as PowerPoint**



Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 2

Open in figure viewer | Download as PowerPoint


Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding (performance bias and detection bias): Participants
Blinding (performance bias and detection bias): Clinical staff
Blinding (performance bias and detection bias): Outcome assessor
Incomplete outcome data (attrition bias)
Other bias
Bundsen 1982
Champagne 1984
Chao 2007
de Orange 2003
Harrison 1986
Hughes 1988
Labrecque 1999
Nesheim 1981
Neumark 1978
Steptoe 1984
Thakur 2004
Thomas 1988
Tsen 2000
Tsen 2001
van der Ploeg 1996
Vasegh 2010
Wang 2007
Wattrisse 1993

Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Effects of interventions

Presentation of results

The review includes three different types of TENS devices: TENS applied to the back (operated by women); TENS applied to acupuncture points (applied by trained staff); and TENS applied to the cranium (applied by trained staff). In addition, the control conditions also varied; TENS was compared with usual care or placebo devices; in three studies TENS was an adjunct to epidural analgesia; and in one study TENS was compared to sterile water injection.

To simplify the way we have reported results we have presented together, in one comparison, those studies where TENS was compared with routine care or placebo devices. For each outcome, studies examining each type of TENS machines (TENS to the back, acupuncture points or cranium) have been grouped together and combined in meta-analyses (with sub-totals for each group). We have not pooled the results for different types of devices, and similarly, results in the text are reported separately for different types of TENS.

The results from studies where TENS was an adjunct to epidural or where compared to sterile water injections, have been examined in a separate comparisons.

For some outcomes there were high levels of heterogeneity and these results should therefore be examined with caution. For analyses where there are high levels of unexplained heterogeneity, we have used a random-effects model.

TENS versus placebo or usual care (14 studies, 1256 women)

Primary outcomes

Pain in labour

There was considerable variation in the way that pain was measured in the included studies. We have combined studies where pain was measured either as a dichotomous variable or as a continuous variable in separate analyses, but in view of the fact that definitions and measurement scales varied between studies, results should be viewed with some caution.

Severe pain in labour

Two studies including 147 women compared the numbers of women reporting severe pain during labour for women receiving TENS (to the back) versus placebo or routine care; women in the TENS group were less likely to report severe pain, but the evidence of a difference between groups did not reach statistical

significance (average risk ratio (RR) 0.67, 95% confidence interval (CI) 0.32 to 1.40, P = 0.28 (as there was substantial heterogeneity for this outcome we used a random-effects model)), Analysis 1.1.

Two studies (including 190 women) examining TENS applied to acupuncture points also found that women in the TENS group were less likely to report having severe pain compared with controls (RR 0.41, 95% CI 0.31 to 0.54), Analysis 1.1.

Pain scores

Two studies examining TENS to the back (including 299 women) used visual analogue scales to measure women's pain in labour, the evidence of a difference between groups was not statistically significant (average standardised mean difference (SMD) -1.01, 95% CI -3.00 to 0.97, (as there was substantial heterogeneity for this outcome we used a random-effects model)), Analysis 1.2. (Both studies measured pain on scales with scores recorded in millimetres, it was not clear how the 10 cm scale was labelled in the Labrecque 1999 study, and the length of the scale (maximum score) was not clear in the Thomas 1988 study. The standard deviations reported for the Labrecque 1999 study are much smaller than would be expected with this type of scale, therefore results should be interpreted with caution.)

Satisfaction with pain relief in labour

There was variability in the way satisfaction with pain relief was defined in different studies and again, we would advise caution in the interpretation of results.

Five studies (including 452 women) examining TENS to the back compared with placebo TENS or routine care collected information on women's satisfaction with pain relief in labour. While women in the TENS group were more likely to express satisfaction the difference between groups did not reach statistical significance (RR 1.25, 95% CI 0.98 to 1.60), Analysis 1.3. The single study (including 90 women) examining TENS to acupuncture points and measuring satisfaction with pain relief reported that women in the TENS group were more satisfied with their pain relief compared with women in the control group (who received no pain relief whatsoever) (RR 4.10, 95% CI 1.81 to 9.29), Analysis 1.3.

Several studies examining TENS to the back versus placebo/sham TENS included an outcome relating to women's willingness to use TENS again in a future labour. In four studies, including 583 women, those in the active TENS group were more likely to be willing to use TENS again in a future labour compared with women with inactive machines (average RR 1.50 95% CI 1.23 to 1.83, (as there was substantial heterogeneity for this outcome we used a random-effects model)), Analysis 1.4. While 63% of women in the active TENS group would use TENS again, 41% using inactive devices reported that they too would be willing to use TENS in a future labour (unweighted percentages). A single study, including 100 women, comparing TENS versus placebo TENS to acupuncture points similarly reported that women in the active TENS group would be more likely to express a willingness to use TENS again (RR 1.45 95% CI 1.18 to 1.79), Analysis 1.4 . (Although again, relatively large numbers in the placebo group expressed positive views about the intervention).

Secondary outcomes

Duration of labour

There was no significant evidence of a difference in the duration of either the first and second stages of labour (various definitions) for women receiving TENS to the back or to acupuncture points compared with women in control groups (Analysis 1.10; Analysis 1.11).

Sense of control in labour

One study reported that here was no significant evidence of a difference in reported sense of control during labour for women receiving TENS to the back compared with women receiving standard care (Labrecque 1999). Standard deviations reported in the paper appeared inconsistent and we have therefore not included data in an analysis.

Use of other analgesia and augmentation of labour

There was no significant evidence of any differences in the numbers of women receiving epidural analgesia for women in control groups compared with women receiving TENS to back (average RR 0.99 95% CI 0.59 to 1.67) (as there was substantial heterogeneity for this outcome we used a random-effects model), Analysis 1.12, or acupuncture TENS (average RR 0.40, 95% CI 0.08 to 1.97) Analysis 1.12. There was a considerable difference in the use of epidural analgesia in the trial examining the use of Limoge current to the cranium, with nine of ten women in the control group going on to have an epidural, compared with only one women of ten in the experimental group Analysis 1.12.

There was no evidence of significant differences between groups in terms of the numbers receiving other analgesia, or in the mean amounts of other analgesia used (Analysis 1.7; Analysis 1.8).

Few studies collected information on the augmentation of labour and there was no evidence of differences between groups (Analysis 1.9)

Mode of delivery

In eight studies (including 868 women) comparing TENS to the back versus placebo TENS or routine care, there was no significant evidence of a difference between TENS and control groups in the numbers of women undergoing caesarean section (RR 1.35, 95% CI 0.84 to 2.17), Analysis 1.5. In the single study (100 women) including this outcome where acupuncture TENS was compared with a placebo, again there was no strong evidence of a difference between groups (RR 1.50 95% CI 0.26 to 8.60), Analysis 1.5. In the study examining the use of Limoge current to the cranium, one woman in both the experimental and control groups had a caesarean section.

Seven studies examining TENS to the back (840 women) reported the numbers of women having assisted vaginal deliveries. There was no evidence of a difference between groups (RR 0.82, 95% CI 0.56 to 1.19), Analysis 1.6. In the single study (100 women) looking at TENS to acupuncture points versus placebo, women in the TENS group were more likely to have an assisted delivery although the confidence intervals were very wide for this outcome (RR 4.50, 95% CI 1.02 to 19.79), Analysis 1.6. In the study examining the use of TENS to the cranium, there was no evidence of a difference between groups for this outcome.

Satisfaction with childbirth experience

There was no significant evidence of a difference in satisfaction with labour and delivery for women in the control group compared with women receiving TENS to the back in a single study with a small sample (Labrecque 1999). Standard deviations reported in the paper appeared inconsistent and we have therefore not included data in an analysis.

Outcomes for babies

There was little information in the included studies on outcomes for babies. No study reported information on admission to NICU/SCBU or infant outcomes at long-term follow-up. None of the studies reported information on the number of babies with Apgar scores less than seven at five minutes (pre-specified outcome). While there was information provided on mean Apgar scores in some studies, these data are very difficult to interpret. Similarly, the number of babies with cord pH less than 7.1 was not reported, but again mean values were sometimes reported but were difficult to interpret. Two studies included information on fetal distress; small numbers of babies were reported as experiencing distress and no statistically significant differences between groups were reported (Analysis 1.13). Electrical interference with fetal heart rate monitoring equipment was reported in one case in one study (Hughes 1988).

Other pre-specified outcomes

No studies reported information on cervical dilatation on admission to hospital; breastfeeding; effect on mother/baby interaction; or cost. All of the studies included women randomised in early labour in hospital settings. No studies examined the use of TENS at home in early labour and so there was no information on whether the use of TENS delayed admission to hospital. No studies reported side effects of TENS.

TENS as an adjunct to epidural analgesia (three studies, 200 women)

Three studies examined TENS as an adjunct to epidural. In two studies TENS was applied to the back (Tsen 2000; Tsen 2001) and in one, TENs was applied to the cranium (Wattrisse 1993).

Primary outcomes

Two studies (including 80 women) examined TENS to the back as an adjunct to epidural analgesia, and pain scores measured at 60 minutes after insertion of the epidural were very similar in the active TENS and placebo groups (mean difference (MD) 0.23, 95% CI -8.71 to 9.16), Analysis 2.1. The study examining cranial TENS with epidural compared with epidural alone also revealed no significant differences in pain scores between groups (Analysis 3.1).

Secondary outcomes

In the studies where TENS was used as an adjunct to epidural there was no evidence of a difference between groups in terms of the number of women undergoing caesarean section or having assisted deliveries (Analysis 2.2; Analysis 2.3; Analysis 3.2; Analysis 3.3).

In the single study (120 women) examining the use of cranial TENS as an adjunct to epidural analgesia, the length of the first stage of labour was similar in both groups (Analysis 3.6). In this study, the analgesic effect of the first dose of epidural lasted longer when cranial TENs was applied as an adjuvant therapy (Analysis 3.4), but this did not result in any overall reduction in the total dose of epidural used by women in the two groups (Analysis 3.5).

The following outcomes were not reported in studies: cervical dilatation on admission to hospital; breastfeeding; effect on mother/baby interaction; or cost. All of the studies included women randomised in early labour in hospital settings. No studies examined the use of TENS at home in early labour and so there was no information on whether the use of TENS delayed admission to hospital. No studies reported side effects of TENS.

TENS versus sterile water injection (one study, 23 women)

Primary outcomes

Pain intensity

One small study examining TENS to the back compared with sterile water injection used visual analogue scales to measure women's pain in labour (millimetres) Labrecque 1999. Women in the TENS group were more likely to have a higher mean pain score in labour than women in the sterile water injection group (SMD, 5.45, 95% CI 3.49 to 7.42), Analysis 4.1. (The study measured pain on a scale with scores recorded in millimetres, it was not clear how the 10 cm scale was labelled and the reported standard deviations are much smaller than would be expected with this type of scale, therefore results should be interpreted with caution).

Secondary outcomes

Sense of control in labour

There was no significant evidence of a difference in sense of control during labour for women receiving TENS to the back compared with women receiving sterile water injections (Labrecque 1999). Standard deviations reported in the paper appeared inconsistent and we have therefore not included data an analysis.

Use of other methods for pain relief in labour

There was no significant evidence of any differences in the numbers of women receiving epidural analgesia for women in the TENS group compared with women receiving sterile water injections (RR 1.07, 95% CI 0.64 to 1.80), Analysis 4.2.

Caesarean section

There was no significant evidence of any difference in the numbers of women undergoing caesarean section for women in the TENS group compared with women receiving sterile water injections (RR 7.62, 95% CI 0.46 to 126.40), Analysis 4.3.

Satisfaction with childbirth experience

There was no significant evidence of a difference in satisfaction with labour and delivery for women receiving TENS to the back compared with women receiving sterile water injections (Labrecque 1999). Standard deviations reported in the paper appeared inconsistent and we have therefore not included data in an analysis.

The following outcomes were not reported in studies: satisfaction with pain relief during labour; duration of labour; augmentation of labour; induction of labour; assisted vaginal birth; side effects; cervical dilatation on admission to hospital; breastfeeding; effect on mother/baby interaction; Apgar score less than seven at five minutes; cord blood pH less than 7.1; adverse events; admission to NICU/SCBU; infant outcomes at long-term follow-up; or cost.

Sub-group analysis

We had intended to carry out sub-group analysis examining the effect of TENS in early versus active labour, however, the studies did not provide consistent definitions of stage of labour and there was variability in inclusion and exclusion criteria. One study (Thomas 1988) provided information on pain scores in early and late labour; while scores were higher in later labour there was no evidence of any difference between women in the TENS and control groups at either stage (Analysis 5.1). One small study (Bundsen 1982) examined whether women reported severe pain in early and later labour and suggested that TENS was associated with fewer reports of severe pain in the later stages of labour (Analysis 5.2).

Few of the studies provided a breakdown of findings by parity. Four of the studies included primiparous women only (Champagne 1984; Steptoe 1984; Wang 2007; Wattrisse 1993); the rest included both primiparous and multiparous women. For pain outcomes, only one study reported separate breakdowns for

primiparous and multiparous women and no differences were apparent between subgroups (Analysis 6.1: Analysis 6.2.)

In this updated version of this review we planned subgroup analysis examining possible differences between women who had spontaneous versus induced labours, term versus preterm births and continuous support in labour versus no continuous support in labour. Insufficient information was reported in the included studies to carry out this planned analysis.

Sensitivity analysis

We had intended to carry out sensitivity analysis excluding studies with high risk of bias from analyses to see if this affected results. However, few of the included studies provided sufficient information on study methods to allow us to separate out those studies with low and high risk of bias. If we assume that those studies failing to provide information (or providing only limited information) on, for example, allocation concealment were at high risk of bias, then all but three of the included studies would be excluded in the sensitivity analyses (and two of the studies with adequate information and methods examined TENS as an adjunct to epidural analgesia).

Discussion

Summary of main results

There is some evidence from the studies included in this review that women receiving TENS were less likely to report experiencing severe pain in labour compared with women in control groups. However, the evidence was not strong and was not consistent. In studies where women rated their pain on visual analogue scales, there was no significant evidence of differences between groups. There was no evidence of differences between groups in their requirements for other types of pain relief, including epidural analgesia (except for one study examining the use of cranial TENS).

Three studies examining the use of TENS with epidural suggest that TENS is not an effective adjuvant therapy when used alongside epidural or combined spinal epidural analgesia.

We did not find consistent evidence that women receiving TENS were more satisfied with their pain relief in labour compared with controls. At the same time, approximately two-thirds of women receiving TENS reported that they would be willing to use TENS again in a future labour, although this also applied to approximately 40% of those women who had been provided with inactive placebo devices.

TENS seems to have little impact on other labour outcomes. There was no strong evidence that the use of TENS made any difference (in either direction) to the mode of delivery, to the length of labour or to obstetric interventions such as augmentation. Few studies collected information on outcomes for babies, and although these studies did not suggest that TENS is associated with harm, much larger randomised and observational studies would be needed to establish the safety of TENS. There was very limited information on several important outcomes including: breastfeeding, effect on mother/baby interaction, side effects, admission to NICU/SCBU, infant outcomes at long-term follow-up, number of babies with Apgar scores less than seven at five minutes and number of babies with cord pH less than 7.1

We had hoped to examine whether the use of TENS at home in early labour would delay admission to hospital; none of the included studies provided information on this outcome.

Overall completeness and applicability of evidence

The studies included in this review were carried out in a variety of countries and settings and this may increase their applicability; however they included relatively small samples and altogether have included only 1456 women. The studies had varied inclusion and exclusion criteria, but tended to include women at term, in spontaneous labour and at low obstetric risk. Women requesting epidural analgesia at the outset were generally excluded although one study examined the effects of TENS before epidural, and two looked at TENS as an adjunct to epidural. Women who had other preferences regarding analgesia may also have been excluded. Most studies did not provide information on the numbers of women approached compared with those actually recruited and randomised. Without such information it is difficult to judge the generalisability of findings.

Two studies examined the use of acupuncture TENS; it was not clear whether in these study hospitals acupuncture was a standard and accepted part of care, nor was it clear whether staff applying the technology were highly skilled and trained, so as to reduce the likelihood of the technology being adopted elsewhere.

It was very difficult to assess the applicability of findings from the included trials because of the wide variety in care received by women in both the TENS and control groups. In some studies TENS was offered alone, in other studies it was an adjuvant therapy. Hence, some women (in one or both groups) had free access to other forms of pain relief, while others may have been denied any other analgesia. So when women expressed satisfaction with their pain relief, it was not clear what exactly women were satisfied with; in one study, for example, all women received pethidine irrespective of group allocation or whether or not they requested it. In some trials, routine management included amniotomy and early oxytocin to augment labour; such interventions are known to have an impact on women's experience of pain. While most of these studies included women randomised in early labour, there were some inconsistencies; sometimes this was defined as cervical dilatation less than, for example, 5 cm. In another study, inclusion criteria was for women with cervical dilation greater than 4 cm; such variability limits our ability to say whether TENS is helpful in

early as opposed to later labour, as there was no clarity about what this means, or when TENS was applied either within or between studies. It is important that in interpreting results, readers examine the characteristics of included studies to appreciate these differences in care.

We have already mentioned the variable ways in which some outcomes were measured in the studies included in the review; for example, the wording of questions relating to satisfaction with pain relief in labour varied between studies. Outcomes such as the length of the first stage of labour are particularly difficult to interpret, as there are no hard and fast rules for determining the starting point of labour. In some studies the start was marked by a given degree of cervical dilation, in others it coincided with hospital admission (and of course, the point at which a woman decides to go to hospital will depend on many factors including her level of anxiety, time of day, distance from the hospital, cultural attitudes, local hospital policy as well as her obstetric history and physiological state). While we have pooled results from such studies, we recognise that differences in the way outcomes have been measured may affect results.

Quality of the evidence

The risk of bias in these studies was generally high. Few studies provided clear information about sequence generation or methods used to conceal group allocation; in the absence of a clear description of methods, the assumption must be that a study is at high risk of bias. While several of the studies claimed that women and care providers were blind to group assignment, these claims must be viewed with some skepticism. Women who have used TENS are aware that the pulses can be felt as a tingling or buzzing on the skin. While some studies specifically excluded women with previous experience of TENS, it is likely that women would have discussed the technology with others, and may well have been aware that they were using an inactive device. It is also likely that women using inactive devices will have reported the fact that they could feel nothing to those 'blinded' midwives providing care and recording outcomes. Although high levels of attrition were not a problem in most of these studies, even relatively low levels of post-randomisation exclusions are likely to have an impact on results if women are excluded for reasons that are likely to relate to outcomes (e.g. women who went on to have a caesarean section, or an epidural were excluded from the analysis in one study). Again, readers are advised to examine the tables of risk of bias to assist in interpreting the results of the review.

Potential biases in the review process

The possibility of introducing bias was present at every stage of the reviewing process. We attempted to minimise bias in a number of ways; two review authors assessed eligibility for inclusion, carried out data extraction and assessed risk of bias. Each worked independently. Nevertheless, the process of assessing risk of bias, for example, is not an exact science and includes many personal judgements. Further, the process of reviewing research studies is known to be affected by prior beliefs and attitudes. Work examining bias in the peer reviewing process has suggested that the content of reviews may make them more or less susceptible

to observer bias, and studies examining "alternative" therapies, such as TENS, may be particularly prone to this sort of bias. In a study where peer reviewers who had written editorial or opinion pieces for or against TENS were asked to assess the methodological quality of a study about TENS, reviewers' assessments tended to reflect their prior beliefs (Ernst 1994). It is difficult to control for this type of bias in the reviewing process.

While we attempted to be as inclusive as possible in the search strategy, the literature identified was predominantly written in English and published in North American and European journals. We are also aware that publication bias is a possibility, as the review includes several small studies reporting a number of statistically significant results. Although we did attempt to assess reporting bias, constraints of time meant that this assessment relied on information available in the published trial report and thus, reporting bias was not usually apparent.

Agreements and disagreements with other studies or reviews

A number of other reviews have examined the use of TENS in labour (Carroll 1997; Gentz 2001; Simkin 1989) and a Cochrane review has examined the use of TENS for other types of pain (Nnoaham 2008). There are some points on which all agree; the evidence relating to TENS is frequently methodologically weak, inconsistent and not easy to interpret. The review by Carroll 1997 et al was used to underpin recent intrapartum care practice guidelines in the UK (NICE 2007). These guidelines concluded that TENS was NOT effective in established labour and there was no evidence that it was effective in early labour, and that TENS should not, therefore, be offered to women in established labour. Our conclusions are not the same. We accept that the results we have described are inconsistent. The studies included in the review do not, in general, demonstrate that compared with controls, women receiving TENS had significantly lower pain scores, or required less pharmacological analgesia. Nevertheless, the majority of women were willing to use TENS again. The experience of pain is complex. There is no simple relationship, for example, between objectively measured physiological changes, women's experience of pain, and their satisfaction with pain relief. For whatever reasons, some women find using TENS in labour helpful. Whether or not the usefulness of TENS is confined to the very earliest stages of labour, or is only helpful as an adjuvant therapy, is not known. The data available to us allowed only very limited subgroup analysis of differences in early and late labour. The variability in inclusion criteria, and the stage of labour at which TENS was applied, did not allow us to draw any conclusions about these matters, except perhaps that TENS is not useful as an adjunct to epidural analgesia. All of the studies included in this review recruited women after admission to hospital; we do not know whether TENS would be helpful to women at home so as to delay hospital admission. None of the studies included a cost analysis, so it is not clear whether TENS is a cost-effective technology.

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Jump to: **included studies** | **excluded studies** | **studies awaiting assessment** | **additional references**

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Characteristics of studies

Characteristics of included studies [ordered by study ID]

Bundsen 1982

Methods	RCT. Little information on study design.
Participants	28 women attending hospital for induction of labour (main indication - postdates). Inclusion criteria: Swedish speaking women with fetus in vertex position. Women were excluded if they "were primarily biased for or against a certain method of pain relief".
Interventions	Intervention group: TENS (2 frequencies) positioned over lower back and/or over the supra-pubic region. Comparison group: routine care. Both groups had amniotomy, an oxytocin infusion and access to other pain relief. Most women in both groups had a pudendal block in the second stage.

Outcomes	Lower back and abdominal pain measured hourly in labour. Pain relief assessed by questionnaire, fetal condition at birth assessed by blinded paediatrician.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Described as "randomly assigned".
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) Participants	High risk	Not feasible.
Blinding (performance bias and detection bias) Clinical staff	High risk	Not feasible.
Blinding (performance bias and detection bias) Outcome assessor	Unclear risk	Partial blinding: assessment of fetal condition at birth by paediatrician not aware of group assignment. Other outcomes assessed by staff aware of allocation.
Incomplete outcome data (attrition bias) All outcomes	High risk	Two women (of 28) were excluded from analysis as they had a caesarean section. Two further excluded as they had an epidural.
Other bias	Unclear risk	Unbalanced groups for most analyses (9 versus 15).

Champagne 1984

Methods	RCT (described as double blind study).

Participants	Study in France. 20 primiparous women in labour requiring analgesia.
Interventions	Intervention group: Limoge current to the cranium (applied by trained staff). Control group: Sham device with no Limoge current.
Outcomes	Use of other analgesia, mode of delivery.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated.
Allocation concealment (selection bias)	Unclear risk	Not stated.
Blinding (performance bias and detection bias) Participants	Unclear risk	Described as a double blind study. It is not clear whether women would have been aware that a sham device was being used.
Blinding (performance bias and detection bias) Clinical staff	Unclear risk	It was stated that the staff applying the TENS were not otherwise providing care for the women.
Blinding (performance bias and detection bias) Outcome assessor	Unclear risk	Not stated.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not clear.
Other bias	Unclear risk	Not clear.

Chao 2007

Methods	Randomised trial with placebo device.

Participants	Hospital obstetrics department in Taiwan. 105 women. Inclusion criteria: women were recruited in the first stage of labour (less than or equal to 5 cm cervical dilatation). Women aged 20 to 40 with term pregnancy, vertex presentation, who had not requested an epidural, planned to give birth vaginally and had no medical or obstetric complications. Exclusion criteria: women were excluded if they had previous experience of TENS, acupuncture, epidural analgesia or poor pregnancy outcome.
Interventions	Intervention Group: TENS to 4 acupuncture points on hands and lower legs for 30 minutes and then on request. Comparsion group: placebo TENS to same positions on hands and legs (the placebo emitted very low level electrical stimulation).
Outcomes	Pain relief (measured on VAS) at 30 and 60 minutes, mode of delivery, epidural and other analgesic use, progress in labour, willingness to use TENS again, Apgar score at 5 minutes and adverse events.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly, by permuted blocks with stratification for parity".
Allocation concealment (selection bias)	Unclear risk	"neither medical personnel nor participants knew which group was assigned".
Blinding (performance bias and detection bias) Participants	Unclear risk	Described as double blind. Placebo device with low current, however, it was not clear whether the attempt to blind women was successful.
Blinding (performance bias and detection bias) Clinical staff	Unclear risk	Not clear.

Blinding (performance bias and detection bias) Outcome assessor	Unclear risk	Not clear.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Five of the 105 women randomised delivered before the intervention could take place and were excluded from some of the analysis (included in ITT for main outcome).
Other bias	Unclear risk	Results relating to pain were difficult to interpret.

de Orange 2003

Methods	Randomised trial.
Participants	Study in Recife, Brazil. 22 women. Inclusion criteria: women with singleton, term pregnancy with cephalic presentation, fetus alive and in good condition. Exclusion criteria: women with severe pre-eclampsia, conditions associated with haemorrhage, women planning caesarean or not suitable for epidural analgesia.
Interventions	Intervention group: TENS to back prior to combined spinal epidural. Comparison group: combined spinal epidural only (no TENS intervention).
Outcomes	Mode of delivery, length of time before epidural was requested.
Notes	Original paper in Portuguese. Translation used for data extraction.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated table of random numbers.
Allocation concealment (selection bias)	Unclear risk	Sealed envelopes.

Blinding (performance bias and detection bias) Participants	High risk	Not reported.
Blinding (performance bias and detection bias) Clinical staff	High risk	Not reported.
Blinding (performance bias and detection bias) Outcome assessor	High risk	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No apparent loss to follow up apparent.
Other bias	Unclear risk	Only 22 of 73 eligible women were recruited.

Harrison 1986

Methods	RCT.
Participants	150 women (100 primiparous and 50 parous) recruited in the study hospital in Dublin, Ireland. Inclusion criteria: women in their first or third labour admitted to the labour ward with no particular preferences re analgesia. Exclusion criteria: women at high risk or requiring monitoring. Women admitted for induction of labour.
Interventions	Intervention: TENS to back. Comparison Group: placebo TENS device. Other analgesia were available on request to women in both groups and other management was as usual.
Outcomes	Pain, requests for other analgesia, cord pH and Apgar score, midwife assessment of pain relief.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Allocated "randomly" to one of the 6 numbered machines.

Allocation concealment (selection bias)	Unclear risk	No information. Machines of similar appearance.
Blinding (performance bias and detection bias) Participants	Unclear risk	Authors state that women and midwives were not aware which were the active and placebo TENS machines. The numbers on the machines were changed regularly by a 3rd party.
Blinding (performance bias and detection bias) Clinical staff	Unclear risk	Unclear.
Blinding (performance bias and detection bias) Outcome assessor	Unclear risk	Unclear.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Some loss to follow up for some outcomes (e.g. 18% missing for pain outcome at one hour).
Other bias	Unclear risk	Unclear.

Hughes 1988

Methods	RCT.
Participants	90 women attending a San Francisco (USA) hospital in active labour who had not received medication prior to study entry. Inclusion criteria: healthy women with term pregnancies (37 to 42 weeks). 5 cm or less cervical dilatation. Vertex presentation. No previous experience of using TENS. No significant medical problems, history of drug abuse or signs of fetal distress.
Interventions	Intervention group: active TENS. Comparsion group 1: Placebo TENS. Comparison group 2: Usual care with medication as required. Analgesia available to all groups on request.
Outcomes	Pain relief (assessed by nurse and woman), Apgar score, cord gas, baby neurological condition.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly assigned".
Allocation concealment (selection bias)	Unclear risk	No information.
Blinding (performance bias and detection bias) Participants	High risk	Placebo device, but one group had routine care in this three-arm trial.
Blinding (performance bias and detection bias) Clinical staff	High risk	Placebo device, but one group had routine care in this three-arm trial.
Blinding (performance bias and detection bias) Outcome assessor	High risk	Placebo device, but one group had routine care in this three-arm trial.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Only very limited loss to follow up.
Other bias	Unclear risk	Unclear.

Labrecque 1999

Methods	RCT.
Participants	Study in Quebec, Canada at a rural hospital. Women at low risk admitted for delivery. 35 women included in the analyses. Inclusion criteria: term pregnancy (more than 36 weeks' gestation), women in active first stage labour who complained of low back pain with no obstetric or medical complications.

Interventions	Intervention group: TENS to lower back operated by women. Comparison group 1: intracutaneous sterile water to lumbar sacral region (4 injections). Comparison group 2: routine care with massage, whirlpool baths and ambulation encouraged.
Outcomes	Low back pain, use of other analgesia, satisfaction with labour and delivery measured in postnatal period. Pain measured on a 10 cm VAS in millimetres.
Notes	The SDs reported for the pain scores were very much lower than might be expected with a VAS and appeared incorrect for some results; where SDs appeared incorrect we have not included data in data and analyses tables.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Table of random numbers in balanced blocks.
Allocation concealment (selection bias)	Low risk	Sealed, sequentially numbered, opaque envelopes.
Blinding (performance bias and detection bias) Participants	High risk	Different interventions.
Blinding (performance bias and detection bias) Clinical staff	High risk	Different interventions.
Blinding (performance bias and detection bias) Outcome assessor	High risk	Different interventions.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Small loss to follow up but very low recruitment to this study.
Other bias	Unclear risk	Of 304 women informed of the study, only 35 were recruited.

Nesheim 1981

Methods	RCT.
Participants	70 women in established labour admitted to a hospital in Norway for delivery. Inclusion criteria: cervical dilation 4 cm or more, expected to have normal birth, at term after a normal pregnancy.
Interventions	Intervention group: TENS to lower back. Comparison group: placebo TENS of identical appearance. Conventional drugs available to both groups.
Outcomes	Women's views of pain relief and use of other analgesics.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not described.
Allocation concealment (selection bias)	High risk	Coin tossed after recruitment to decide group allocation.
Blinding (performance bias and detection bias) Participants	Unclear risk	Placebo device, but not clear whether it was convincing to women and staff.
Blinding (performance bias and detection bias) Clinical staff	Unclear risk	Unclear.
Blinding (performance bias and detection bias) Outcome assessor	Unclear risk	Unclear.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No apparent loss to follow up.
Other bias	Unclear risk	Some baseline imbalance between groups with more primiparous women in the intervention group.

Neumark 1978

Methods	Randomised trial (methods unclear).
Participants	25 women (30 women were recruited to this 5-arm trial, we have not included data for the arm where women (n = 5) were allocated to receive pethidine). Inclusion criteria: "co-operative patients" with no drug dependency. Various ages and social groups. Exclusion criteria: unclear.
Interventions	5 study groups: 1) TENS group - TENS to lower back (10 women). 2) 50 mg pethidine (5 women). 3) Placebo TENS (no current) (5 women). 4) "Wrong" TENS (electrodes applied to wrong positions) (5 women). 5) No analgesia or intervention (5 women).
Outcomes	Pain measured on a VAS over 70-minute period. Progress in labour.
Notes	Paper in German. Translation notes used for data extraction. In the analysis in this review study groups 3 to 5 have been combined to form the control group.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described - "randomly divided".
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding (performance bias and detection bias) Participants	Unclear risk	The study included two placebo TENS devices (TENS with no current or TENS with the electrodes in the wrong position). It is not clear if the placebo devices were convincing to women or others.
Blinding (performance bias and detection bias) Clinical staff	Unclear risk	It is not clear if the placebo devices were convincing to women or others.

Blinding (performance bias and detection bias) Outcome assessor	Unclear risk	It is not clear if the placebo devices were convincing to women or others.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	One woman was lost to follow up.
Other bias	Unclear risk	Small study and results were difficult to interpret.

Steptoe 1984

Methods	RCT.
Participants	Study in Denmark. 26 women. Inclusion criteria: first birth, expecting normal delivery, no pacemaker, nerve problems, skin problems or psychiatric illness. Cervical dilatation 3 to 5 cm at recruitment.
Interventions	Intervention group: TENS to back. Control group: placebo equipment (with flashing lights but no current).
Outcomes	Other analgesics used.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated.
Allocation concealment (selection bias)	Unclear risk	Not stated.
Blinding (performance bias and detection bias) Participants	Unclear risk	Placebo device provided.
Blinding (performance bias and detection bias) Clinical staff	Unclear risk	Placebo device provided; unclear whether it was convincing to staff.

Blinding (performance bias and detection bias) Outcome assessor	Unclear risk	Placebo device provided; unclear whether it was convincing to staff.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear.
Other bias	Unclear risk	Unclear.

Thakur 2004

Methods	RCT.
Participants	200 women in established labour attending for care in a hospital in India. The participants were described as being predominantly from low-socio-economic groups and from urban areas. (300 women were recruited to this 3-arm trial but data for those women (n = 100) in the arm allocated to receive IM tramadol have not been included in this review.) Inclusion criteria: term pregnancy (37 to 42 weeks), vertex presentation, cervical dilatation 3 cm or more with contractions. Exclusion criteria: previous uterine scar, malpresentation, multiple pregnancy, cephalo-pelvic disproportion, antepartum haemorrhage, pre-eclampsia or other medical disorders.
Interventions	Intervention group: TENS to back. Comparison group 1: 100 mg IM tramadol. Comparison group 2: no intervention.
Outcomes	Satisfaction with pain relief, progress in labour, Apgar score, mode of delivery and maternal side effects.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Described as "randomly allocated" but groups were of identical size with identical numbers of primiparous and multiparous women in each group.

Allocation concealment (selection bias)	Unclear risk	Method of randomisation not described.
Blinding (performance bias and detection bias) Participants	High risk	Each group had different interventions.
Blinding (performance bias and detection bias) Clinical staff	High risk	Each group had different interventions.
Blinding (performance bias and detection bias) Outcome assessor	High risk	Each group had different interventions.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Apparently there was no loss to follow up.
Other bias	Unclear risk	Groups were unusually similar and it was not clear that there had been stratification to achieve such balanced groups.

Thomas 1988

Methods	RCT with placebo device.
Participants	280 women recruited in early labour (both spontaneous and induced). Exclusion criteria: women in advanced labour with cervical dilatation 7 cm or over, those who had already received analgesia, non-English speaking, unable to give consent, with malpresentation, in premature labour, multiple pregnancy, previous exposure to TENS or booked for Caesarean section.

Interventions	Intervention group: TENS to lower back. Comparison group: non-active placebo TENS. Both groups instructed in use. Both groups were able to request other analgesia.
Outcomes	Pain assessment hourly in labour, satisfaction with TENS.
Notes	Pain was assessed on a VAS recorded in millimetres.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random number tables.
Allocation concealment (selection bias)	Unclear risk	TENS applied by staff not involved in the trial.
Blinding (performance bias and detection bias) Participants	Unclear risk	Placebo device (identical in appearance but it was not clear whether women or staff could detect whether the units were working or not).
Blinding (performance bias and detection bias) Clinical staff	Unclear risk	Placebo device (identical in appearance but it was not clear whether women or staff could detect whether the units were working or not).
Blinding (performance bias and detection bias) Outcome assessor	Unclear risk	Unclear.
Incomplete outcome data (attrition bias) All outcomes	High risk	High levels of missing data (approximately 50%) for some outcomes measured in labour and many women withdrew from the study in the later stages of labour.

Other bias	Unclear risk	Baseline imbalance. More primiparous women in the TENS group (57%) than in the placebo group (45%).

Tsen 2000

Methods	RCT examining active TENS versus a placebo device.
Participants	Study carried out in a Boston hospital (USA). 40 women receiving a combined spinal epidural were included. Inclusion criteria: women recruited in active spontaneous labour, at term with singleton baby in vertex position, requesting analgesia. Cervical dilatation at recruitment less than 5 cm.
Interventions	Intervention group: active TENS to lower back. Comparison group: inactive TENS to lower back (placebo). Women in both groups received a combined spinal epidural.
Outcomes	Pain score measured at several time points on a VAS. Rate of cervical dilatation, amount of oxytocin and analgesia, fetal heart rate, Apgar score and side effects.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Described as "randomized in a double blinded fashion".
Allocation concealment (selection bias)	Low risk	"Sequentially numbered, opaque, shuffled envelopes".
Blinding (performance bias and detection bias) Participants	Unclear risk	Described as double blinded study. It was stated that care staff and assessors were not aware of group allocation. The placebo device was switched off after the combined spinal epidural had been set up.
Blinding (performance bias and detection bias) Clinical staff	Unclear risk	Inactive device provided.

Blinding (performance bias and detection bias) Outcome assessor	Unclear risk	Unclear.
Incomplete outcome data (attrition bias) All outcomes	Low risk	One woman withdrew from the study.
Other bias	Unclear risk	Some baseline imbalance. Fewer women (30%) in the intervention group were nulliparous compared with 80% in the control group.

Tsen 2001

Methods	RCT.
Participants	40 women attending a Boston (USA) hospital. Inclusion criteria: women in active, spontaneous labour with singleton, vertex, term pregnancy, requesting epidural. Cervical dilatation less than 5 cm on recruitment.
Interventions	All women had a Bupivacaine epidural. Intervention: TENS to lower back. Comparison Group: placebo/inactive TENS.
Outcomes	VAS pain scores, use of oxytocin, fetal heart rate, Apgar scores and maternal side effects.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No information provided.
Allocation concealment (selection bias)	Low risk	"Sequentially numbered, opaque, shuffled envelopes".
Blinding (performance bias and detection bias) Participants	Unclear risk	Described as double-blind trial. TENS machines were in pouches so women could not see if they were on or off.
Blinding (performance bias and detection bias) Clinical staff	Unclear risk	Unclear.

Blinding (performance bias and detection bias) Outcome assessor	Unclear risk	Unclear.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women included in the analysis.
Other bias	Unclear risk	Some baseline differences, 7/20 women in the intervention group and 3/20 in the control group had opiate analgesia before entry to the study.

van der Ploeg 1996

Methods	RCT.
Participants	Study carried out in the Netherlands in an area where 40% of the deliveries occur at home. 96 women recruited in 3rd trimester and attending hospital for delivery (72 primiparous and 22 multiparous women). Inclusion criteria: women requiring pain relief in the first stage of labour. Exclusion criteria: not specified.
Interventions	Intervention: TENS to the back allowing both low and high intensity stimulation, from admission until full cervical dilatation. Comparison group: placebo TENS device which looked identical to the active TENS unit. BOTH GROUPS received patient-controlled pethidine (75 mg) and promethazine (25 mg).
Outcomes	Length of first and second stages of labour; mode of delivery, Apgar score, VAS score for satisfaction with pain relief and TENS.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not stated.
Allocation concealment (selection bias)	Unclear risk	Not clear, described as a "prospective randomized trial".

Blinding (performance bias and detection bias) Participants	Unclear risk	A placebo device was provided which was described as appearing identical to the active device. It was not clear whether women and clinical staff would be able to ascertain whether or not women had received an active TENS device.
Blinding (performance bias and detection bias) Clinical staff	Unclear risk	Unclear.
Blinding (performance bias and detection bias) Outcome assessor	Unclear risk	Unclear.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow up apparent.
Other bias	Unclear risk	Women attending hospital for delivery may have been a high risk group in a context with high home delivery rates.

Vasegh 2010

Methods	RCT.
Participants	84 primiparous women.
Interventions	Intervention group: (42 women) TENS to back. Comparison group: (42 women) TENS to acupuncture points.
Outcomes	Satisfaction with intervention, duration of labour, mode of birth, use of oxytocin, Apgar score and fetal heart rate.
Notes	We have not included any data from this study in our data and analyses tables. No data were reported by randomisation group for any outcome. It was reported by the authors that the amount of oxytocin use was lower and the active phase of labour was shorter in the group receiving TENS to acupuncture points but no other differences between groups were reported.

Risk of bias

Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Unclear risk	Not described.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding (performance bias and detection bias) Participants	High risk	TENS to different areas of the body.
Blinding (performance bias and detection bias) Clinical staff	High risk	Not feasible.
Blinding (performance bias and detection bias) Outcome assessor	High risk	Not described.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported.
Other bias	Unclear risk	There was insufficient information on study methods to allow full assessment of risk of bias.

Wang 2007

Methods	Randomised trial.

Participants	120 women recruited in a hospital in the Zhongshan region of China. Inclusion criteria: primiparous women with normal fetal position. Exclusion criteria: women with congenital heart disease, twin pregnancy or hypertension.
Interventions	Intervention: TENS to 4 bilateral acupuncture points. The frequency and intensity of TENS was adjusted according to tolerance. It was not clear how or by whom the TENS were operated. Comparison groups: two groups each of 30 women, one group received oxytocin and one group received no intervention ("all drugs and therapeutic methods were suspended"). The latter group were used as the control group for this review.
Outcomes	Rating of pain (assessed by clinician and women), pain progression, length of time for full cervical dilatation, blood cortisol content and measures of uterine contraction.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described.
Allocation concealment (selection bias)	Unclear risk	Described as "randomly divided".
Blinding (performance bias and detection bias) Participants	High risk	The control group received no intervention.
Blinding (performance bias and detection bias) Clinical staff	High risk	Not feasible.
Blinding (performance bias and detection bias) Outcome assessor	High risk	Not described.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusions or drop-outs from the study apparent.

Other bias	Unclear risk	Unclear.

Wattrisse 1993

Methods	RCT.
Participants	120 primiparous women. Inclusion criteria: primiparous women at term, cephalic presentation and cervical dilatation of 3 cm. Exclusion criteria: women who refused consent or unable to understand and complete the VAS used in the study.
Interventions	Intervention group: Limoge current applied to the cranium (TENS). Control group: routine care. Both groups had epidural analgesia (Bupivacaine).
Outcomes	Pain scores, duration of labour, amount of analgesia used, mode of delivery.
Notes	Report in French, data were extracted using translation notes.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not stated.
Allocation concealment (selection bias)	Unclear risk	Not clear, allocation by drawing names.
Blinding (performance bias and detection bias) Participants	High risk	Blinding not attempted.
Blinding (performance bias and detection bias) Clinical staff	High risk	Blinding not attempted.
Blinding (performance bias and detection bias) Outcome assessor	High risk	Not described.

Incomplete outcome data (attrition bias) All outcomes	Low risk	No apparent loss to follow up.
Other bias	Unclear risk	Not clear whether outcomes relating to duration of labour excluded those women going on to have caesarean or assisted deliveries.

IM: Intramuscular
ITT: intention-to-treat
RCT: randomised controlled trial
SD: standard deviation
TENS: Transcutaneous electrical nerve stimulation
VAS: Visual analogue scale

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Anonymous 1995	Brief conference abstract. No results for groups reported (P values provided but no other data). We attempted to follow up this reference through the conference organisers but were unable to contact the author.
Canino 1987	This study examined the use of TENS after Caesarean section rather than in labour.
Chia 1990	20 women were included in this randomised cross-over trial; TENS to the back was compared with Entonox®. This comparison is not relevant for this review. (This study was originally included in the review but this updated version is one in a series of Cochrane reviews examining pain management in labour which contribute to an overview of systematic reviews of pain management for women in labour (Jones 2011b) and which share a generic protocol (Jones 2011a). In order to comply with the generic protocol which has specific inclusion criteria relating to comparison interventions, this trial has been moved to a review examining inhaled analgesia as it no longer meets the inclusion criteria for the TENS review.
Dunn 1989	Study examining acupuncture-point TENS for the induction of labour rather than for pain relief in labour. Main outcome was the strength of uterine contractions.
Erkkola 1980	Not random allocation. Women were assigned to groups alphabetically.
Hulkko 1979	This study carried out in 1977 included women with post-dates pregnancies admitted to hospital for induction. Allocation to groups was not randomised.
Merry 1983	This study involving 17 women used non-random methods of allocation (hospital number). The study was reported in a brief abstract.

Study	Reason for exclusion
Tajali-Awal 1995	Not clear that this is a RCT. Randomisation described as sequential. There were high levels of attrition - 30% were excluded (for reasons that may have been related to outcomes of the review, e.g. if they used any other form of pain relief or had a caesarean section).
Tawfik 1982	This study was originally included in this review. This review is one in a series of Cochrane reviews examining pain management in labour. These reviews contribute to an overview of systematic reviews of pain management for women in labour (Jones 2011b) and share a generic protocol (Jones 2011a). In order to comply with the generic protocol which has specific inclusion criteria relating to comparison interventions, the Tawfik 1982 trial (TENS versus pethidine) has been moved to the Parenteral opioids review (Ullman 2010), as it no longer meets the inclusion criteria for this updated TENS review.

Characteristics of studies awaiting assessment [ordered by study ID]

Knobel 2005

Methods	RCT.
Participants	60 women in labour.
Interventions	3 arms. Two types of TENS were compared with placebo (false) TENS.
Outcomes	Use of other analgesia, satisfaction with pain relief.
Notes	The paper is published in Portuguese and we are awaiting translation so that we can assess eligibility for inclusion.

RCT: randomised controlled trial
TENS: Transcutaneous electrical nerve stimulation

Data and analyses

Comparison 1. TENS versus placebo TENS or routine care **Open in table viewer**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Severe pain (various definitions) measured in labour Show forest plot	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

Analysis 1.1

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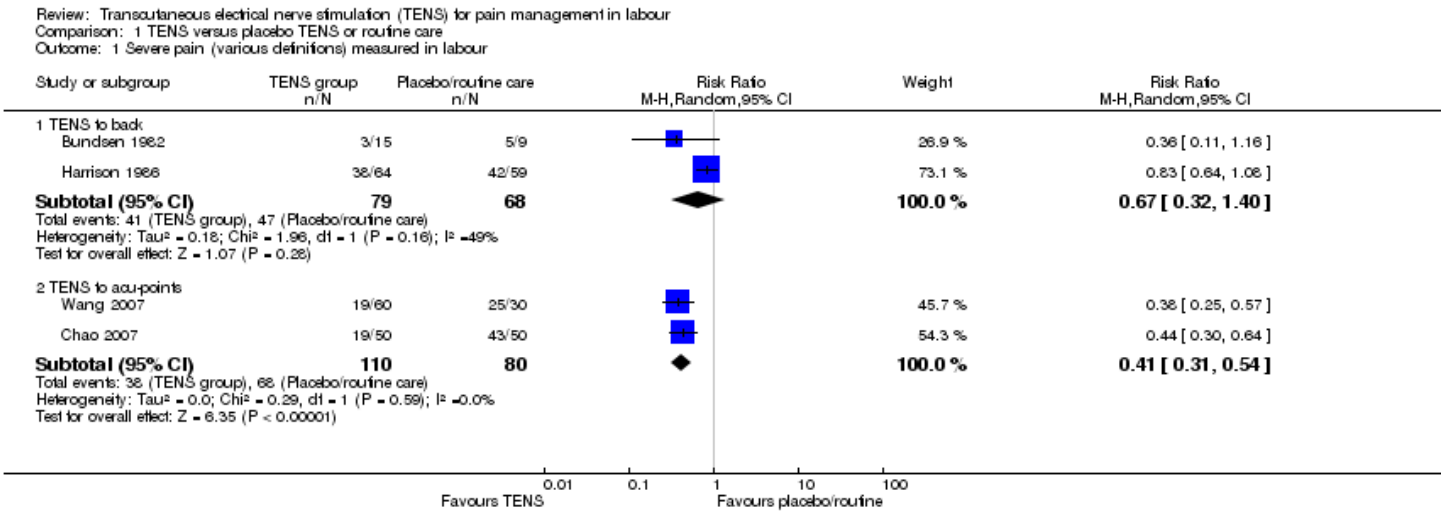

Comparison 1 TENS versus placebo TENS or routine care, Outcome 1 Severe pain (various definitions) measured in labour.

1.1 TENS to back	2	147	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.32, 1.40]
1.2 TENS to acu-points	2	190	Risk Ratio (M-H, Random, 95% CI)	0.41 [0.31, 0.54]
2 Mean pain score in labour (measured on various VASs) Show forest plot	2	299	Std. Mean Difference (IV, Random, 95% CI)	-1.01 [-1.00, 0.97]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 1.2

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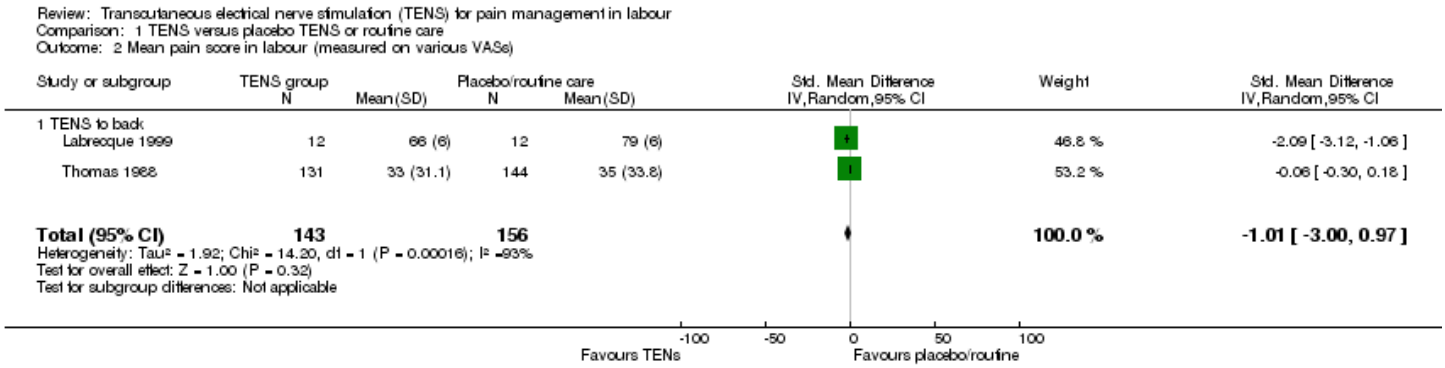

Comparison 1 TENS versus placebo TENS or routine care, Outcome 2 Mean pain score in labour (measured on various VASs).

2.1 TENS to back	2	299	Std. Mean Difference (IV, Random, 95% CI)	-1.01 [-1.00, 0.97]
3 Women satisfied with pain relief (various definitions) Show forest plot	6		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 1.3

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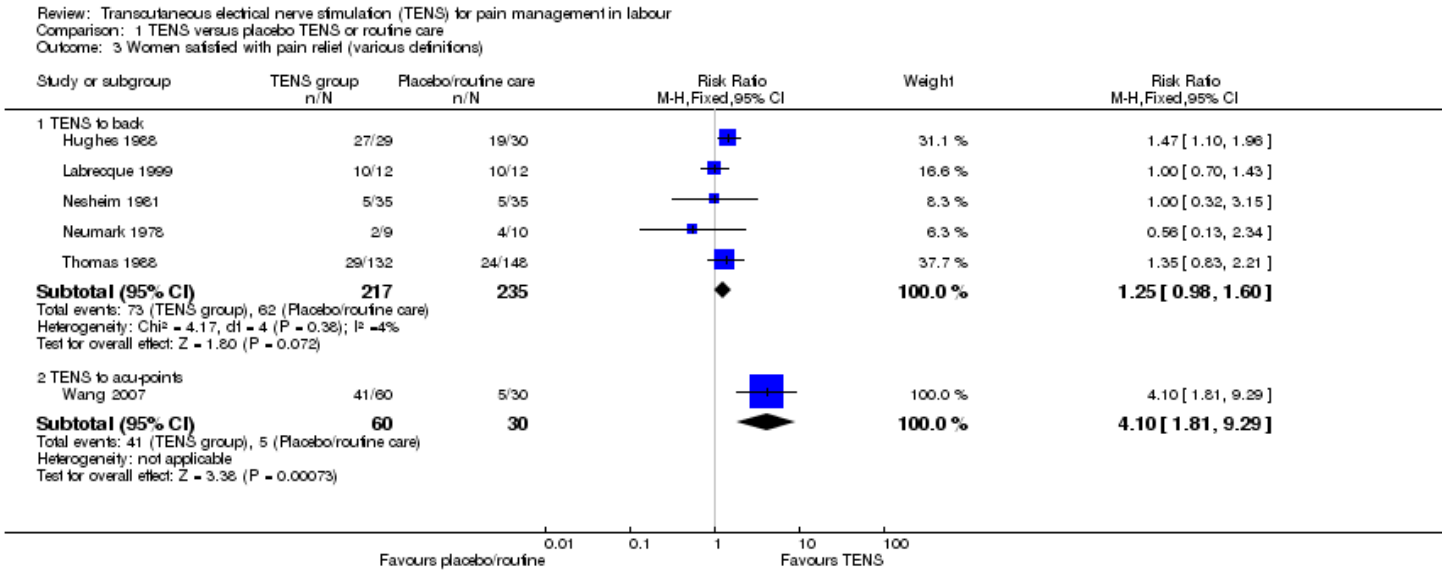

Comparison 1 TENS versus placebo TENS or routine care, Outcome 3 Women satisfied with pain relief (various definitions).

3.1 TENS to back	5	452	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [0.98, 1.60]
3.2 TENS to acu-points	1	90	Risk Ratio (M-H, Fixed, 95% CI)	4.1 [1.81, 9.29]
4 Women would use TENS again in a future labour Show forest plot	5		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 1.4

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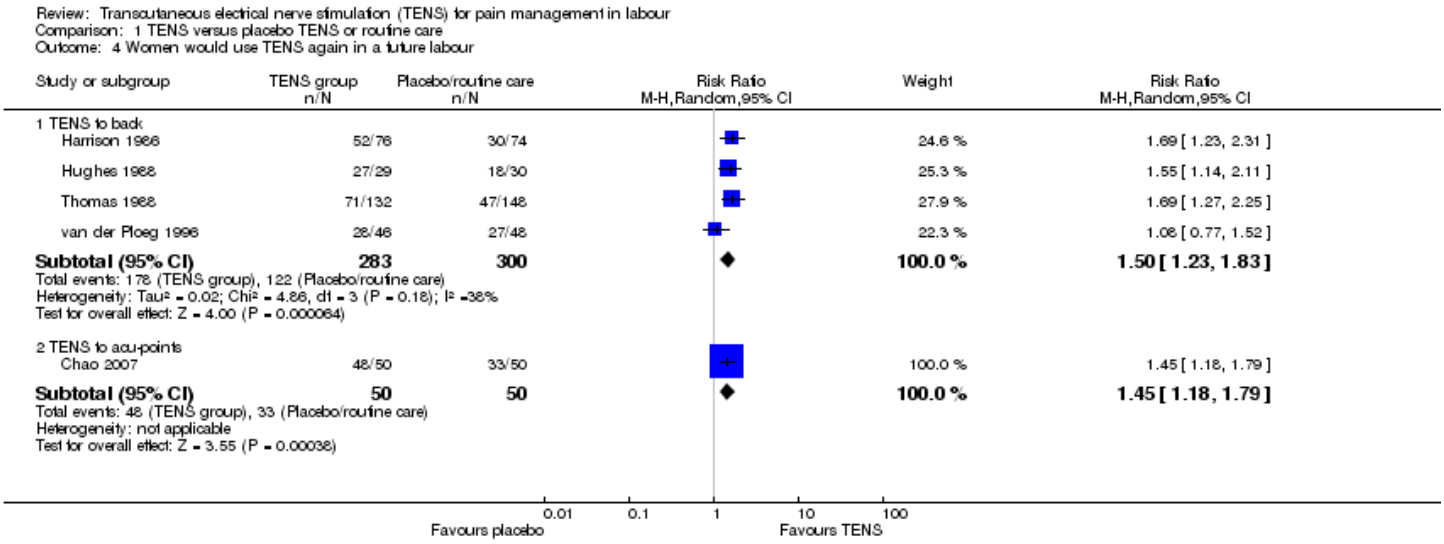

Comparison 1 TENS versus placebo TENS or routine care, Outcome 4 Women would use TENS again in a future labour.

4.1 TENS to back	4	583	Risk Ratio (M-H, Random, 95% CI)	1.50 [1.23, 1.83]
4.2 TENS to acu-points	1	100	Risk Ratio (M-H, Random, 95% CI)	1.45 [1.18, 1.79]
5 Caesarean section rate Show forest plot	10		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 1.5

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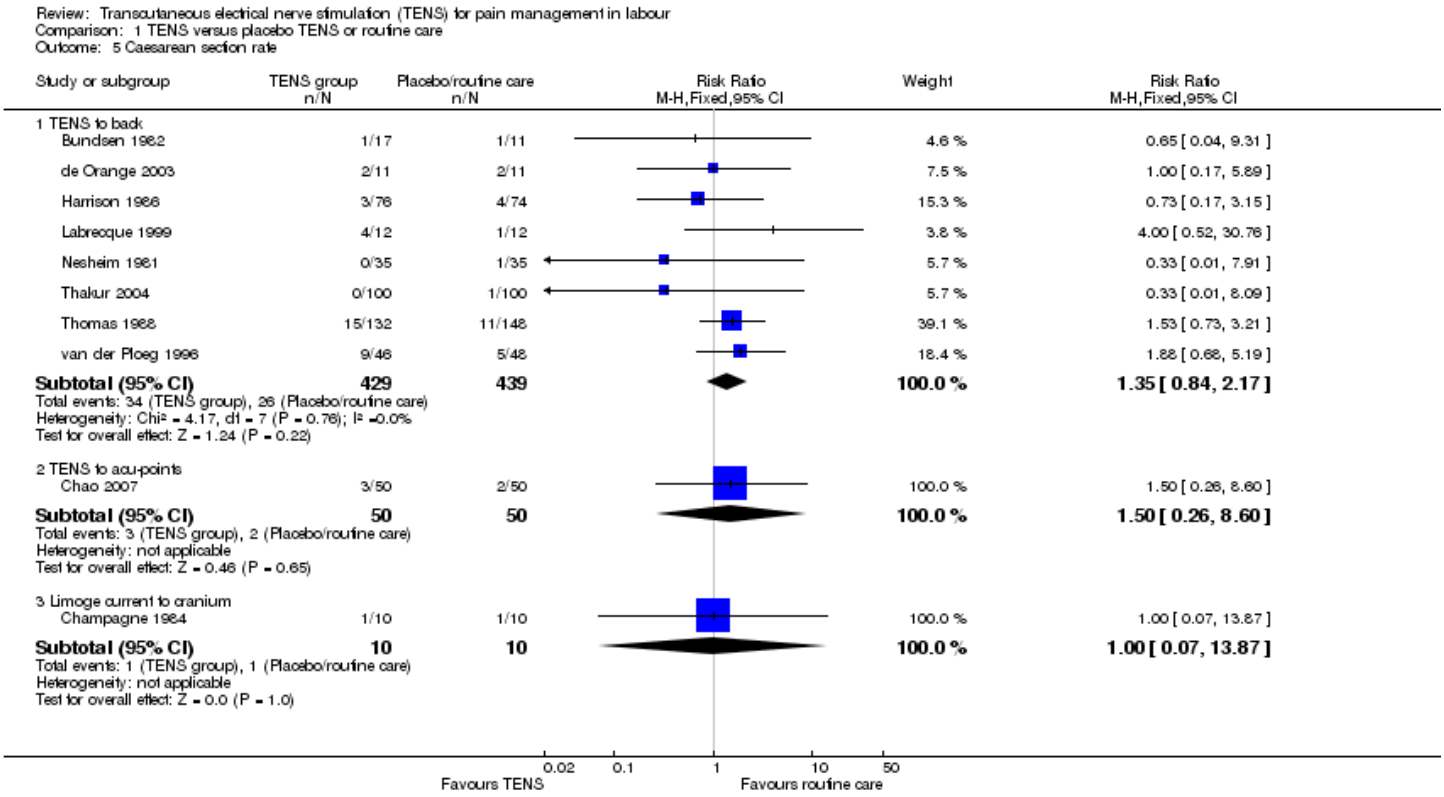

Comparison 1 TENS versus placebo TENS or routine care, Outcome 5 Caesarean section rate.

5.1 TENS to back	8	868	Risk Ratio (M-H, Fixed, 95% CI)	1.35 [0.84, 2.17]
5.2 TENS to acu-points	1	100	Risk Ratio (M-H, Fixed, 95% CI)	1.5 [0.26, 8.60]
5.3 Limoge current to cranium	1	20	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.07, 13.87]
6 Assisted delivery Show forest plot	9		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 1.6

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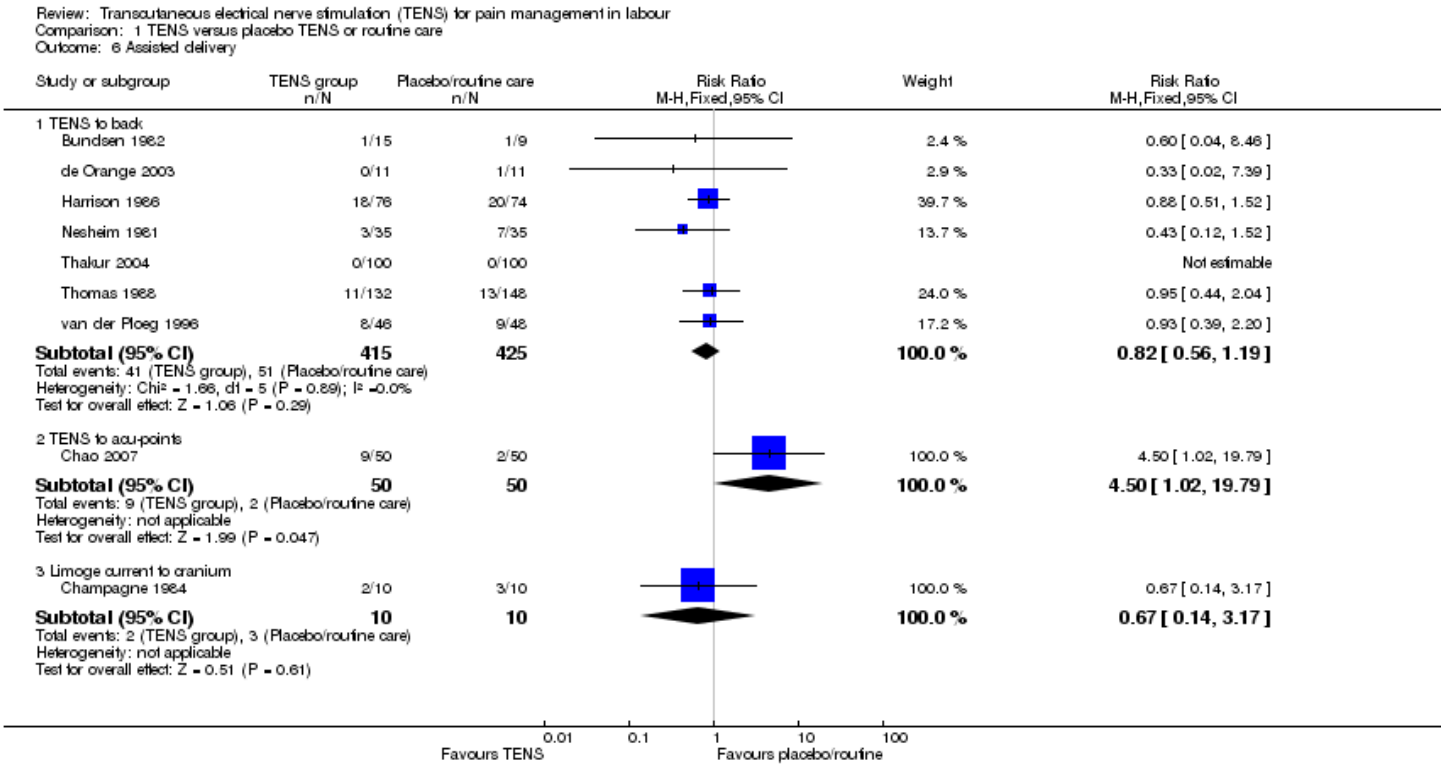

Comparison 1 TENS versus placebo TENS or routine care, Outcome 6 Assisted delivery.

6.1 TENS to back	7	840	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.56, 1.19]
6.2 TENS to acu-points	1	100	Risk Ratio (M-H, Fixed, 95% CI)	4.5 [1.02, 19.79]
6.3 Limoge current to cranium	1	20	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.14, 3.17]
7 Other pharmacological pain relief required (various definitions)	6		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Show forest plot

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 1.7

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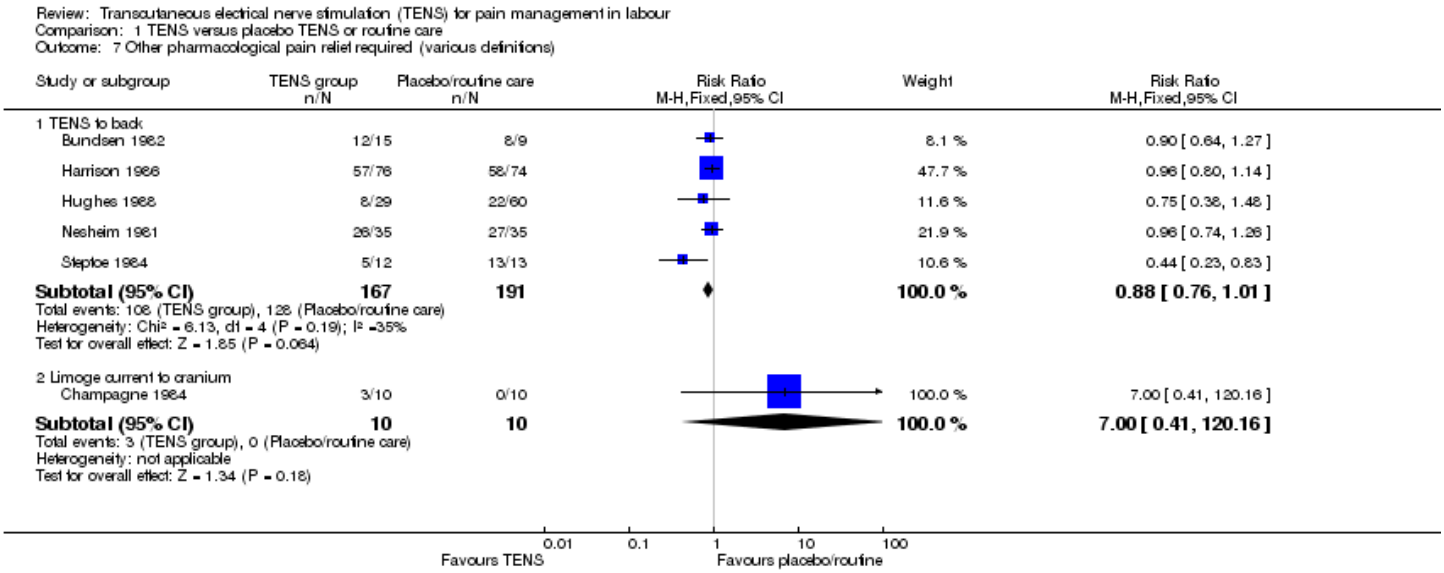

Comparison 1 TENS versus placebo TENS or routine care, Outcome 7 Other pharmacological pain relief required (various definitions).

7.1 TENS to back	5	358	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.76, 1.01]
7.2 Limoge current to cranium	1	20	Risk Ratio (M-H, Fixed, 95% CI)	7.0 [0.41, 120.16]
8 Amount of other medication (various drugs) **Show forest plot**	2	282	Std. Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.33, 0.14]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 1.8

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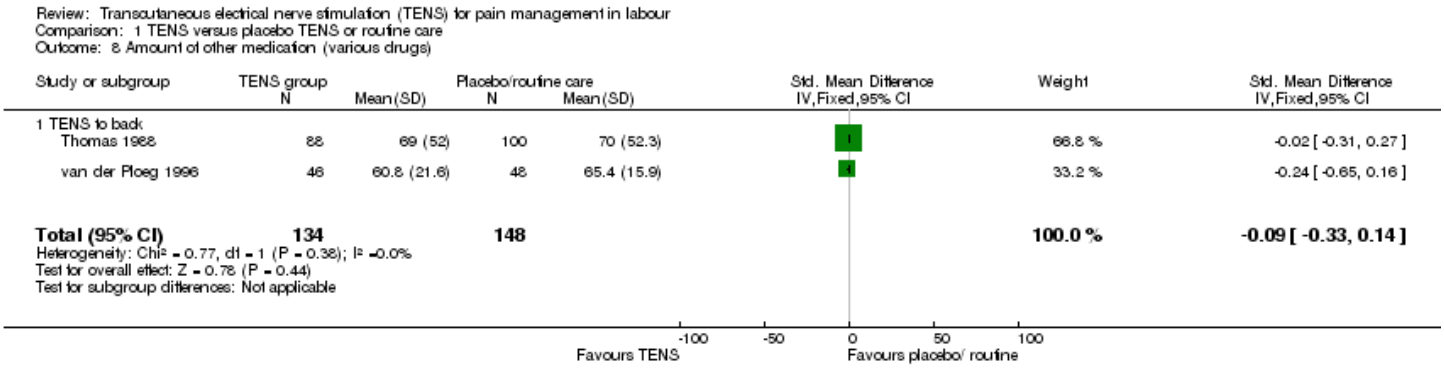

Comparison 1 TENS versus placebo TENS or routine care, Outcome 8 Amount of other medication (various drugs).

8.1 TENS to back	2	282	Std. Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.33, 0.14]
9 Augmentation of labour Show forest plot	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 1.9

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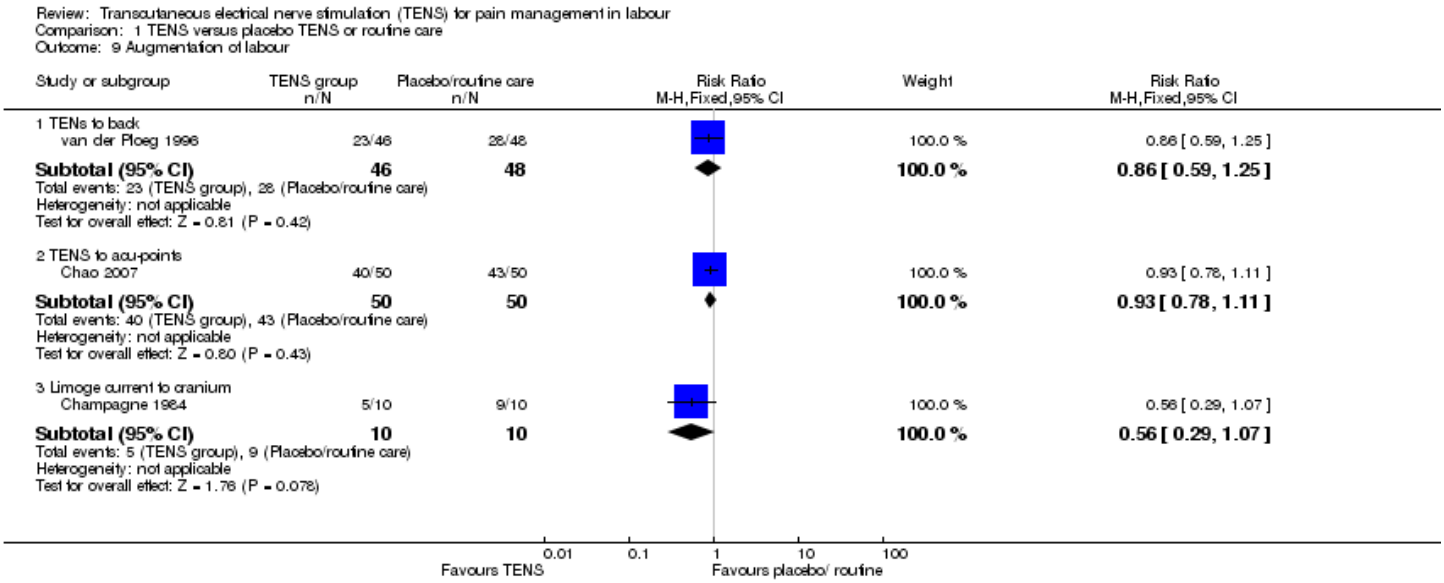

Comparison 1 TENS versus placebo TENS or routine care, Outcome 9 Augmentation of labour.

9.1 TENs to back	1	94	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.59, 1.25]
9.2 TENS to acu-points	1	100	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.78, 1.11]
9.3 Limoge current to cranium	1	20	Risk Ratio (M-H, Fixed, 95% CI)	0.56 [0.29, 1.07]
10 Duration of first stage of labour in minutes (various starting points) Show forest plot	5		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 1.10

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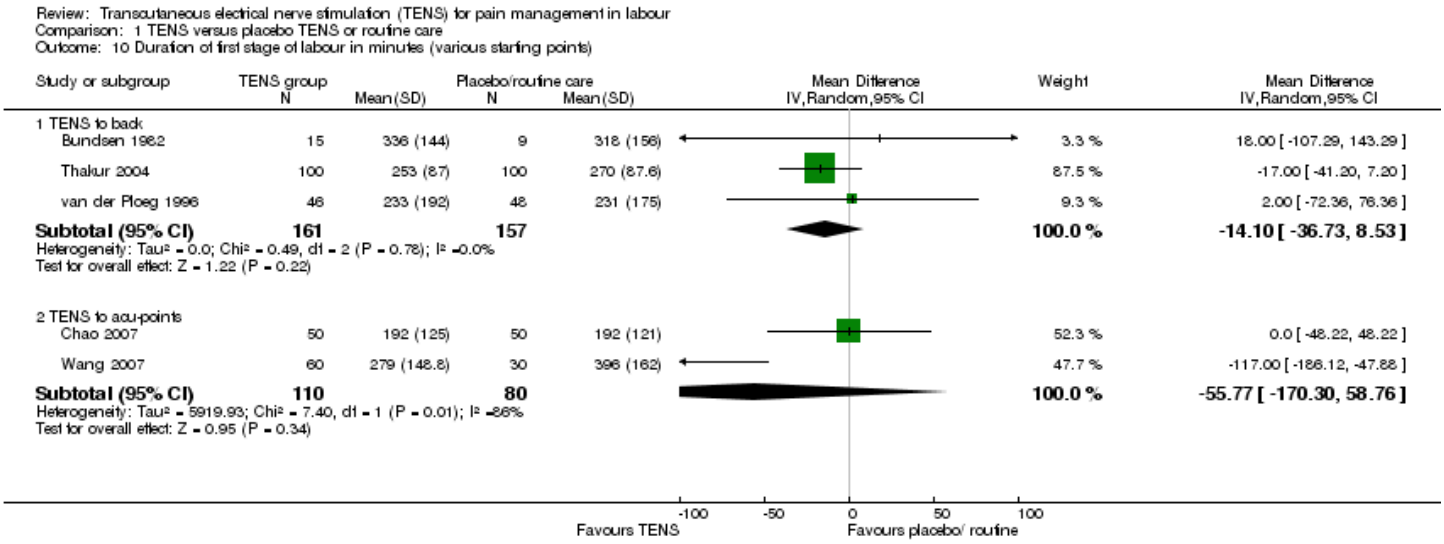

Comparison 1 TENS versus placebo TENS or routine care, Outcome 10 Duration of first stage of labour in minutes (various starting points).

10.1 TENS to back	3	318	Mean Difference (IV, Random, 95% CI)	-14.10 [-36.73, 8.53]
10.2 TENS to acu-points	2	190	Mean Difference (IV, Random, 95% CI)	-55.77 [-170.30, 58.76]
11 Duration of second stage of labour in minutes Show forest plot	4		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 1.11

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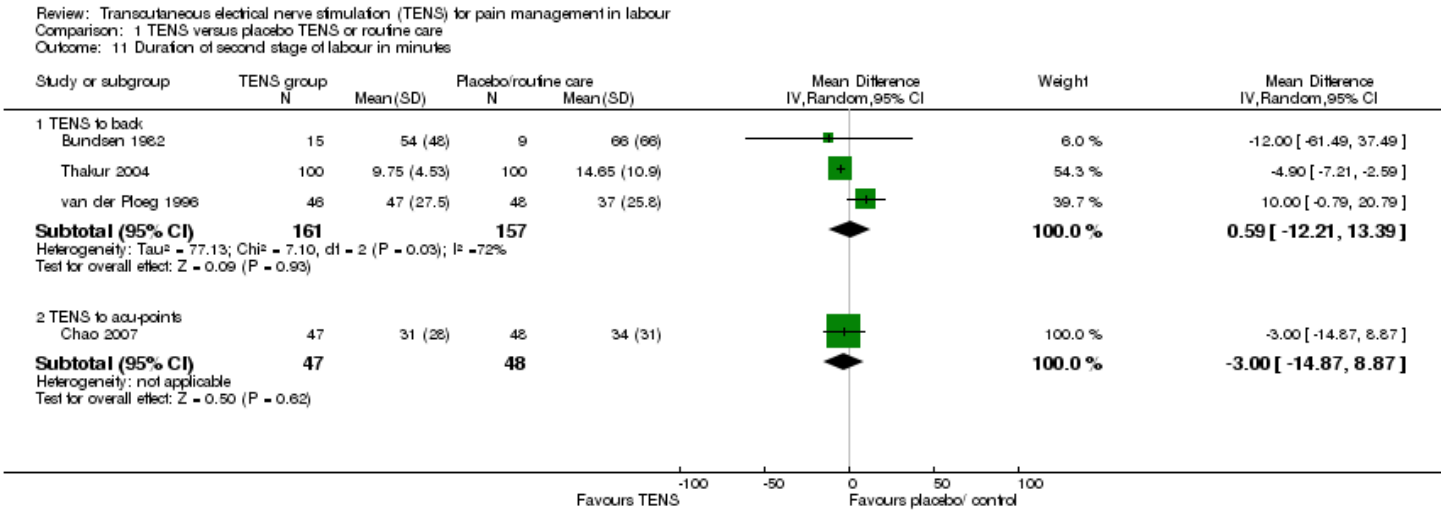

Comparison 1 TENS versus placebo TENS or routine care, Outcome 11 Duration of second stage of labour in minutes.

11.1 TENS to back	3	318	Mean Difference (IV, Random, 95% CI)	0.59 [-12.21, 13.39]
11.2 TENS to acu-points	1	95	Mean Difference (IV, Random, 95% CI)	-3.0 [-14.87, 8.87]
12 Epidural required Show forest plot	7		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 1.12

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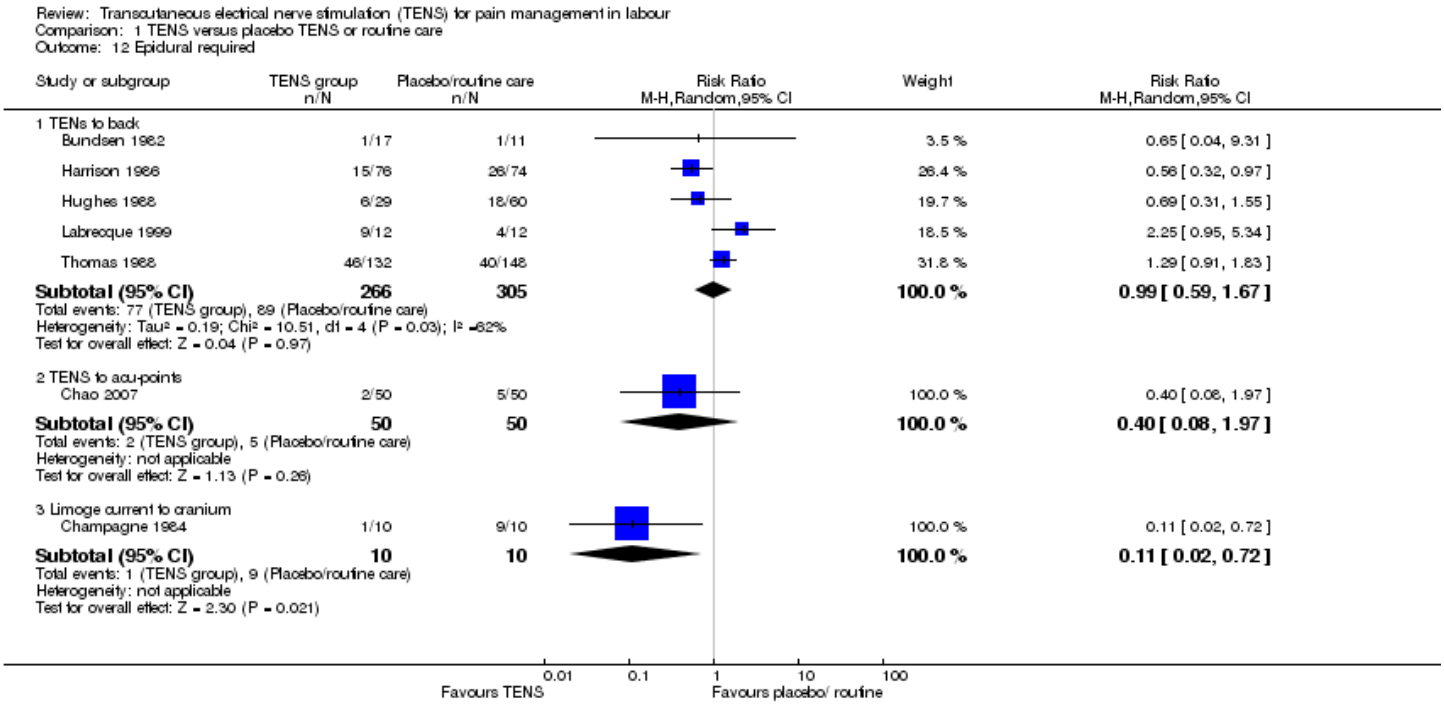

Comparison 1 TENS versus placebo TENS or routine care, Outcome 12 Epidural required.

12.1 TENs to back	5	571	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.59, 1.67]
12.2 TENS to acu-points	1	100	Risk Ratio (M-H, Random, 95% CI)	0.40 [0.08, 1.97]
12.3 Limoge current to cranium	1	20	Risk Ratio (M-H, Random, 95% CI)	0.11 [0.02, 0.72]
13 Fetal distress Show forest plot	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 1.13

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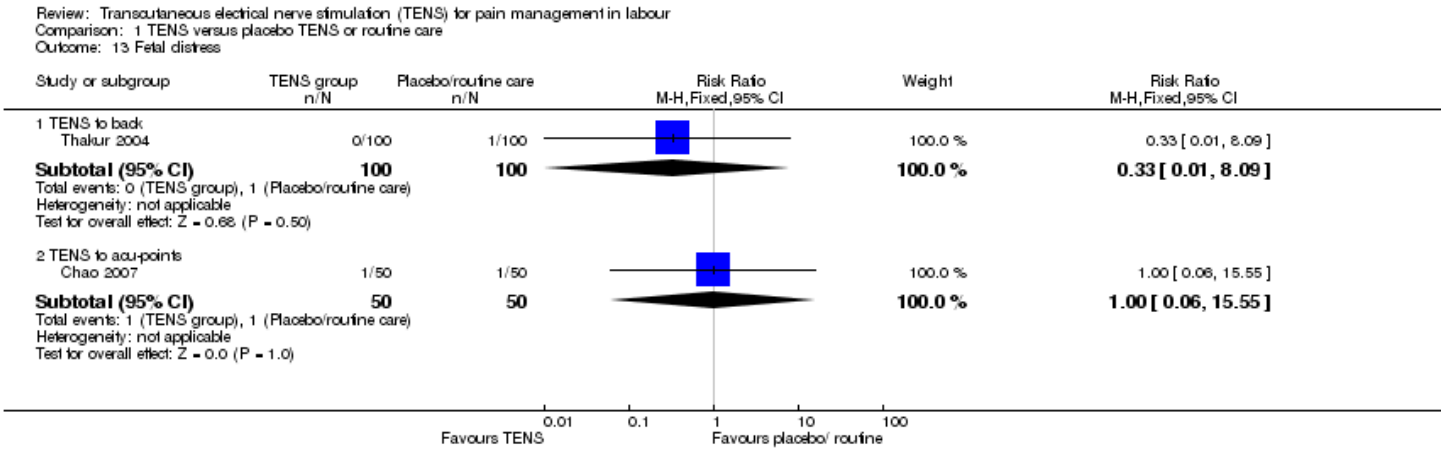

Comparison 1 TENS versus placebo TENS or routine care, Outcome 13 Fetal distress.

13.1 TENS to back	1	200	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.01, 8.09]
13.2 TENS to acu-points	1	100	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.06, 15.55]

Comparison 2. TENS with epidural versus epidural alone

Open in table viewer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain score (VAS) at 60 minutes Show forest plot	2	80	Mean Difference (IV, Fixed, 95% CI)	0.23 [-8.71, 9.16]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 2.1

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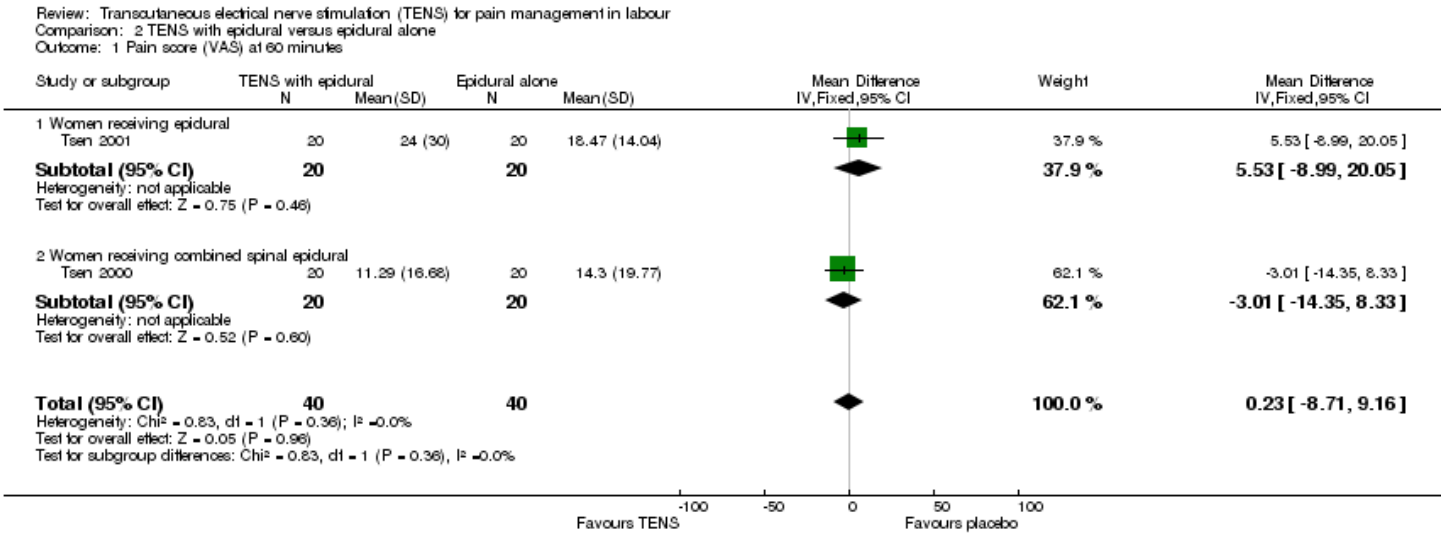

Comparison 2 TENS with epidural versus epidural alone, Outcome 1 Pain score (VAS) at 60 minutes.

1.1 Women receiving epidural	1	40	Mean Difference (IV, Fixed, 95% CI)	5.53 [-8.99, 20.05]
1.2 Women receiving combined spinal epidural	1	40	Mean Difference (IV, Fixed, 95% CI)	-3.01 [-14.35, 8.33]
2 Caesarean section rate Show forest plot	1	40	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.01, 7.72]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 2.2

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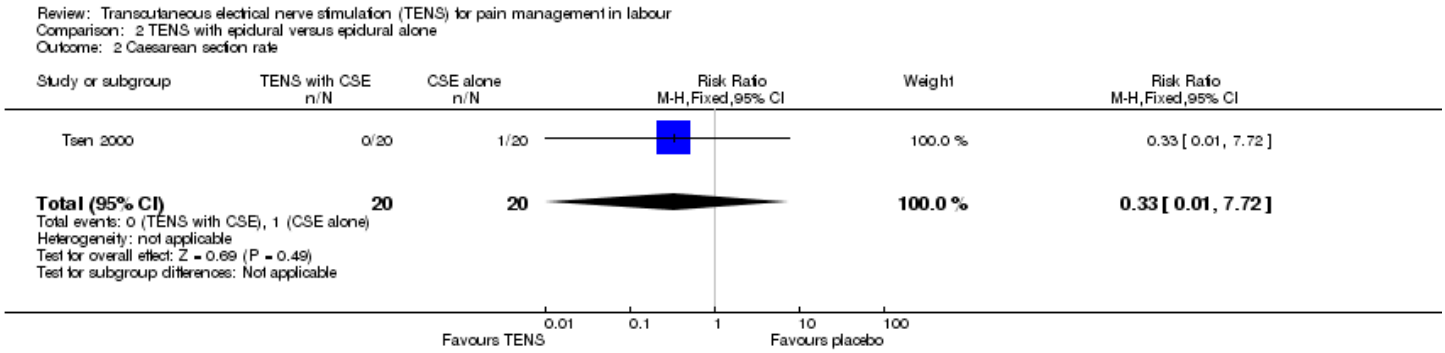

Comparison 2 TENS with epidural versus epidural alone, Outcome 2 Caesarean section rate.

3 Assisted delivery	1	40	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.07, 14.90]
Show forest plot				

Analysis 2.3

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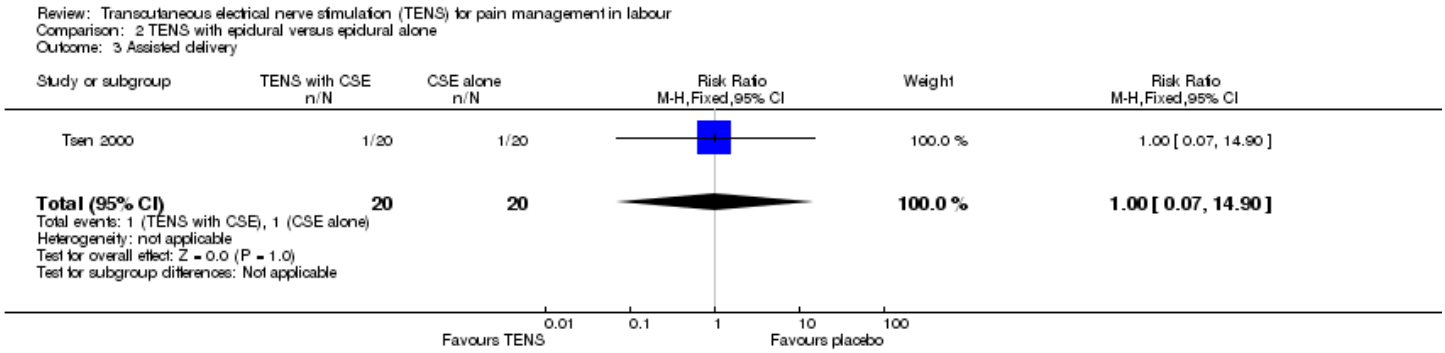

Comparison 2 TENS with epidural versus epidural alone, Outcome 3 Assisted delivery.

Comparison 3. Cranial TENS with epidural versus epidural alone

Open in table viewer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain score during the first stage of labour Show forest plot	1	120	Mean Difference (IV, Fixed, 95% CI)	0.06 [-0.66, 0.78]

Analysis 3.1

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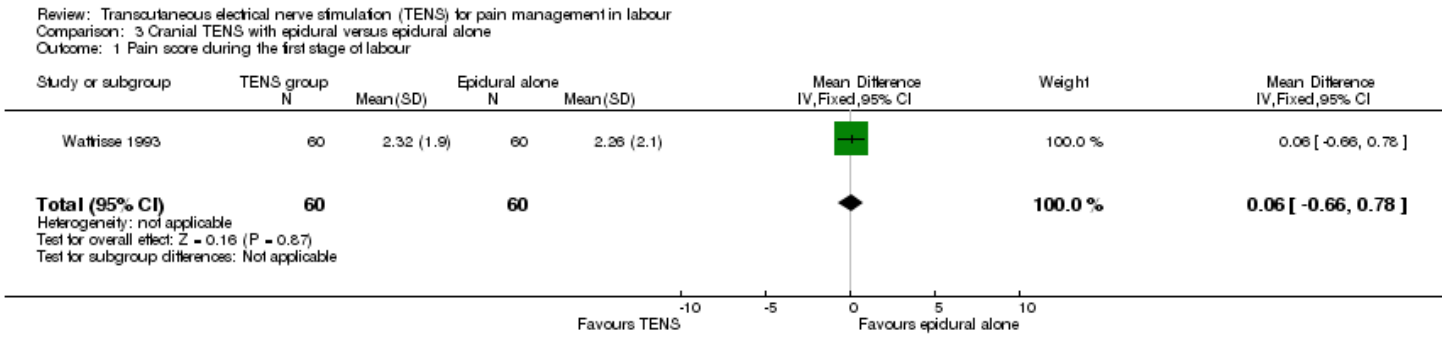

Comparison 3 Cranial TENS with epidural versus epidural alone, Outcome 1 Pain score during the first stage of labour.

2 Caesarean section rate Show forest plot	1	113	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.21, 4.83]

Analysis 3.2

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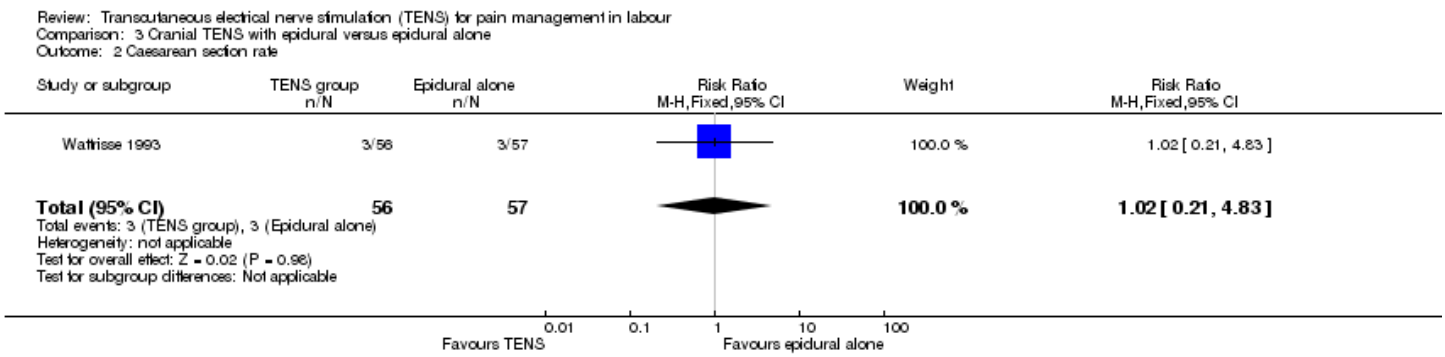

Comparison 3 Cranial TENS with epidural versus epidural alone, Outcome 2 Caesarean section rate.

3 Instrumental delivery Show forest plot	1	113	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.54, 1.16]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 3.3

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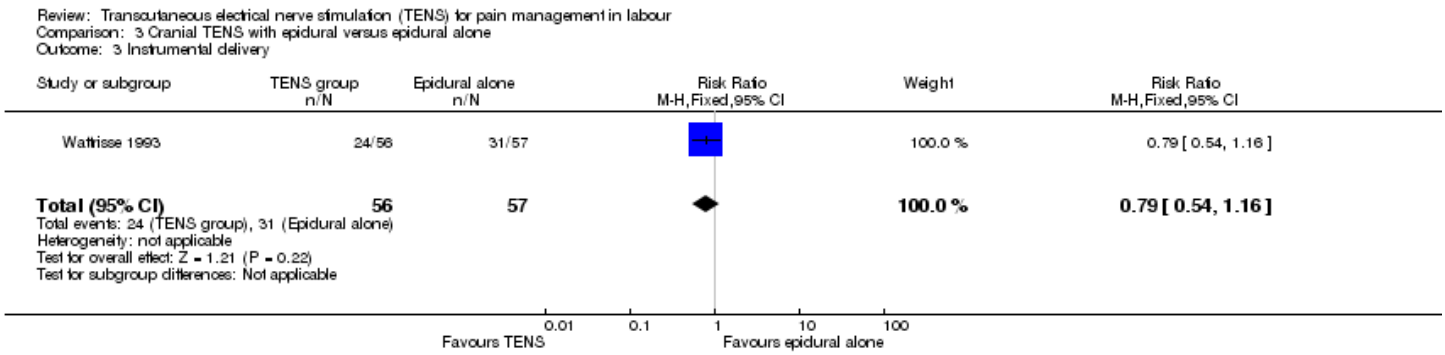

Comparison 3 Cranial TENS with epidural versus epidural alone, Outcome 3 Instrumental delivery.

4 Duration of pain relief in minutes (first injection) Show forest plot	1	120	Mean Difference (IV, Fixed, 95% CI)	22.00 [9.09, 34.91]

Analysis 3.4

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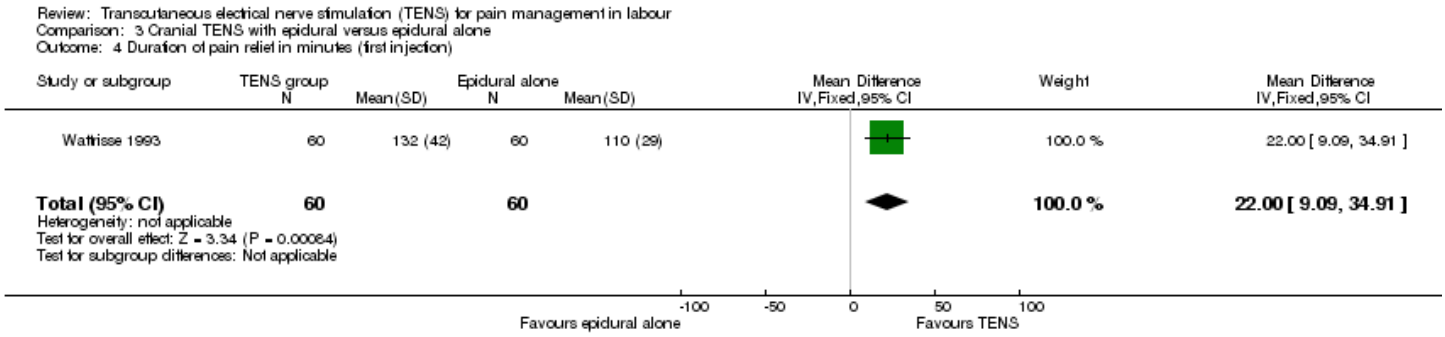

Comparison 3 Cranial TENS with epidural versus epidural alone, Outcome 4 Duration of pain relief in minutes (first injection).

5 Mean dose of epidural analgesia (Bupivacaine) Show forest plot	1	113	Mean Difference (IV, Fixed, 95% CI)	-1.80 [-11.46, 7.86]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 3.5

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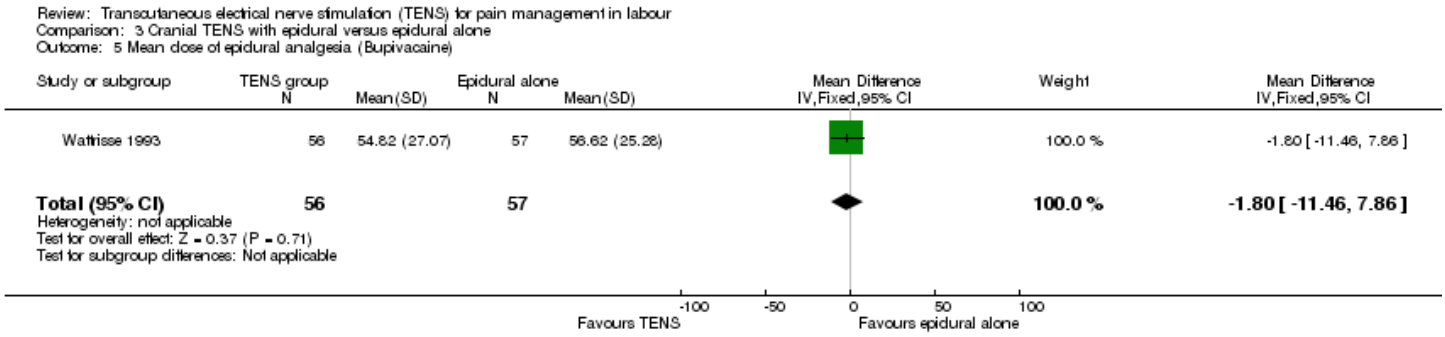

Comparison 3 Cranial TENS with epidural versus epidural alone, Outcome 5 Mean dose of epidural analgesia (Bupivacaine).

6 Duration of first stage of labour in minutes Show forest plot	1	120	Mean Difference (IV, Fixed, 95% CI)	22.79 [-27.81, 73.39]

Analysis 3.6

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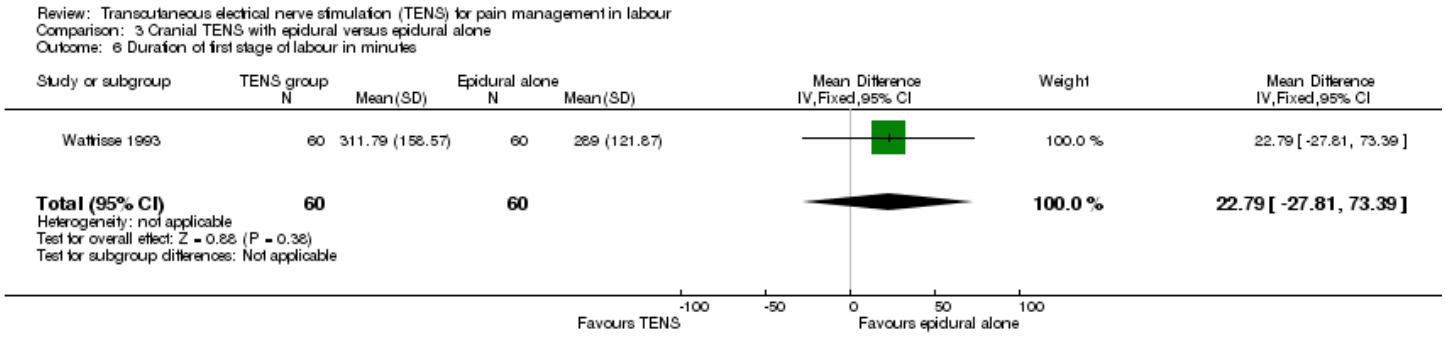

Comparison 3 Cranial TENS with epidural versus epidural alone, Outcome 6 Duration of first stage of labour in minutes.

Comparison 4. TENS versus sterile water injection

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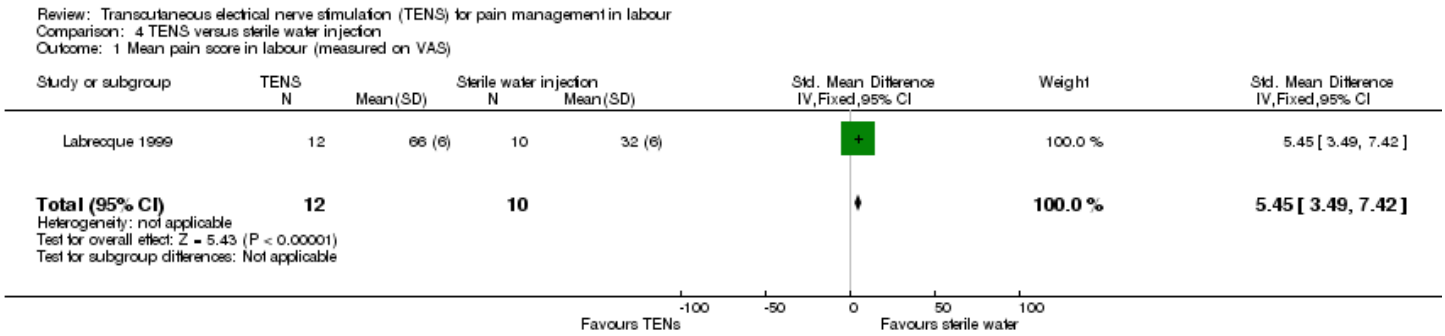
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean pain score in labour (measured on VAS)	1	22	Std. Mean Difference (IV, Fixed, 95% CI)	5.45 [3.49, 7.42]
Show forest plot				

Analysis 4.1

Open in figure viewer | Download as PowerPoint



Comparison 4 TENS versus sterile water injection, Outcome 1 Mean pain score in labour (measured on VAS).

2 Epidural required	1	22	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.64, 1.80]
Show forest plot				

Analysis 4.2

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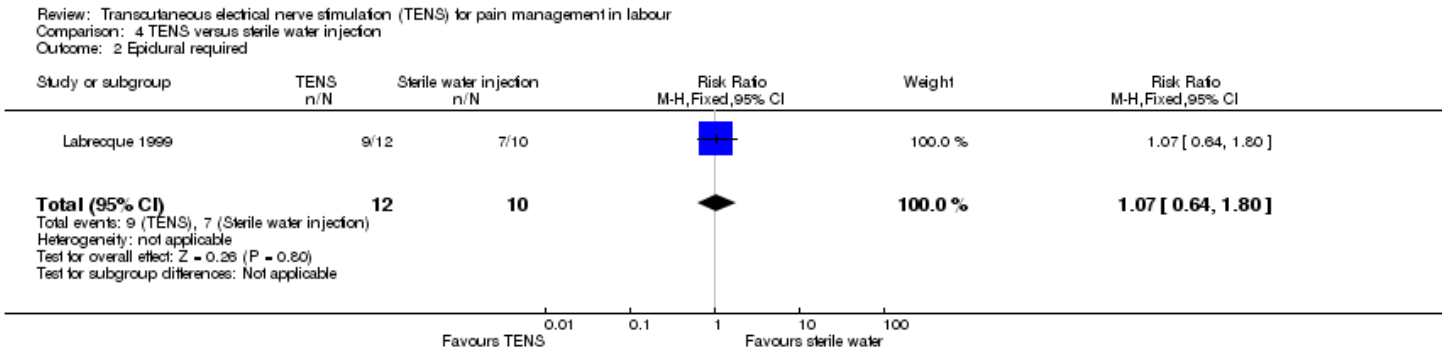

Comparison 4 TENS versus sterile water injection, Outcome 2 Epidural required.

3 Caesarean section rate	1	22	Risk Ratio (M-H, Fixed, 95% CI)	7.62 [0.46, 126.40]
Show forest plot				

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 4.3

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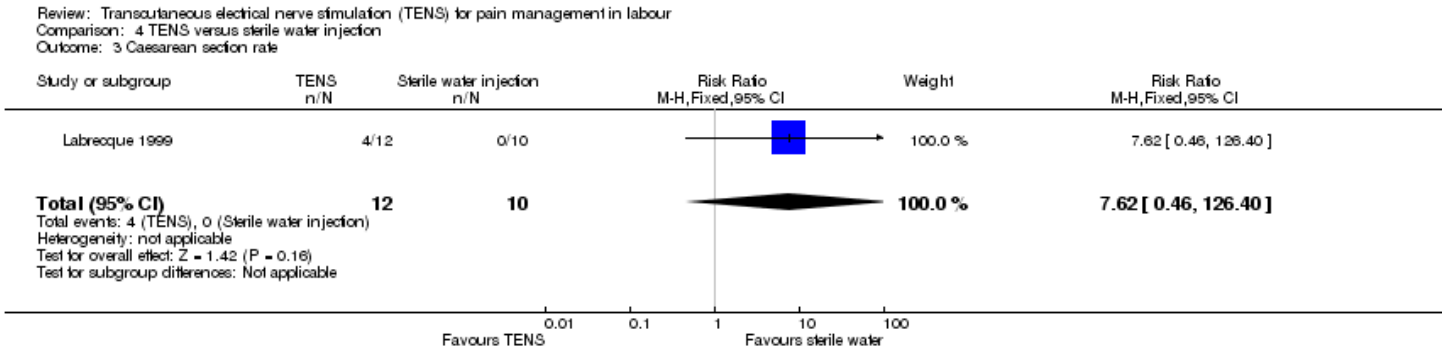


Comparison 4 TENS versus sterile water injection, Outcome 3 Caesarean section rate.

Open in table viewer

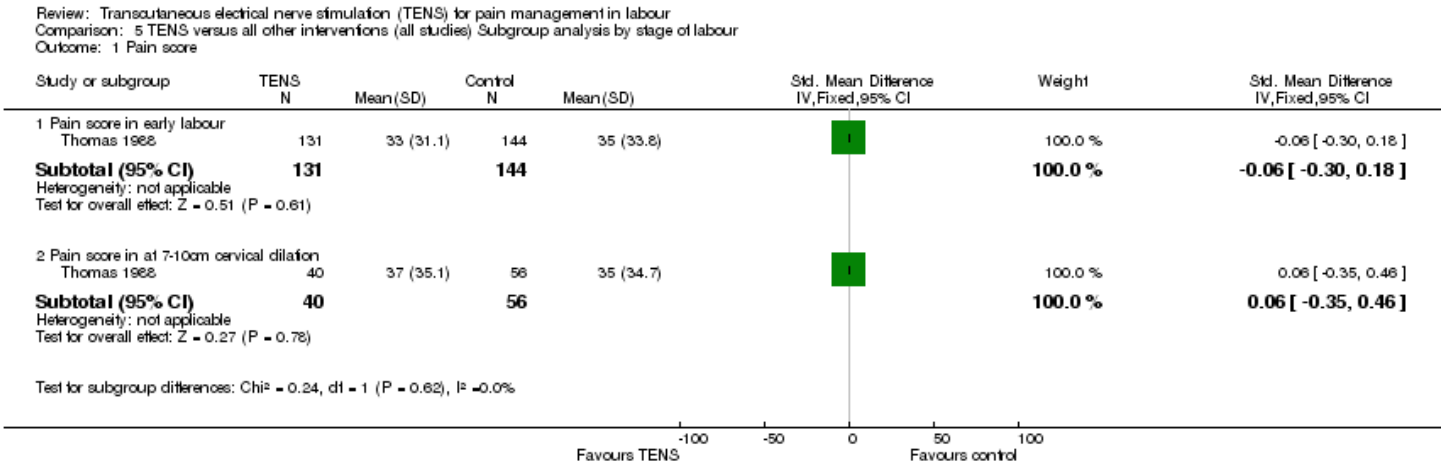
Comparison 5. TENS versus all other interventions (all studies) Subgroup analysis by stage of labour

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain score Show forest plot	1		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 5.1

Open in figure viewer | Download as PowerPoint



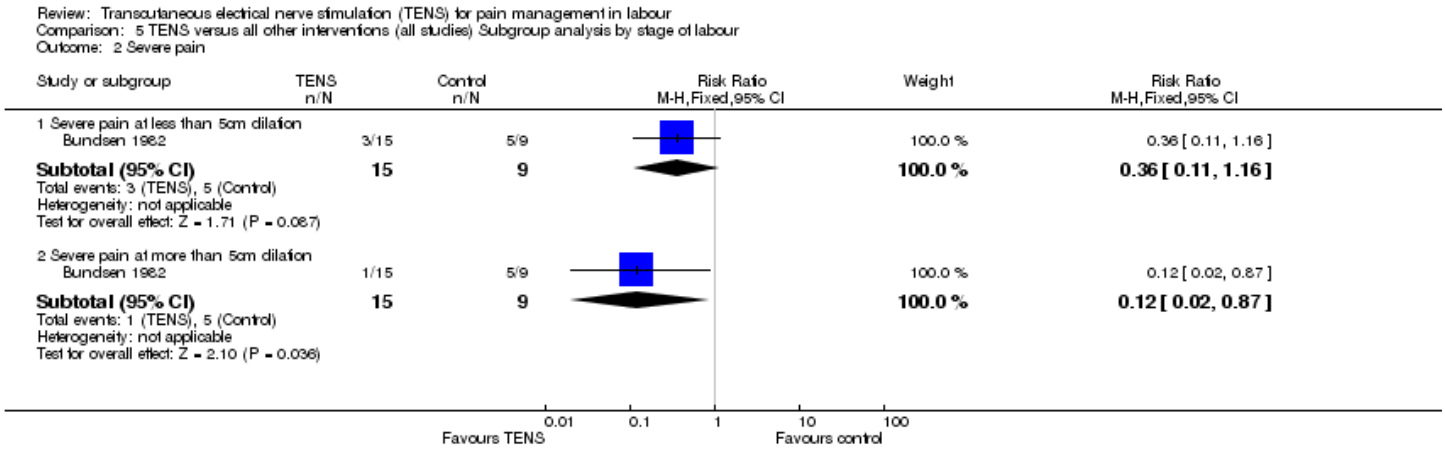
Comparison 5 TENS versus all other interventions (all studies) Subgroup analysis by stage of labour, Outcome 1 Pain score.

1.1 Pain score in early labour	1	275	Std. Mean Difference (IV, Fixed, 95% CI)	-0.06 [-0.30, 0.18]
1.2 Pain score in at 7-10cm cervical dilation	1	96	Std. Mean Difference (IV, Fixed, 95% CI)	0.06 [-0.35, 0.46]
2 Severe pain Show forest plot	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 5.2

Open in figure viewer | Download as PowerPoint



Comparison 5 TENS versus all other interventions (all studies) Subgroup analysis by stage of labour, Outcome 2 Severe pain.

2.1 Severe pain at less than 5cm dilation	1	24	Risk Ratio (M-H, Fixed, 95% CI)	0.36 [0.11, 1.16]
2.2 Severe pain at more than 5cm dilation	1	24	Risk Ratio (M-H, Fixed, 95% CI)	0.12 [0.02, 0.87]

Comparison 6. TENS versus placebo. Subgroup analysis by parity

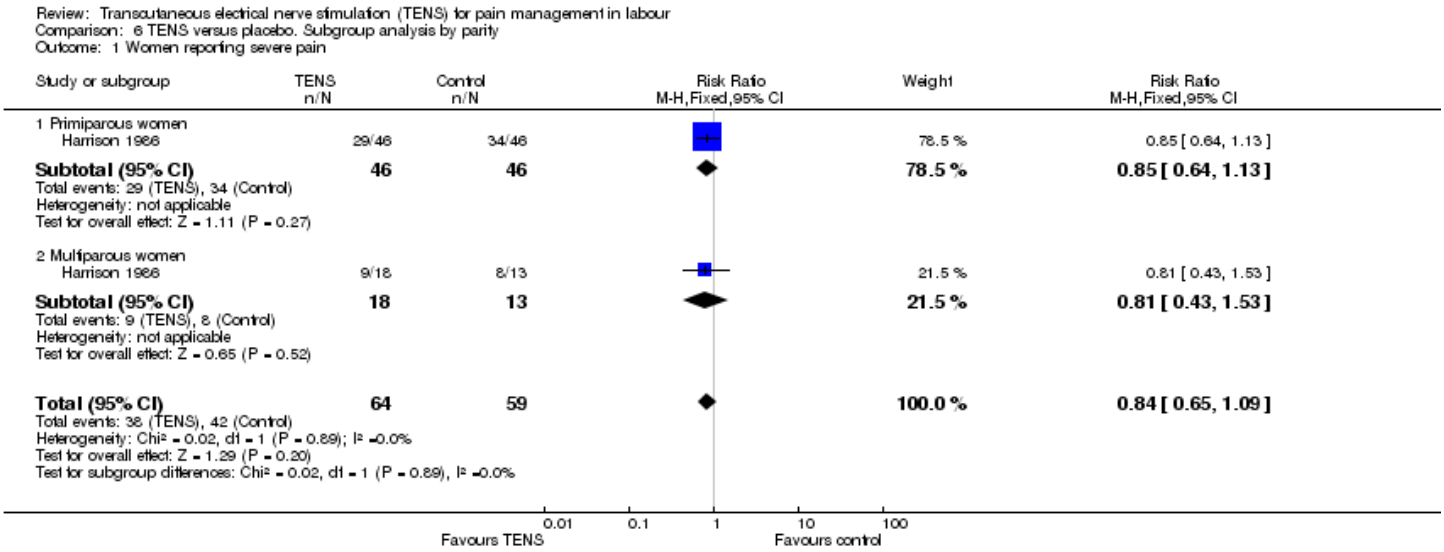
Open in table viewer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Women reporting severe pain Show forest plot	1	123	Risk Ratio (M-H, Fixed, 95% CI)	0.84 [0.65, 1.09]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 6.1

Open in figure viewer | Download as PowerPoint



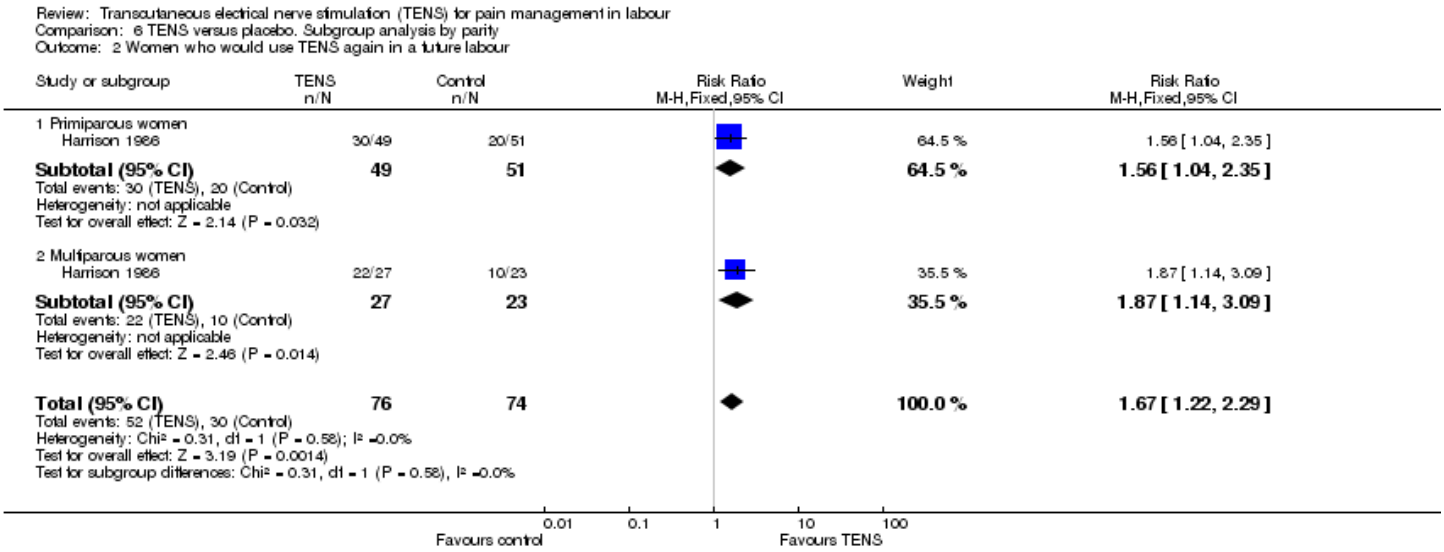
Comparison 6 TENS versus placebo. Subgroup analysis by parity, Outcome 1 Women reporting severe pain.

1.1 Primiparous women	1	92	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.64, 1.13]
1.2 Multiparous women	1	31	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.43, 1.53]
2 Women who would use TENS again in a future labour Show forest plot	1	150	Risk Ratio (M-H, Fixed, 95% CI)	1.67 [1.22, 2.29]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 6.2

Open in figure viewer | Download as PowerPoint



Comparison 6 TENS versus placebo. Subgroup analysis by parity, Outcome 2 Women who would use TENS again in a future labour.

2.1 Primiparous women	1	100	Risk Ratio (M-H, Fixed, 95% CI)	1.56 [1.04, 2.35]
2.2 Multiparous women	1	50	Risk Ratio (M-H, Fixed, 95% CI)	1.87 [1.14, 3.09]

Information

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10.1002/14651858.CD007214.pub2 Check for updates

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Intervention

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Contributions of authors

Therese Dowswell wrote the first draft of the review and revised subsequent drafts; assessed study eligibility, carried out data extraction and entered data. Carol Bedwell assessed study eligibility, carried out data extraction, checked data and commented on drafts of the review. James P Neilson and Tina Lavender commented on drafts.

For this update, Therese Dowswell prepared the first draft with input and comment from the other authors.

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Declarations of interest

None known.

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Several papers considered for inclusion in the review were not reported in English. Thanks to Jill Hampson for organising translations; to Lotta Jansson for translating Hulkko 1979, Alice Dowswell for translating de Orange 2003, Neumark 1978 and Tajali-Awal 1995, Angela Cooke for translating Steptoe 1984 and Sara Roden-Scott for translating Champagne 1984 and Wattrisse 1993.

This updated review forms part of a series of reviews focusing on pain management in labour that will be included in a Cochrane overview of reviews (Jones 2011b); contributing reviews share a generic protocol (Jones 2011a). We would like to thank Leanne Jones for her valuable help in updating this review so as to improve consistency between this and other pain management reviews.

Thanks to staff in the editorial office of the Cochrane Collaboration Pregnancy and Childbirth Group for their help in preparing the review, and to the editor and referees for their helpful comments on earlier drafts. Three peers (an editor and two referees who are external to the editorial team), a member of the Pregnancy and Childbirth Group's international panel of consumers and the Group's Statistical Adviser commented on the first version of this review.

What's new

Last assessed as up-to-date: 21 June 2011.

Date	Event	Description

Date	Event	Description
20 June 2011	New search has been performed	New search conducted. The review is one of a series of reviews included in an overview of reviews examining methods of pain management in labour and which share a generic protocol (Jones 2011a). This update includes a new comparison (TENS versus sterile water injection). A comparison that was included in previous versions of the review (TENS versus opioid analgesia) is no longer included; rather, it is now included in a review focusing on parenteral opioids (Ullman 2010). These changes were made to comply with the generic protocol and have not altered the conclusions of the review.

Version history

Title	Stage	Authors	Version	Publication Date
Transcutaneous electrical nerve stimulation (TENS) for pain management in labour	Review	Therese Dowswell, Carol Bedwell, Tina Lavender, James P Neilson	https://doi.org/10.1002/14651858.CD007214.pub2	15 April 2009
Transcutaneous electrical nerve stimulation for pain relief in labour	Protocol	Therese Dowswell, James P Neilson, Tina Lavender	https://doi.org/10.1002/14651858.CD007214	16 July 2008

Differences between protocol and review

This update includes a new comparison (TENS versus sterile water injection). A comparison that was included in previous versions of the review (TENS versus opioid analgesia) is no longer included; rather, it is now included in a review focusing on parenteral opioids (Ullman 2010). These changes were made to comply with the generic protocol on pain management for women in labour (Jones 2011a).

What's new

Last assessed as up-to-date: 21 June 2011.

Date	Event	Description
20 June 2011	New search has been performed	New search conducted. The review is one of a series of reviews included in an overview of reviews examining methods of pain management in labour and which share a generic protocol (Jones 2011a). This update includes a new comparison (TENS versus sterile water injection). A comparison that was included in previous versions of the review (TENS versus opioid analgesia) is no longer included; rather, it is now included in a review focusing on parenteral opioids (Ullman 2010). These changes were made to comply with the generic protocol and have not altered the conclusions of the review.

Appendices

Appendix 1. Methods used to assess trials included in previous versions of this review

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs). We have not included quasi-randomised trials.

Types of participants

Women in labour.

Types of interventions

There are various models and types of TENS equipment available; we have not restricted the inclusion criteria to any particular device specification. We have included studies where women were randomised to receive TENS versus routine care, a placebo TENS device, or other pharmacological or non-pharmacological interventions. We are aware that the use of sham TENS devices may not be an adequate means of blinding women to group allocation, and the use of such devices may influence caregiver behaviour. We have taken this into account in the interpretation of results.

Types of outcome measures

Primary outcomes

(1) Pain intensity in labour (measured as a continuous variable using visual analogue scales or by validated questionnaires or as a dichotomous variable has/has not severe pain)
(2) Satisfaction with pain relief

Secondary outcomes

Maternal

(3) Duration of labour
(4) Sense of control in labour
(5) Augmentation of labour
(6) Other pain relief
(7) Assisted vaginal delivery
(8) Caesarean section
(9) Side effect - local skin irritation
(10) Satisfaction with childbirth experience
(11) Cervical dilatation on admission to hospital

Fetal/neonate

(12) Apgar score less than seven at five minutes
(13) Cord pH less than 7.1
(14) Adverse events as defined by trialists

Search methods for identification of studies

Electronic searches

We contacted the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group's Trials Register (November 2008).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. handsearches of 30 journals and the proceedings of major conferences;
4. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

Searching other resources

We searched the reference lists of relevant papers. We did not apply any language restrictions.

Data collection and analysis

Selection of studies

Two review authors (T Dowswell and C Bedwell) independently examined abstracts of all potential studies identified by the search to ascertain which met the inclusion criteria. Where we did not have enough information to determine eligibility we sought further information from the study authors. We resolved any disagreement through discussion between all review authors.

The reasons for excluding studies have been set out in the tables of excluded studies.

Data extraction and management

All authors were involved in designing, piloting and revising the data extraction form. Two review authors (TD, CB) independently extracted data using the agreed form. We resolved any disagreement through discussion. After checking (by TD), we entered data into Review Manager software (RevMan 2008) and then data were re-checked (by CB).

When information regarding study methods and findings were unclear, we attempted to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Assessment of methodological quality of included studies

We assessed the validity of each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008). We have described methods used for generation of the randomisation sequence for each trial and assessed them as adequate (any truly random process), unclear, or inadequate.

(1) Selection bias (allocation concealment)

We assessed the quality of each trial, using the following criteria:

- adequate concealment of allocation: such as telephone randomisation, consecutively numbered sealed opaque envelopes;
- unclear whether adequate concealment of allocation: such as list or table used, sealed envelopes, or study does not report any concealment approach;
- inadequate concealment of allocation: such as open list of random number tables, use of case record numbers, dates of birth or days of the week.

(2) Attrition bias (loss of participants, eg withdrawals, dropouts, protocol deviations)

We assessed completeness to follow up, and where information was available, specified the numbers lost to follow up at each stage.

Where loss to follow up was greater than 20%, we have noted the reasons for attrition. Where, in the judgement of review authors, attrition rates seriously compromise the interpretation of results, we have excluded studies or subjected them to a sensitivity analysis. Again, we have documented reasons for excluding studies.

(3) Performance bias (blinding of participants, researchers and outcome assessment)

We assessed blinding using the following criteria:

(A) blinding of women;
(B) blinding of caregiver;
(C) blinding of outcome assessment (yes/no/unclear).

We are aware that blinding women and caregivers where TENS has been compared with sham TENS may not be possible. We have recorded where an attempt at blinding has been made.

Measures of treatment effect

We have carried out statistical analysis using the Review Manager software (RevMan 2008). We had anticipated that studies evaluating TENS were likely to include a range of comparison groups and that data on different outcomes (measured in different ways and at different time points) would have been recorded. Where trials were not sufficiently similar, results were analysed and presented separately. However, where possible, and at least for the primary outcome (pain in labour) we have used fixed-effect meta-analysis for combining data to produce a summary statistic.

Dichotomous data

Where, for example, outcome data such as maternal perceptions of pain have been measured as a dichotomous variable (e.g. severe pain versus no severe pain) we have presented results as summary risk ratio with 95% confidence intervals.

Continuous data

For continuous data (e.g. pain measured on visual analogue scales), we have used the mean difference where outcomes have been measured in the same way between trials. We have used the standardised mean difference to combine trials that measure the same outcome, but using different methods.

Unit of analysis issues

Cluster-randomised trials

We had intended to include cluster-randomised trials in the analyses along with individually randomised trials. Their sample sizes would have been adjusted using the methods described in Gates 2005 using an estimate of the intracluster correlation co-efficient (ICC) derived from the trial (if possible), or from another source. We did not identify any cluster-randomised trials for this review, but will include them in updates if such trials are identified in the future.

Cross-over trials

We did not anticipate that there would be any cross-over trials for an intervention carried out during labour, but one was identified (Chia 1990) and to avoid the risk of bias associated with treatment order effect, we prespecified that we would only include data from the first stage of such studies.

Dealing with missing data

We have analysed data on all participants with available data in the group to which they were allocated, regardless of whether or not they received the allocated intervention, and irrespective of whether they used additional interventions. If, in the original reports, participants were not analysed in the group to which they were randomised, and there was sufficient information in the trial report, we have attempted to restore them to the correct group.

For included studies levels of attrition have been noted.

Where data were not reported for some outcomes or groups we attempted to contact the study authors.

Assessment of heterogeneity

As part of the meta-analyses we examined heterogeneity between trials using the I^2 statistic. Where we have identified unexplained heterogeneity among the trials we have made this explicit, so that this can be taken into account in the interpretation of results.

Subgroup analysis and investigation of heterogeneity

We planned subgroup analyses classifying whole trials by interaction tests as described by Deeks 2001.

For the primary outcome, where data were available, we planned the following subgroup analyses.

- Parity (nulliparous versus multiparous women).
- Stage of labour (first stage latent versus active phase).

Sensitivity analysis

We planned to carry out sensitivity analyses to explore the effect of trial quality assessed by concealment of allocation, high attrition rates, or both, with poor quality studies being excluded from the analyses in order to assess whether this made any difference to the overall result.

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Transcutaneous electrical nerve stimulation for acute pain

Cochrane Systematic Review - **Intervention** | Version published: 15 June 2015 see what's new

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Mark I Johnson | Carole A Paley | Tracey E Howe | Kathleen A Sluka

View authors' declarations of interest

Abstract *available in* English | 日本語

Background

This is a second update of a Cochrane Review originally published in Issue 2, 2009. Transcutaneous Electrical Nerve Stimulation (TENS) is a non-pharmacological agent, based on delivering low voltage electrical currents to the skin. TENS is used by people to treat a variety of pain conditions.

Objectives

To assess the analgesic effectiveness of TENS, as a sole treatment, for acute pain in adults.

Search methods

We searched the following databases up to 3 December 2014: the Cochrane Central Register of Controlled Trials (CENTRAL), in the Cochrane Library; MEDLINE; EMBASE; CINAHL; and AMED. We also checked the reference lists of included trials.

Selection criteria

We included randomised controlled trials (RCTs) of adults with acute pain (< 12 weeks) if they examined TENS given as a sole treatment and assessed pain with subjective pain scales. Trials were eligible if they compared TENS to placebo TENS, no treatment controls, pharmacological interventions or non-pharmacological interventions. We excluded trials on experimental pain, case reports, clinical observations, letters, abstracts or reviews. Also we excluded trials investigating the effect of TENS on pain during childbirth

(labour), primary dysmenorrhoea or dental procedures. Studies where TENS was given with another treatment as part of the formal trial design were excluded. We did not restrict any articles based on language of publication.

Data collection and analysis

Two review authors independently assessed study eligibility and carried out study selection, data extraction, 'Risk of bias' assessment and analyses of data. We extracted data on the following: types of participants and pain condition, trial design and methods, treatment parameters, adverse effects, and outcome measures. We contacted trial authors for additional information if necessary.

Main results

We included 12 trials in the original review (2009) and included no further trials in the first update (2011). An additional seven new trials met the inclusion criteria in this second update. In total, we included 19 RCTs involving 1346 participants at entry, with 11 trials awaiting classification either because the full text was unavailable or information in the full text failed to clarify eligibility. We excluded most trials because TENS was given in combination with another treatment as part of the formal study design or TENS was not delivered using appropriate TENS technique. The types of acute pain included in this Cochrane Review were procedural pain, e.g. cervical laser treatment, venepuncture, screening flexible sigmoidoscopy and non-procedural pain, e.g. postpartum uterine contractions and rib fractures. We pooled data for pain intensity for six trials (seven comparisons) comparing TENS with placebo but the I^2 statistic suggested substantial heterogeneity. Mean difference (MD) with 95% confidence intervals (CIs) on a visual analogue scale (VAS, 100 mm) was -24.62 mm (95% CI -31.79 to -17.46) in favour of TENS. Data for the proportion of participants achieving ≥ 50% reduction in pain was pooled for four trials (seven comparisons) and relative risk was 3.91 (95% CI 2.42 to 6.32) in favour of TENS over placebo. We pooled data for pain intensity from five trials (seven comparisons) but the I^2 statistic suggested considerable heterogeneity. MD was -19.05 mm (95% CI -27.30 to -10.79) in favour of TENS using a random-effects model. It was not possible to pool other data. There was a high risk of bias associated with inadequate sample sizes in treatment arms and unsuccessful blinding of treatment interventions. Seven trials reported minor adverse effects, such as mild erythema and itching underneath the electrodes and participants disliking TENS sensation.

Authors' conclusions

This Cochrane Review update includes seven new trials, in addition to the 12 trials reviewed in the first update in 2011. The analysis provides tentative evidence that TENS reduces pain intensity over and above that seen with placebo (no current) TENS when administered as a stand-alone treatment for acute pain in adults. The high risk of bias associated with inadequate sample sizes in treatment arms and unsuccessful blinding of treatment interventions makes definitive conclusions impossible. There was incomplete reporting of treatment in many reports making replication of trials impossible.

Plain language summary *available in* English | Hrvatski | 日本語 | தமிழ்

Transcutaneous Electrical Nerve Stimulation (TENS) to treat acute pain in adults

Background

Acute pain is pain of recent onset and limited duration. Acute pain is associated with surgery, physical trauma (e.g. broken bones, burns and cuts) and medical procedures (e.g. venepuncture and sigmoidoscopy). Transcutaneous Electrical Nerve Stimulation (TENS) is a treatment to relieve pain by administering mild electrical currents to the body using electrode pads attached to the surface of the skin.

Review question

Does TENS relieve acute pain in adults?

Study characteristics

We included 19 clinical trials published up to 3 December 2014, which examined 1346 people. The trials administered TENS to produce a strong non painful 'tingling' sensation at the site of acute pain. The trials assessed TENS for cervical laser treatment, venepuncture, sigmoidoscopy, rib fractures and uterine contractions after childbirth. We did not include trials that assessed TENS for pain associated with childbirth, dental procedures and menstruation because they have been the subject of other Cochrane Reviews. Eleven trials are awaiting classification.

Key results

TENS was better than placebo TENS (delivering no electrical current) at reducing the intensity of acute pain but the reduction in pain was not consistent across all trials. This finding was based on an analysis of only six of the 19 trials. There was an insufficient number patients to make a firm conclusion.

A small number of patients experienced itching and redness beneath the TENS pads or disliked the sensation produced by TENS.

Overall we concluded that TENS may reduce the intensity of acute pain in some patients but the quality of evidence was weak. TENS is inexpensive, safe and can be self-administered. We recommended that TENS should be considered as a treatment option given on its own or in combination with other treatments.

Quality of the evidence

The quality of the evidence was moderate to low because sample sizes were small and some patients were aware that they were receiving TENS or placebo.

Authors' conclusions

Implications for practice

In this update we identified seven additional trials to the 12 trials reviewed in 2011. The analysis of 19 RCTs with 1346 participants provides tentative evidence that TENS reduces pain intensity over and above that seen with placebo (no current) TENS when administered as a stand-alone treatment for acute pain in adults. However, the high risk of bias associated with inadequate sample sizes in treatment arms and unsuccessful blinding of treatment interventions makes definitive conclusions impossible. The additional analyses conducted in this second update strengthen evidence presented in Walsh 2009. Whether TENS should be considered as a potential treatment option for patients and clinicians managing acute pain remains a matter for debate, although TENS compares favourably to many alternatives because it can be self-administered, safe, inexpensive and readily available to patients over the counter.

Implications for research

There was incomplete reporting of treatment in many reports, making replication of trials impossible. Further adequately powered research trials are required to provide a comprehensive assessment of the role of TENS as a sole treatment in acute pain management. Bennett 2011 has provided criteria and operational guidelines for the design of a robust RCT on TENS. PaPaS guidance suggests that a sample size of ≥ 200 participants per treatment arm is necessary for a low risk of bias in RCTs. The Consolidated Standards of Reporting Trials (CONSORT) statement has been revised for non-pharmacological treatments (Boutron 2008); this should be adopted to ensure better reporting of all aspects of trial design and subsequent reporting. In particular, appropriate sequence generation and allocation concealment methods should be used and reported. Sample size calculations should be performed to determine appropriate participant numbers. Complete details of the TENS application should be provided to allow subgroup analysis between trials. Appropriate TENS technique should be used including a strong non-painful TENS sensation at the site of pain. A clear description of missing data and how they are analysed is required. Outcome assessor blinding should be adopted as a key element of future trial design. Blinding of participants is accepted as a challenge in TENS trials but should be addressed nevertheless. Finally, future trials should adopt a common policy of reporting means and SDs for continuous data to enable data extraction for subsequent meta-analysis.

Background

This Cochrane Review is a second update of Walsh 2009, and replaces the 2011 update.

Description of the condition

The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (Merskey 1994). Acute pain is defined as pain "of recent onset and probable limited duration which usually has an identifiable temporal and causal relationship to the injury or disease". In clinical practice acute pain is categorised as pain of less than three months duration (Strong 2002). Current approaches to acute pain management include pharmacological agents (drugs) and a number of non-pharmacological agents, one of which is Transcutaneous Electrical Nerve Stimulation (TENS) (Schug 2014).

Description of the intervention

TENS is the delivery of pulsed electrical currents across the intact surface of the skin to stimulate peripheral nerves principally for pain relief (Johnson 2014). In clinical practice TENS is administered using a portable, battery-powered device that generates electrical currents that are delivered to the body via electrodes attached to the intact surface of the skin. TENS is inexpensive and can be self-administered. The safety profile of TENS compares positively compared with medication. Safety guidelines published by professional bodies guide judgements about whether it is appropriate to use TENS (Houghton 2010). Contradictions include TENS for patients who also have electronic implants, such as cardiac pacemakers and implantable cardioverter defibrillators. Precautions include pregnancy, epilepsy, active malignancy, deep-vein thrombosis, and frail or damaged skin.

How the intervention might work

Natural forms of electricity (e.g. electrogenic fish) have been used as a method of pain relief since the Egyptian era (Johnson 2014). A theoretical foundation for electroanalgesia (pain relief by electrical methods) was established in 1965 through the publication of Melzack and Wall's gate control theory of pain (Melzack 1965). This theory proposed that a metaphorical gate consisting of excitatory and inhibitory synapses existed in the dorsal horn of the spinal cord. The gate could regulate the amount of nociceptive traffic (painful stimuli) being transmitted onwards to the brain. This gate could be opened by noxious stimuli that excited high threshold small diameter peripheral afferents and could be closed by non-noxious stimuli (e.g. touch, pressure and electrical currents) that excited low threshold large diameter peripheral afferents.

Technological advances have produced a variety of TENS devices with a wide range of stimulation parameters for clinicians and patients to choose from (e.g. pulse frequency, pulse amplitude, pulse duration and electrode placement site). TENS interventions tend to be described according to technical characteristics as either high frequency, low intensity (conventional TENS) or low frequency, high intensity (acupuncture-like TENS, AL-TENS). This technical approach fails to specify the physiological intention of

delivering TENS. In this regard, the physiological intention when administering conventional TENS is to activate selectively non-noxious low threshold afferent nerve fibres in the skin (Aβ-fibres) which are claimed to inhibit transmission of nociceptive information at the level of the spinal cord (i.e. segmental modulation) (DeSantana 2008). In practice, Aβ nerve fibre activity is recognised by the user reporting strong electrical paraesthesia (pins and needles) beneath the electrodes. The physiological intention of AL-TENS is to generate a muscle twitch which is believed to increase activity in small diameter afferent nerve fibres in muscles (Aδ) leading to activation of descending pain inhibitory pathways. In practice, AL-TENS is achieved by administering low frequency and high intensity, but non-painful, currents over muscles (Francis 2011). Interestingly, experimental evidence to establish the roles of different afferent fibres in TENS outcome is inconclusive (Garrison 1994; Levin 1993; Radhakrishnan 2005). Research suggests that different frequencies of TENS may act through different neurotransmitter systems. Sluka and colleagues conducted a series of animal studies that have shown that low frequency TENS-induced antihyperalgesia (decreased sensitivity to pain) is mediated by activation of serotonin and mu opioid receptors, while high frequency TENS activates delta opioid receptors (Kalra 2001; Radhakrishnan 2003; Sluka 1999). In 2008, a systematic review evaluating frequency dependent effects on experimentally induced pain in humans was inconclusive due to an insufficient number of high quality trials (Chen 2008). In recent years frequency-dependent effects have been confirmed in human subjects by high quality research studies (Chen 2010a; Chen 2010b; Chen 2011; Claydon 2011; Leonard 2010; Léonard 2011; Liebano 2011).

Why it is important to do this review

TENS is used extensively by people with acute and chronic pain (DeSantana 2008; Johnson 2011). Meta-analyses on the effectiveness of TENS for chronic musculoskeletal pain (Johnson 2007) and for osteoarthritis of the knee (Bjordal 2007) demonstrated a significant effect on pain over placebo. Cochrane Reviews on TENS for specific chronic pain conditions have been hindered by methodological weaknesses in randomised controlled trials (RCTs) (Bennett 2011; Johnson 2010; Johnson 2014; Sluka 2013). An all-encompassing Cochrane Review on TENS for a variety of chronic pain conditions (i.e. pain > three months' duration) reported inconclusive results (Nnoaham 2008). However, this review has now been withdrawn and is being replaced by new reviews on TENS for neuropathic pain in adults, led by Gibson (protocol in press) and TENS for fibromyalgia, led by Claydon et al (protocol in press). There is also a title registered for an overview of Cochrane Reviews of TENS for chronic pain (protocol in press).

Cochrane Reviews on TENS for specific types of acute pain have been inconclusive for labour pain (Dowswell 2009) and dysmenorrhoea (Proctor 2002). An early systematic review of TENS for post-operative pain found TENS to be no better than controls for postoperative pain (Carroll 1996) although pain measures were taken when patients were allowed free access to analgesic medication. This compromises pain scores because patients in placebo and TENS groups titrate analgesic medication to achieve effective pain relief, and therefore exhibit similar pain scores. Review authors also included trials that underdosed TENS or used an inappropriate TENS technique, or both. A meta-analysis with subgroup analysis demonstrated a significantly

better outcome for TENS when applied using adequate (optimal) stimulation techniques when compared to non-adequate stimulation techniques (Bjordal 2003); optimal TENS techniques were defined as an intensity that was strong enough to generate a strong paraesthesia and electrodes applied at the site of the operative scar. Recent evidence from systematic reviews suggests that TENS is superior to placebo TENS when used in combination with analgesic medication for thoracotomy and post-sternotomy pain (Freynet 2010; Sbruzzi 2012). To date, there has been no all-encompassing systematic review on TENS for acute pain. A systematic review, which takes account of adequate TENS techniques, is necessary to assist clinicians and researchers to make informed decisions on the effectiveness of this modality for acute pain. TENS can be given either as a sole treatment, i.e. stand alone treatment, or combined with other interventions. This Cochrane Review will focus on TENS given as a sole treatment only to see if it has sufficient efficacy in its own right.

Objectives

Primary objective

To assess the analgesic effectiveness of TENS, as a sole treatment, for acute pain in adults.

Secondary objectives

To assess whether:

1. TENS effectiveness is influenced by the type of TENS (i.e. conventional TENS versus AL-TENS);
2. TENS effectiveness is influenced by the time of recording the outcome measure, i.e. if outcome is influenced by measurements taken when TENS is switched on (during TENS measurement) compared to when TENS has been turned off after the treatment (post-TENS measurement);
3. TENS effectiveness is influenced by duration of TENS treatment;
4. TENS effectiveness differs for different acute pain conditions; and,
5. TENS is safe for the treatment of acute pain.

Methods

Criteria for considering studies for this review

Types of studies

We included all prospective RCTs. Both cross-over and parallel trial designs were acceptable. We excluded data from the following: trials that were non-randomised; studies of experimental pain; case reports; clinical observations; and letters, abstracts and reviews (unless they provided additional information from published RCTs that met the criteria).

Types of participants

Study participants were required to be adults (i.e. 16 years and over) with a diagnosis of acute pain (less than 12 weeks) by any cause including injury or surgical intervention. Acute pain conditions included, but were not limited to, the following: angina; back pain; fractures; headache; musculoskeletal pain and procedural pain. We included postpartum pain trials if the pain investigated was due to episiotomy or Caesarean section irrespective of the presence of uterine cramps. We excluded trials including patients with pain due to uterine contractions (i.e. labour) alone and trials including patients with acute pain due to primary dysmenorrhoea as these conditions have been covered by previous Cochrane Reviews (Dowswell 2009; Proctor 2002). In addition, we excluded trials on electrical stimulation for dental procedures as this is a subject for a separate review.

Types of interventions

We only included trials which evaluated surface electrical nerve stimulation for the treatment of acute pain (i.e. transcutaneous as opposed to percutaneous electrical stimulation). We defined appropriate delivery of TENS as follows:

1. A 'standard TENS device' was used which delivered biphasic or monophasic (type of waveform) pulsed electrical currents in the mA range. TENS had to be delivered using at least two surface electrodes. We excluded TENS delivered using single probes (i.e. TENS pens). Neuromuscular electrical stimulation (NMES) devices and Interferential Current devices were excluded;

2. TENS was administered to produce a strong electrical paraesthesia that was felt by the patient. We included AL-TENS delivered at strong intensities to generate muscle twitches. We excluded trials if the active TENS intervention was delivered at intensities reported to be 'barely perceptible', 'faint' or 'mild';

3. TENS was administered on an area of the body which was sensate (where pain is being felt) at either (a) the site of pain or (b) over nerve bundles proximal (or near) to the site of pain. We only included TENS delivered at acupuncture stimulation points if the point was lying over nerve bundles proximal (or near) to the site of pain. We considered any parameters of treatment meeting these criteria as were any duration or frequency of treatment and either self-applied or therapist-applied treatments.

The interventions to be compared included the following:

- TENS versus placebo TENS (i.e. use of a sham TENS device). We defined a sham TENS device as a device similar to the one used in the active group but the output was modified in some way so that either no electrical current or a barely perceptible electrical current is delivered through the electrodes;
- TENS versus no treatment controls;
- TENS versus a pharmacological intervention;
- TENS versus a non-pharmacological intervention.

We excluded trials if TENS was given in combination with any other treatment as part of the formal trial design, e.g. analgesic medication, exercise.

Types of outcome measures

Primary outcomes

- Standard subjective scales for pain intensity, pain relief or both (e.g. visual analogue scales (VAS), numerical rating scales (NRS); verbal rating scales (VRS) McGill Pain Questionnaire (MPQ)).

Secondary outcomes

- Other measures of pain.

We recorded adverse events associated with the intervention. Also, we sought information on the level of compliance with the intervention, the magnitude and duration of effect.

Search methods for identification of studies

Electronic searches

We developed detailed search strategies for each electronic database searched. We based these on the search strategy developed for MEDLINE but revised each strategy appropriately for each database. The search strategy combined the subject specific search with phase one and two of the Cochrane Sensitive Search Strategy for RCTs (as published in chapter sections 6.4.11.1, 6.3.2.1 and 6.3.3.2 in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). The subject specific search used a combination of MeSH (upper case) and free text (lower case) terms based on the MEDLINE search strategy via OVID which can be seen in Appendix 1. We attempted to identify all relevant trials irrespective of language. We assessed non-English papers and translated articles when necessary.

We performed the literature search for Walsh 2009 up to 8 August 2008 and subsequent searches up to 7 January 2011 for the 2011 review update. For this second search update we performed searches up to 3 December 2014. We searched the following databases:

- Cochrane Pain, Palliative and Supportive Care Group (PaPaS) Specialized Register (4 August 2008; as data are captured in CENTRAL, we did not include this database in the 2011 or 2013 update search) Appendix 2;
- Cochrane Central Register of Controlled Trials, CENTRAL (the Cochrane Library, Issue 11 of 12, 2014) Appendix 3;
- MEDLINE (1950 to Nov week 3 2014) Appendix 1;
- EMBASE (1980 to 2 Dec 2014) Appendix 4;
- CINAHL (1982 to 6 Dec 2014) Appendix 5;
- AMED (1985 to 6 November 2014) Appendix 6;
- PEDro (www.pedro.org.au) accessed 7 January 2011. We excluded this database from the 2013 update search Appendix 7;
- OTseeker (www.otseeker.com) accessed 7 January 2011. We excluded this database from the 2013 update search Appendix 8; and,
- OpenSIGLE (http://opensigle.inist.fr) accessed 7 January 2011. We excluded this database from the 2013 update search Appendix 9.

Searching other resources

We searched the reference lists of all included trials, key textbooks and previous systematic reviews for additional trials.

Data collection and analysis

Selection of studies

From the title, abstract, and descriptors, pairs of review authors independently reviewed the results of the literature searches to identify potentially relevant trials for full review. We resolved any disagreements by consensus. We did not blind the review authors from authors' names, institutions, and journal name or trial results at this stage or any stage of the review. After screening full text articles, we included trials that met the inclusion criteria. We sought additional information or clarification from the primary trial author if incompletely reported.

Data extraction and management

Pairs of review authors independently extracted data using a customised data extraction tool tested prior to use. We resolved any disagreements by consensus or by consulting a third review author. We contacted trial authors where there was incomplete reporting of data. We extracted data on the following trial

characteristics for entry into RevMan 2014:

- **Study participants:** age, gender, condition, inclusion/exclusion criteria, number of participants randomised, number of, and reasons for, withdrawals or dropouts;
- **Study:** design and location, methods of sequence generation and allocation concealment, blinding, intention-to-treat (ITT) or per protocol analysis, outcome measures for pain, and results of statistical analysis;
- **Interventions used:** where TENS was applied and by whom, stimulation parameters (frequency, waveform, pulse amplitude/intensity, pulse duration), electrode details, treatment time and frequency, and adverse effects.

Assessment of risk of bias in included studies

We originally intended to assess the methodological quality of trials using the scale devised by Jadad 1996 as detailed in the protocol. However, with the launch of Review Manager (RevMan) in 2008, we decided to use the Cochrane Collaboration's 'Risk of bias' assessment tool as described in Chapter 8 of Higgins 2011. Two review authors independently assessed the following: sequence generation, allocation concealment, blinding of participants and outcome assessors, incomplete outcome data, and other sources of bias (funding and size of trial). We resolved any disagreement by consensus or by consulting a third review author.

Measures of treatment effect

Where available and appropriate, we presented quantitative data for the outcomes listed in the inclusion criteria. For each trial, we calculated relative risk and 95% confidence intervals (CI) for dichotomous outcomes. For continuous outcomes reported using the same scale, we determined mean differences (MD) and 95% CIs. Where results for continuous outcomes were presented on different scales, we calculated standardised mean differences (SMD) and 95% CIs. We planned to calculate the number needed to treat for an additional beneficial outcome (NNTB) for treatment effect.

Dealing with missing data

In cases of missing data due to withdrawals or dropouts, we only used the data analysed in the trial for analysis in this Cochrane Review.

Assessment of heterogeneity

We had intended that, where appropriate, we would pool results of comparable groups of trials using the fixed-effect model and calculate 95% CIs. We planned to test heterogeneity between comparable trials using a standard Chi^2 test considered statistically significant at a P value < 0.1, after due consideration of the I^2

statistic value. We interpreted the I^2 statistic value according to the following thresholds (Higgins 2011): 0% to 40%, might not be important; 30% to 60%, may represent moderate heterogeneity; 50% to 90%, may represent substantial heterogeneity; and 75% to 100%, considerable heterogeneity. We planned to investigate any evidence of heterogeneity to determine if there were obvious differences in the trials that were likely causes of the heterogeneity. If the heterogeneity was regarded as likely to have serious effects on the validity of the results, then we did not combine the data. Where there was significant heterogeneity, we intended to view the results of the random-effects model and present these when appropriate.

Subgroup analysis and investigation of heterogeneity

Where the data allowed, we planned separate outcome analyses to test the following null hypotheses that there is no difference in analgesia:

1. Between AL-TENS (visible phasic muscle contractions) and conventional TENS (no visible muscle contraction);
2. If the outcome measure is recorded during TENS application;
3. Between different TENS treatment durations; and,
4. Between different acute pain conditions.

Results

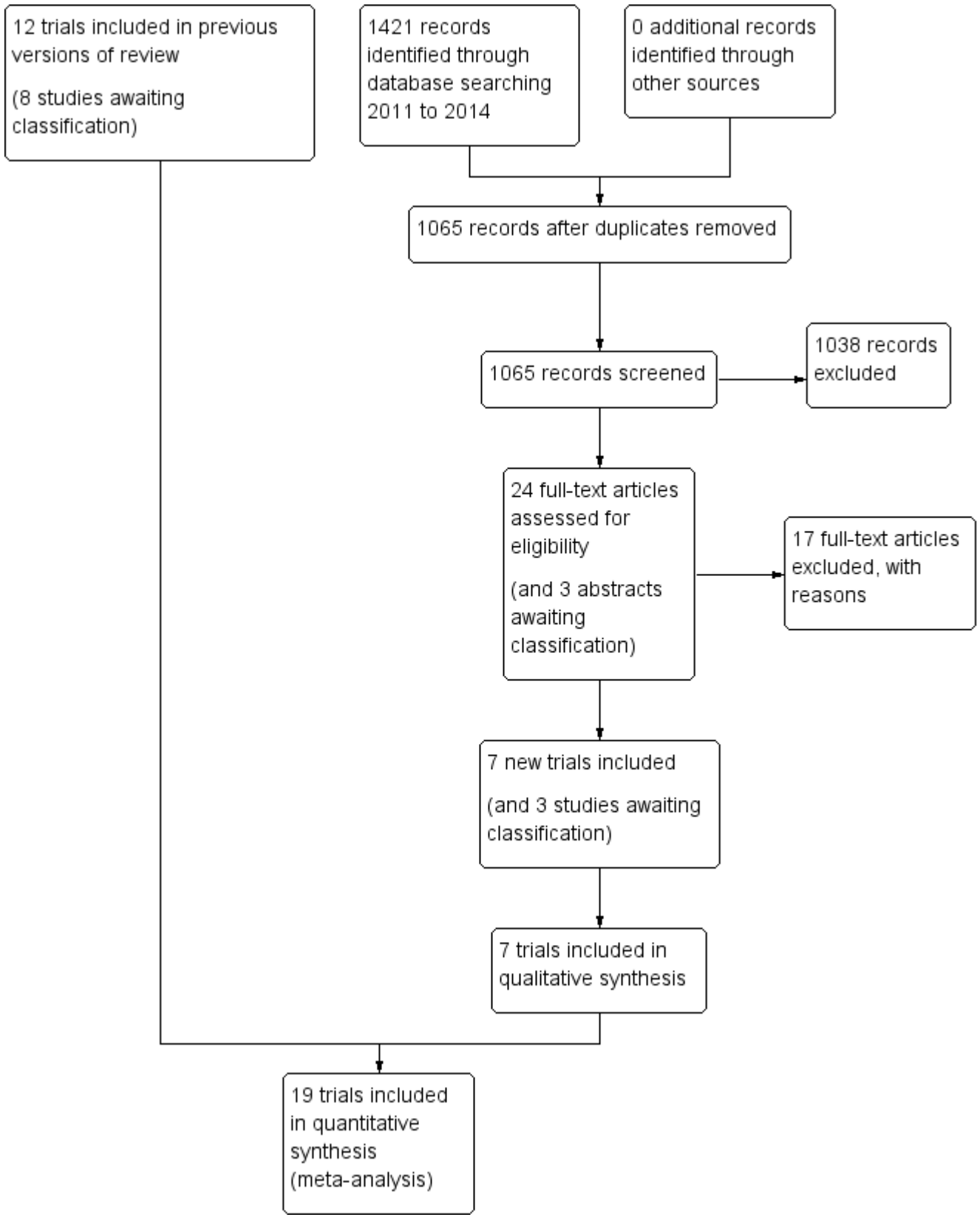
Description of studies

Results of the search

For the 2011 update we identified 1775 reports in the literature searches. For this update, 1421 records were identified through database searching between 2011 and 2014. After removal of duplicates we screened the abstracts of 1065 reports (Figure 1). Of these 1065 reports, 1038 were removed because they were not relevant, did not meet the inclusion criteria, had administered TENS in combination with another treatment as part of the formal trial design (n=120) or had not administered TENS using appropriate technique as defined in the Types of interventions section (n=32). Hence this update included seven new trials (Amer-Cuenca 2011; de Sousa 2014; Ekblom 1987; Gregorini 2010; Keskin 2012; Kim 2012; Pitangui 2012), including two of the trials that were awaiting classification in the 2011 update (Ekblom 1987; Gregorini 2010). In total there were 19 trials included for review (Characteristics of included studies) and all were published in

English. Eleven trials were awaiting classification (Cambiaghi 2013; de Paiva Tosato 2007; França 2012; Hsueh 1997; Liebano 2013; Park 2014; Rajpurohit 2010; Salvador 2005; Salvino 2013; Silva 2012; Treacy 2011).

Figure 1 **Open in figure viewer** | **Download as PowerPoint**



Study flow diagram.

Included studies

Participants

The 19 included trials had 1346 participants at entry (Amer-Cuenca 2011; Cheing 2005; Coyne 1995; Crompton 1992; De Angelis 2003; de Sousa 2014; Ekblom 1987; Gregorini 2010; Hansson 1983; Hruby 2006; Keskin 2012; Kim 2012; Limoges 2004; Liu 1985; Olsén 2007; Oncel 2002; Ordog 1987; Pitangui 2012; Roche 1985). Two trials did not indicate the gender of participants (Ordog 1987; Roche 1985), six trials included only women (Crompton 1992; De Angelis 2003; de Sousa 2014; Keskin 2012; Olsén 2007; Pitangui 2012) and the remaining 11 trials included women and men. There were 429 males and 759 females with an age range of 11 to 81 years in reports that provided information about age. One report did not provide details about the age of participants (Ordog 1987). Two trials included at least one participant under 16 years of age in the sample population (age range: Cheing 2005: 15 to 58 years; Oncel 2002: 11 to 81 years) but we included these trials because the mean age for both sample populations was > 30 years. Seven trials investigated the effect of TENS on procedural pain. Procedures included cervical laser treatment (Crompton 1992), office hysteroscopy (De Angelis 2003), screening flexible sigmoidoscopy (Limoges 2004), flexible cystoscopy (Hruby 2006), unsedated colonoscopy (Amer-Cuenca 2011) and venepuncture (Coyne 1995; Kim 2012). The remaining trials investigated the effect of TENS on haemophilia pain (Roche 1985), acute trauma such as sprains or fractures (Ordog 1987), postpartum uterine contractions (de Sousa 2014; Olsén 2007), acute low back pain (LBP) during pregnancy (Keskin 2012) acute orofacial pain (Ekblom 1987; Hansson 1983), post thoracotomy (Liu 1985), post-cardiac surgery (Gregorini 2010), post-episiotomy (Pitangui 2012), rib fractures (Oncel 2002) and neuropathic pain (Cheing 2005).

Setting

Studies were conducted in Europe (UK, Sweden, Turkey, Italy, Spain), North America , Brazil and China, Hong Kong and South Korea. Eighteen trials were conducted in a hospital or specialised clinic with participants in one of these trials continuing to use TENS at home after discharge (Oncel 2002). In one trial, participants received TENS instruction in hospital but only used it at home (Ordog 1987).

Design

All included RCTs used a parallel group design.

Sample sizes

The number of participants randomised to each treatment group ranged from eight (Olsén 2007; Roche 1985) to 71 (De Angelis 2003). Ten trials had at least 20 participants in each of the treatment groups (Amer-Cuenca 2011; Crompton 1992; De Angelis 2003; Hansson 1983; Hruby 2006; Kim 2012; Limoges 2004; Oncel 2002; Ordog 1987; Pitangui 2012). Four trials performed a prospective sample size calculation to determine the appropriate number of participants required (Amer-Cuenca 2011; Crompton 1992; de Sousa 2014; Keskin

2012). Olsén 2007 reported that they based their sample size on results from previous trials in the area but did not provide *a priori* power analysis details; they performed a *post hoc* power analysis on the data they collected and claimed that the numbers they recruited (N = 13 and 8 in the two groups) were adequate.

TENS device and application

Electrodes were placed at the painful site in all trials except Amer-Cuenca 2011, where electrodes were placed over the sensory nerves supplying the colon for unsedated colonoscopy, and Roche 1985, where electrodes were placed over the painful area or close to the area of bleeding for pain associated with haemophilia. Five trials did not provide full details of the type, size, number of electrodes used (Crompton 1992; De Angelis 2003; Hruby 2006; Liu 1985; Ordog 1987). TENS was administered using two self-adhesive electrodes or two rubber/silicone electrodes smeared with gel in most trials. Crompton 1992 used four electrodes over the anterior abdominal wall (painful area) and two over the sacrum for pain experienced during cervical laser treatment. Limoges 2004 placed two electrodes over the abdomen (painful area) and two electrodes parallel to the spinal cord at L1-S3 level for screening flexible sigmoidoscopy pain. Ordog 1987 used metal electrodes. Details of the model or manufacturer of the TENS device used, or both, was provided in all reports. Two trials used a device from the same Swedish manufacturer (Hansson 1983; Olsén 2007) and two trials used a Chattanooga Intelect Advanced combination Therapy System (Amer-Cuenca 2011; Keskin 2012).

Only three reports described both the intensity (i.e. subjective description) and current amplitude (mA) of TENS (Hruby 2006; Liu 1985; Olsén 2007). Twelve reports described the intensity but not current amplitude (Amer-Cuenca 2011; Cheing 2005; Coyne 1995; Crompton 1992; De Angelis 2003; de Sousa 2014; Hansson 1983; Keskin 2012; Kim 2012; Oncel 2002; Ordog 1987; Roche 1985) and one report described pulse amplitude but not intensity (Limoges 2004). Two trials delivered TENS using a fixed pulse amplitude: Limoges 2004 used 30 mA; Olsén 2007 used 50 mA in the high pulse amplitude TENS group and 10 to 15 mA in the low pulse amplitude TENS group. Seven reports indicated that the pulse amplitude was adjusted during treatment (Amer-Cuenca 2011; Coyne 1995; De Angelis 2003; Gregorini 2010; Hansson 1983; Hruby 2006; Pitangui 2012). This information was unclear or not provided in the remaining trials. A variety of subjective descriptors were used to describe the intensity of TENS including: tingling, non-painful sensation from stimulated area (high frequency TENS group) or non-painful muscular contractions in stimulated area (low frequency TENS group (Hansson 1983); strong but tolerable tingling (Amer-Cuenca 2011; Cheing 2005); subjective level of comfort (Liu 1985); highest level that did not make participants uncomfortable (Oncel 2002); definite but comfortable perception with no muscle activation (Roche 1985); and below pain threshold (Coyne 1995). De Angelis 2003 used the term 'tickle' to describe the level of intensity. This is an unusual term and may be a result of translation from non-English language. Most trials used high pulse frequencies, ranging from 51 Hz (Liu 1985) to 160 Hz (Coyne 1995). Two trials used trains of pulses delivered at a low frequency (Hansson 1983; Roche 1985). One trial, Ekblom 1987, had two TENS groups, one with a pulse frequency of 2 Hz and one with a frequency of 100 Hz. Pulse duration ranged between 50 µs (Oncel

2002) and 400 µs (Amer-Cuenca 2011). One trial used a pulse duration of 310 to 400 µs (Coyne 1995). de Sousa 2014 reported using a pulse duration of 75 msec, which seems excessively large. We suspect that this is a typographical error in the trial report as technical specifications for the device used was listed as 45 to 300 µs by the manufacturer. Ordog 1987 did not specify frequency or pulse duration settings.

There was a wide variation in the number of treatments and individual treatment times across the included trials. TENS was administered in a single treatment session in 14 trials (Amer-Cuenca 2011; Coyne 1995; Crompton 1992; De Angelis 2003; de Sousa 2014; Ekblom 1987; Gregorini 2010; Hansson 1983; Hruby 2006; Kim 2012; Limoges 2004; Pitangui 2012; Roche 1985; Olsén 2007) and in multiple treatment sessions in five trials (Cheing 2005; Keskin 2012; Liu 1985; Oncel 2002; Ordog 1987). Often it was difficult to ascertain exactly how often and for how long TENS was administered in trials using multiple TENS treatment sessions. Three of the seven reports of trials on procedural pain did not specify treatment duration (Crompton 1992; De Angelis 2003; Hruby 2006); in those that did, treatment duration varied from five minutes to four hours (Coyne 1995; Kim 2012; Limoges 2004) or was described as being for the duration of the procedure (Amer-Cuenca 2011). In the non-procedural pain trials, treatment duration varied from one minute (Olsén 2007) to applying TENS as often as required (Ordog 1987). Only two trials involved TENS being self-administered at home where compliance could be assessed (Oncel 2002; Ordog 1987). In these trials participants continued to use TENS at home for two days (Oncel 2002) or used TENS at home for as long as needed with mean duration of use being three days and no participants using TENS at one month follow-up (Ordog 1987).

Comparison groups

Eleven trials included a placebo TENS intervention (Amer-Cuenca 2011; Cheing 2005; Coyne 1995; Ekblom 1987; Gregorini 2010; Hansson 1983; Hruby 2006; Kim 2012; Limoges 2004; Ordog 1987; Roche 1985) and one trial included a placebo pill (Oncel 2002). In most trials placebo TENS was operationalised as a sham TENS device with no current output that was similar in appearance to the active TENS device but had no batteries, or the internal circuit disconnected, or the device was not switched on. Gregorini 2010 administered placebo TENS using an active device with an inter-pulse interval of 33 seconds and claimed that this would avoid an analgesic effect. Liu 1985 applied a low pulse amplitude stimulus (fixed at 2.5 mA) as they felt this was a more valid control than a no stimulus placebo; for the purposes of this review, this was treated as low pulse amplitude TENS rather than placebo TENS. Only four of the trials that included placebo TENS also included TENS naive participants. Coyne 1995 specified "no previous TENS exposure" as an inclusion criterion and Cheing 2005 and Amer-Cuenca 2011 had previous experience of TENS as an exclusion criterion. Ordog 1987 indicated that none of their participants had used TENS previously. Olsén 2007 did not include a placebo group but did use TENS naive participants. Eight trials included a no treatment comparison group (Amer-Cuenca 2011; Coyne 1995; De Angelis 2003; de Sousa 2014; Hruby 2006; Keskin 2012; Limoges 2004; Pitangui 2012). Four trials included a pharmacological intervention as a comparison group: acetaminophen (paracetamol; Keskin 2012); local anaesthetic (Lignocaine with Octopressin, Crompton 1992); non-steroidal anti-inflammatory drug (NSAID) (Naproxen Sodium; Oncel 2002) and Tylenol (Ordog 1987). Two trials

included a non-pharmacological comparison group: exercise (Keskin 2012) and vibration (Ekblom 1987). Two active TENS groups were compared by Ekblom 1987 (2 Hz versus 100 Hz); Hansson 1983 (conventional TENS (100 Hz) to AL-TENS (2 Hz trains with 71 Hz internal frequency); Olsén 2007 (high (50 mA) versus low (10 to 15 mA) pulse amplitude); and Liu 1985 (high (5.86 + 0.96 mA) versus low (2.5 mA) pulse amplitude.

Adverse effects

Ten reports included information about the occurrence of adverse effects with three indicating that there were no adverse effects (Oncel 2002; Ordog 1987; Roche 1985) and seven indicating adverse effects. De Angelis 2003 compared TENS with no treatment in participants undergoing office hysteroscopy and reported nausea (8.5% of TENS group; 11.3% of control group, sample size of 71 per group); shoulder pain (3% of TENS group; 0% of control group); bradycardia (0% of TENS group; 2.8% of control group) and dizziness (8.5% of TENS group; 10% of control group). They did not specifically link these effects to TENS. Limoges 2004 reported that 29 out of 30 participants in the TENS group and six out of 30 participants in the placebo TENS group reported pain, burning or tingling at the electrode site. Hruby 2006 reported that two out of 48 participants could not tolerate TENS and Keskin 2012 reported discomfort with the TENS treatment as an adverse effect in one participant. Kim 2012 reported erythema and itching as adverse effects in seven out of 50 participants in the placebo TENS group and eight out of 50 in the TENS group. Olsén 2007 reported that TENS was discontinued due to discomfort during stimulation in one out of 13 participants receiving high pulse amplitude TENS. Hansson 1983 reported that most of the 20 participants receiving low frequency TENS found muscle twitch uncomfortable.

Outcomes

All trials used standard pain scales/questionnaires to record pain (VAS; NRS; McGill Pain Questionnaire, MPQ; VRS) but many trials did not provide sufficient information about the exact instruction given to participants about how to rate pain scores. Thus, it was difficult to determine whether pain scores were taken at a specific moment in time (e.g. present pain intensity) or retrospectively for over a specified period of time (e.g. pain intensity for the previous 24 hours) and if taken retrospectively whether scores were for 'average' pain or worst pain episode. Other outcomes included time in minutes until first report of pain reduction and maximum pain reduction (Hansson 1983), overall impression of using TENS (de Sousa 2014; Liu 1985), discomfort during TENS (Amer-Cuenca 2011; Crompton 1992; de Sousa 2014; Olsén 2007). One trial used a Roland Morris Disability Questionnaire (Keskin 2012). It was only possible to ascertain that three trials measured pain intensity whilst TENS was switched on and generating an electrical paraesthesia (Amer-Cuenca 2011; Ekblom 1987; Hruby 2006). Amer-Cuenca 2011 measured pain intensity during non-sedated colonoscopy; Ekblom 1987 measured pain intensity in participants experiencing acute dental pain due to pulpal inflammation, apical periodontitis, pericoronitis or postoperative pain following operative removal of an impacted tooth; and Hruby 2006 measured pain intensity during TENS for discomfort during office-based flexible cystoscopy. Many trials recorded pain after TENS had finished.

Excluded studies

For this update we retrieved 1065 reports from the literature searches after we removed duplicates, of which we considered 1038 irrelevant or excluded against eligibility criteria based on screening of abstracts (Figure 1). We obtained 24 full-text trial reports, of which we excluded 17. Overall we excluded 120 trials on the basis that TENS was given in combination with another treatment as part of the formal trial design, of which 73 were postoperative pain trials (Table 1). In most trials, TENS was given with analgesic medication as part of the formal trial design but some provided TENS in conjunction with non-pharmacological interventions, e.g. TENS given as part of a physiotherapy package of treatment. The reasons for excluding the remaining trials included not using a standard TENS device or TENS intensity in the active intervention was too low (Characteristics of excluded studies).

Table 1. Studies excluded as TENS given in combination with other treatments **Open in table viewer**

Akyuz G, Kayhan O, Babacan A, Gener FA. Transcutaneous electrical nerve stimulation (TENS) in the treatment of postoperative pain and prevention of paralytic ileus. Clinical Rehabilitation 1993; 7(3): 218-21.
Ali J, Yaffe CS, Serrette C. The effect of transcutaneous electric nerve stimulation on postoperative pain and pulmonary function. Surgery 1981; 89(4): 507-12.
Alm WA, Gold ML, Weil LS. Evaluation of transcutaneous electrical nerve stimulation (TENS) in podiatric surgery. Journal of the American Podiatry Association 1979; 69(9): 537-42.
Anderson AF, Lipscomb AB. Analysis of rehabilitation techniques after anterior cruciate reconstruction. American Journal of Sports Medicine 1989; 17(2): 154-60.
Angulo DL, Colwell CWJr. Use of postoperative TENS and continuous passive motion following total knee replacement. The Journal of Orthopaedic and Sports Physical Therapy 1990; 11(12): 599-604.
Ardic F, Sarhus M, Topuz O. Comparison of two different techniques of electrotherapy on myofascial pain. Journal of Back and Musculoskeletal Rehabilitation 2002; 16(1): 11-6.
Arena M, Savoca G, Lednyiczky G. Percutaneous paravertebral infiltration of O2-O3, bioresonance magnetotherapy, transcutaneous electrical nerve stimulation and psychosomatic postural rehabilitation in the treatment of degenerative joint disease of the lumbar spine with functional insufficiency of the vertebral motor unit. International Journal of Ozone Therapy 2008; 7(1): 29-36.
Avraham F, Aviv S, Ya'akobi P, Faran H, Fisher Z, Goldman Y, Neeman G, et al. The efficacy of treatment of different intervention programs for patellofemoral pain syndrome-a single blinded randomized clinical trial. Pilot study. The Scientific World Journal 2007; 7:1256-62.
Baker SB, Wong CC, Wong PC, Jenkins LC. Transcutaneous electrostimulation in the management of postoperative pain: initial report. Canadian Anaesthetists' Society Journal 1980; 27(2): 150-5.

Bayindir O, Paker T, Akpinar B, Erenturk S, Askin D, Aytac A. Use of transcutaneous electrical nerve stimulation in the control of postoperative chest pain after cardiac surgery. Journal of Cardiothoracic and Vascular Anesthesia 1991; 5(6): 589-91.

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Please note we may have had other reasons for exclusion of above studies in addition to the fact that TENS was used in combination with other treatments.

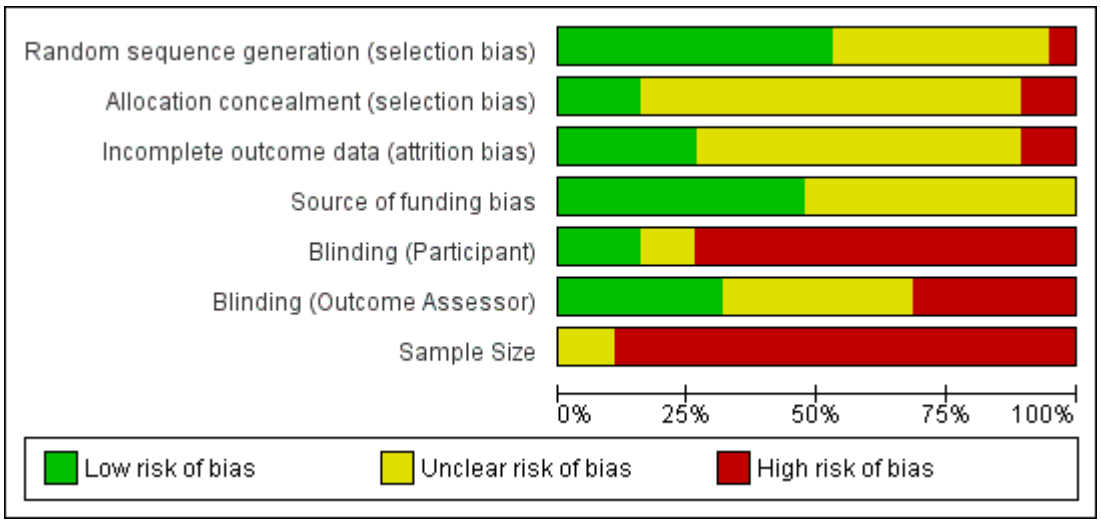
Studies awaiting classification

Eleven trials are awaiting classification (Characteristics of studies awaiting classification). Nine were written in English (Cambiaghi 2013; França 2012; Hsueh 1997; Liebano 2013; Park 2014; Rajpurohit 2010; Treacy 2011; Salvino 2013; Silva 2012) and two in Portuguese that required translation (de Paiva Tosato 2007; Salvador 2005). We contacted the trial authors by e-mail to clarify their eligibility based on three of our inclusion criteria (i.e. if the trial involved acute pain, if it was a randomised trial, or if other treatment was given in addition to TENS). The full trial report of the abstract by Liebano 2013 has been submitted for publication. We have not obtained the information required to classify the other studies yet.

Risk of bias in included studies

The 'Risk of bias' table provides details of judgements on the following items: allocation; blinding; incomplete outcome data; and, sources of funding bias. We have provided the overall 'Risk of bias' assessment of the 19 trials in Figure 2. We have listed details of the judgments about each methodological quality item for each included trial in Figure 3.

Figure 2 **Open in figure viewer** | **Download as PowerPoint**



Methodological quality graph: review authors' judgments about each methodological quality item presented as percentages across all included studies.

Figure 3

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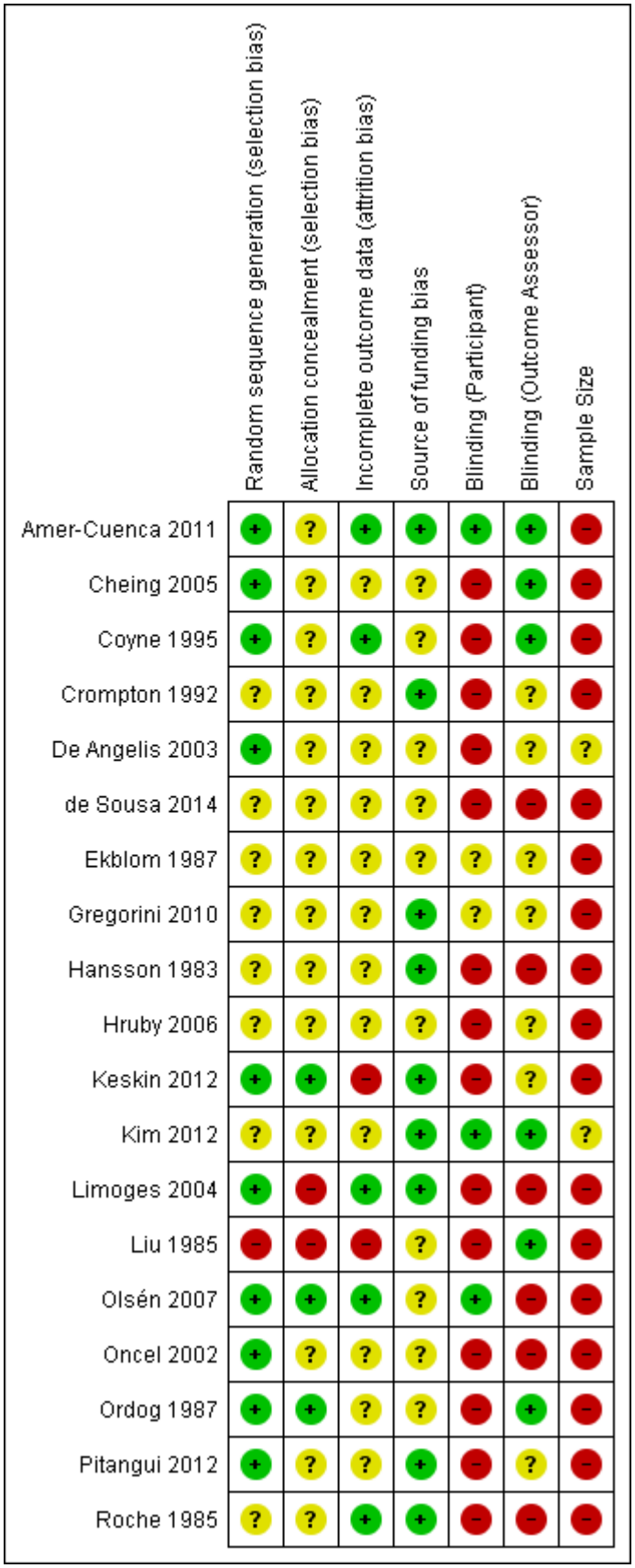


Methodological quality summary: review authors' judgments about each methodological quality item for each included trial.

Allocation

We considered sequence generation to be adequate in 11 trials (Amer-Cuenca 2011; Cheing 2005; Coyne 1995; De Angelis 2003; de Sousa 2014; Keskin 2012; Limoges 2004; Olsén 2007; Oncel 2002; Ordog 1987; Pitangui 2012), and unclear or inadequate in the other eight trials. Six trials used a computer generated list for sequence generation (Amer-Cuenca 2011; De Angelis 2003; de Sousa 2014; Olsén 2007; Oncel 2002; Pitangui 2012). Ordog 1987 mixed active and sham TENS devices during allocation and unblinded group allocation when all devices were returned to the researcher after the trial was completed. Gregorini 2010 used a 'sealed' box for randomisation but did not give specific operational details. Coyne 1995 and Keskin 2012 used a randomisation table. We rated the remaining trials as either inadequate (dividing participants alternatively into groups; Liu 1985) or unclear in their methods of sequence generation (Ekblom 1987; Gregorini 2010; Kim 2012). Only three trials had adequate allocation concealment (Keskin 2012; Olsén 2007; Ordog 1987). Olsén 2007 and Keskin 2012 were the only trials to use pre-sealed opaque envelopes. Ordog 1987 revealed which of the TENS units were active or sham only after they had been returned to the researcher when the trial was completed. Most trials were unclear regarding how allocation was concealed (Amer-Cuenca 2011; Cheing 2005; Coyne 1995; Crompton 1992; De Angelis 2003; de Sousa 2014; Gregorini 2010; Hansson 1983; Hruby 2006; Kim 2012; Oncel 2002; Pitangui 2012; Roche 1985) and deemed inadequate in two trials (Limoges 2004; Liu 1985).

Blinding

Participant blinding

It is impossible to fully blind participants to an electrical current that generates a sensory experience, although participants can be made to be uncertain whether the sensations that they experience are likely to be effective. Four trials that included a placebo control specified that participants were TENS naive (Amer-Cuenca 2011; Cheing 2005; Coyne 1995; Ordog 1987). Studies that used a sham TENS device ensured that it was similar in appearance to the active TENS device but delivered no current (Amer-Cuenca 2011; Cheing 2005; Coyne 1995; Hansson 1983; Hruby 2006; Kim 2012; Limoges 2004; Oncel 2002; Ordog 1987; Roche 1985) or a very low pulse amplitude current (Liu 1985; Gregorini 2010). In addition, participants were told they may or may not feel a sensation during the treatment (Cheing 2005; Kim 2012; Limoges 2004; Oncel 2002; Roche 1985) or that some people may not experience the stimulation (Hansson 1983). Olsén 2007 did not use a placebo TENS intervention and participants experienced TENS sensation in both of the active TENS interventions.

Assessor blinding

In six trials, the person who recorded the outcomes was blind to group allocation (Amer-Cuenca 2011; Cheing 2005; Coyne 1995; Kim 2012; Liu 1985; Ordog 1987). Five trials did not have blinded assessors (de Sousa 2014; Hansson 1983; Limoges 2004; Olsén 2007; Oncel 2002). Oncel 2002 recorded pain scores using

an investigator not blinded to group allocation and also by nurses who were blinded to group allocation. The remaining trials did not provide sufficient details to judge assessor blinding (Crompton 1992; De Angelis 2003; Ekblom 1987; Gregorini 2010; Hruby 2006; Keskin 2012; Pitangui 2012).

Follow-up and exclusions

Amer-Cuenca 2011, Kim 2012, Limoges 2004, Pitangui 2012 and Roche 1985 did not report any participant withdrawals. de Sousa 2014 evaluated 44 participants for eligibility, of which five did not meet the inclusion criteria, six were excluded and one refused to participate in the trial. All 32 participants randomised completed the trial. Coyne 1995 withdrew ten participants post-randomisation as they did not meet blood donor criteria, although such screening for eligibility should have been conducted before randomisation. Crompton 1992 provided details of two withdrawals (one participant failed to record a pain score and another found the cervical laser treatment uncomfortable) but there were no details of which treatment group they belonged to. Oncel 2002 reported that eight participants were withdrawn due to complications from respiratory distress associated with their minor rib fractures but they did not state which treatment group they belonged to. These withdrawals were replaced. Liu 1985 reported the number of participants that data were recorded from on each postoperative day but did not give specific reasons for the incomplete data set. Olsén 2007 reported that one participant dropped out due to discomfort of TENS (high pulse amplitude TENS group). Keskin 2012 reported dropouts due to non-compliance, loss to follow-up or pregnancy-related complications but gave no information on how this data was dealt with. Six trials did not provide details on whether there were any incomplete data (Cheing 2005; De Angelis 2003; Gregorini 2010; Hansson 1983; Hruby 2006; Ordog 1987).

Other potential sources of bias

There was a high risk of bias associated with inadequate sample sizes in treatment arms. Four trials acknowledged sources of funding: loan of TENS units from a TENS manufacturer (Crompton 1992); TENS units provided by a TENS manufacturer and university project grant (Limoges 2004); research foundation (Hansson 1983); and a research council grant (Roche 1985). None of these sources were thought to introduce bias.

Effects of interventions

Primary objective

The primary objective of this Cochrane Review was to assess the analgesic effectiveness of TENS, as a sole treatment, for acute pain in adults. We were unable to extract data from included trials for the following reasons: data presented as median and interquartile (IQ) range (Crompton 1992; Keskin 2012); insufficient data provided (Coyne 1995). We felt that there was sufficient information in reports to assume that De Angelis 2003 and Hruby 2006 presented means with standard deviations (SDs). We also decided to extract

data from the two trials that included at least one participant under 16 years (age range: Cheing 2005 = 15 to 58 years; Oncel 2002 = 11 to 81 years) because the mean ages for the sample populations were above 30 years. We contacted the following authors in an attempt to obtain the data: Crompton 1992 (responded but unable to provide data as mean and SD); Coyne 1995 (responded but unable to provide data); Hruby 2006 and De Angelis 2003 (no response). There were insufficient extractable data to allow us to pool data for meta-analysis for most planned comparisons. We decided to pool data for pain intensity (100 mm VAS) and proportion of participants achieving ≥ 50% reduction in pain, although there was variability in procedures used to measure pain scores including whether scores were for present or retrospective pain and whether TENS was switched on during pain ratings.

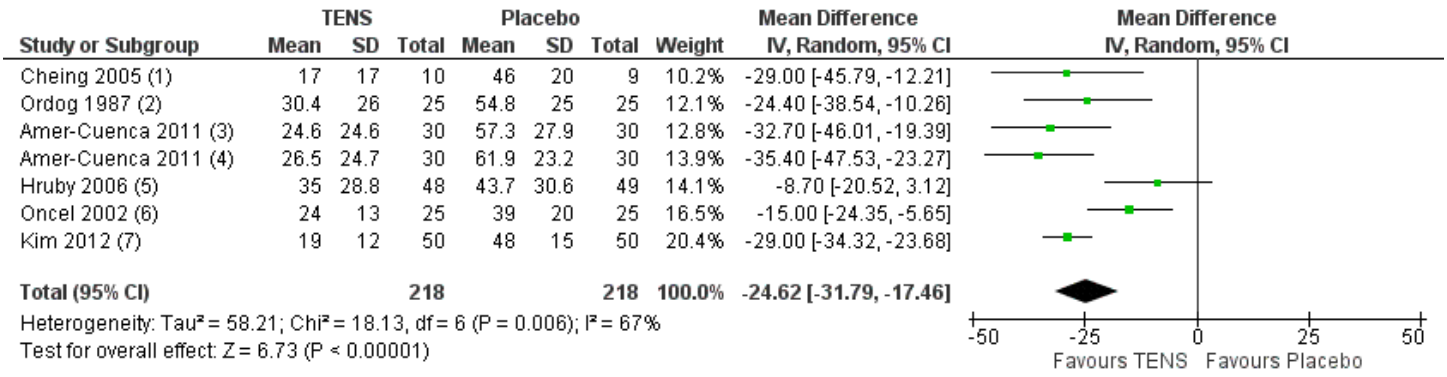
TENS versus placebo TENS

Eleven trials included a comparison between active and placebo TENS. Eight trials reported a statistically significant improvement in favour of TENS of at least one outcome measure at one or more time points (Amer-Cuenca 2011; Cheing 2005; Ekblom 1987; Gregorini 2010; Hansson 1983; Kim 2012; Ordog 1987; Roche 1985). Cheing 2005 reported lower pain scores (VAS) for neuropathic pain in the hand during TENS. Hansson 1983 claimed that more patients experienced > 50% relief of orofacial pain post treatment using a VAS but only reported details of a descriptive analysis. Ordog 1987 reported a significant decrease in pain intensity during TENS after two days of treatment (VAS, WMD -2.44 cm, 95% CI -3.85 to -1.03, P = 0.0007). Roche 1985 reported that more patients achieved 50% relief of pain associated with haemophilia haemorrhage using TENS (P < 0.02). Ekblom 1987 reported that more patients experienced reduction of acute orofacial pain using 100 Hz TENS following statistical analysis using the Chi^2 test but there was insufficient information to evaluate the analysis. Gregorini 2010 reported a significant reduction in post-operative pain intensity (VAS) following cardiac surgery during TENS group (P < 0.001). Amer-Cuenca 2011 reported that more patients achieved > 50% relief of pain associated with colonoscopy during TENS (P < 0.001). Kim 2012 reported significantly lower pain intensity (VAS) during venous cannulation during TENS. Studies that reported no differences in pain outcomes between TENS and placebo TENS found no significant differences between active and placebo TENS for procedural pain associated with venipuncture (Coyne 1995), flexible cytoscopy (Hruby 2006) and flexible sigmoidoscopy (Limoges 2004). One trial included a comparison between active TENS and placebo pill and reported a statistically significant improvement in favour of TENS (Oncel 2002).

We pooled data for pain intensity for six trials (seven comparisons) but the I^2 statistic (67%) suggested substantial heterogeneity (Figure 4). The MD was -24.62 mm (95% CI -31.79 to -17.46; six trials, 436 participants; Analysis 1.1) in favour of TENS using a random-effects model. We pooled data for the proportion of participants achieving ≥ 50% reduction in pain from four trials (seven comparisons). The relative risk was 3.91 (95% CI 2.42 to 6.32; four trials, 280 participants; Analysis 1.2) in favour of TENS with a NNTB of 2.49 (Figure 5). We were unable to pool other data.

Figure 4

Open in figure viewer | Download as PowerPoint



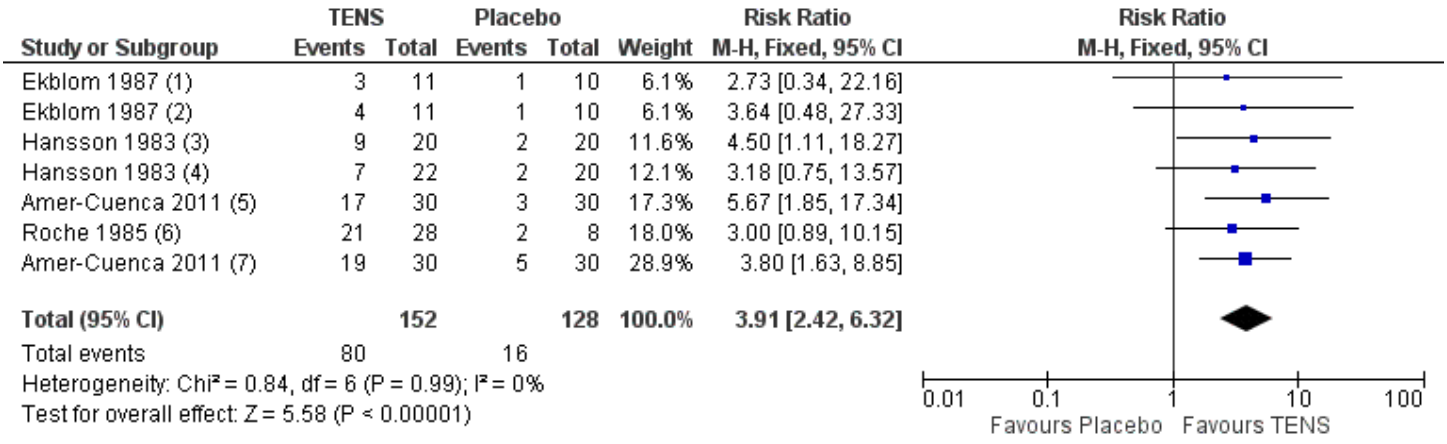
Footnotes

(1) Outcome measured on day 11 after 10 days of TENS treatment. TENS not on during measurement
(2) Outcome measured after day 2 of treatment. NRS (0-10) used presented as mean+SD. TENS not on during measurement
(3) Outcome measured 5 minutes into procedure (mean duration procedure 17-20 min depending on group). TENS on during measurement
(4) Outcome measured at end of procedure (mean duration 17-20 min depending on group). TENS on during measurement
(5) Outcome measured after 1 minute of TENS. TENS on during measurement
(6) NOTE: Comparison with placebo pill. Outcome measured on day 4 receiving TENS for 3 days. TENS not on during measurement.
(7) Outcome measured after 20 minutes of TENS. TENS not on during measurement

Forest plot of comparison: 1 TENS versus placebo TENS, outcome: 1.1 Pain intensity (100 mm VAS).

Figure 5

Open in figure viewer | Download as PowerPoint



Footnotes

(1) 2Hz TENS with muscle contractions (AL-TENS)
(2) 100z sensory TENS (conventional TENS)
(3) 100z sensory TENS (conventional TENS)
(4) 2Hz TENS with muscle contractions (AL-TENS)
(5) Outcome measured at end of procedure (mean duration 17-20 min depending on group). TENS on during measurement
(6) Outcome measured immediatey after 25 minutes of TENS. TENS not on during measurement
(7) Outcome measured 5 minutes into procedure (mean duration procedure 17-20 min depending on group). TENS on during...

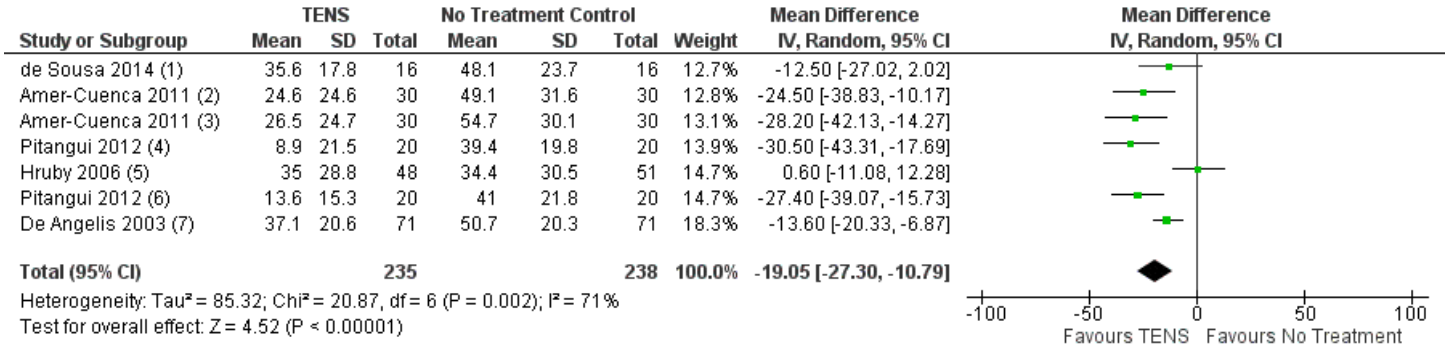
Forest plot of comparison: 1 TENS versus placebo TENS, outcome: 1.2 > 50% reduction in pain.

TENS versus no treatment control

Seven trials included a comparison between TENS and a no treatment control. Five trials reported an improvement in favour of TENS of at least one outcome measure at one or more time points (Amer-Cuenca 2011; De Angelis 2003; de Sousa 2014; Keskin 2012; Pitangui 2012). de Sousa 2014 found that TENS reduced post-partum uterine contraction pain during breast-feeding compared with the no treatment control. De Angelis 2003 found that TENS reduced the intensity of pain during hysteroscopy compared with a no treatment control. Amer-Cuenca 2011 reported that more patients achieved > 50% relief of pain associated with colonoscopy during TENS compared with a no treatment control. Keskin 2012 reported that the pain intensity associated with LBP during pregnancy was lower during TENS compared with a no treatment control. Pitangui 2012 found a significant reduction in resting, sitting and ambulating pain (NRS) following episiotomy immediately after TENS and 60 minutes later when compared with the control group ($P < 0.001$). Hruby 2006 found no significant differences between TENS and no treatment control for the intensity of pain during flexible cytoscopy. Limoges 2004 found no significant difference between TENS and no treatment control groups during screening flexible sigmoidoscopy (NRS, WMD -0.23 points, 95% CI -0.72 to 0.26, $P = 0.36$). We were unable to ascertain whether Coyne 1995 used a no treatment control or an unspecified 'placebo' for procedural pain associated with venipuncture. Coyne 1995 found no significant differences between TENS and the control/placebo.

We pooled data for pain intensity were pooled from five trials (seven comparisons) but the I^2 statistic value (71%) suggested considerable heterogeneity (Figure 6). MD was -19.05 mm (95% CI -27.30 to -10.79; five trials, 473 participants; Analysis 2.1) in favour of TENS using a random-effects model. We were unable to pool other data.

Figure 6 **Open in figure viewer** | **Download as PowerPoint**



Footnotes
(1) Time point used = 2nd assessment/feed. Measurement taken using NRS at rest (converted to 100 unit scale). Data presented as Mean+SD
(2) Outcome measured 5 minutes into procedure (mean duration procedure 17-20 min depending on group). TENS on during measurement
(3) Outcome measured at end of procedure (mean duration 17-20 min depending on group). TENS on during measurement
(4) Outcome measured 60 after start of TENS . TENS on during measurement. Measurement taken using NRS at rest. Data presented as Mean+SD
(5) Outcome measured after 1 minute of TENS. TENS on during measurement
(6) Outcome measured 120 minutes after start of TENS . TENS on during measurement. Measurement taken using NRS at rest. Data presented as Mean+SD
(7) Outcome measured after procedure. TENS not on during measurement

Forest plot of comparison: 2 TENS versus no treatment control, outcome: 2.1 Pain intensity (100 mm VAS).

TENS versus a pharmacological intervention

Four trials included a comparison between TENS and a pharmacological treatment. Three trials reported an improvement in favour of TENS of at least one outcome measure at one or more time points. Crompton 1992 reported that TENS was superior to local anaesthetic for procedural cervical laser treatment. Oncel 2002 reported that TENS was superior to NSAID for rib fractures. Keskin 2012 reported that TENS was superior to acetaminophen (2 x 500 mg/day) for LBP during pregnancy. Ordog 1987 reported that there was no difference between TENS and acetaminophen (300 to 600 mg) plus codeine (30 to 60 mg) for pain associated with acute traumatic injuries including sprains, lacerations, fractures, haematomas and contusions but did not make a direct comparison of TENS alone versus medication. We were unable to pool other data.

TENS versus a non-pharmacological intervention

Two trials included a comparison between TENS and a non-pharmacological treatment. Keskin 2012 reported that TENS produced greater pain relief than exercise for LBP during pregnancy. Ekblom 1987 reported that there were no differences in pain relief between TENS and vibration for acute orofacial pain. We were unable to pool data.

Conventional TENS versus AL-TENS

Two trials included a comparison between conventional and AL-TENS. Hansson 1983 and Ekblom 1987 reported that there were no significant differences in the proportion of participants achieving > 50% reduction in orofacial pain between high frequency, low intensity (conventional) TENS (100 Hz, intensity of

two to three times perception threshold) and low frequency, high intensity (acupuncture-like) TENS (2 Hz pulse train, intensity of three to five times perception threshold). We pooled data for the proportion of participants achieving ≥ 50% reduction in pain. The relative risk was 0.72 (95% CI 0.37 to 1.39; two trials, 64 participants; Analysis 3.1).

High pulse amplitude TENS versus low pulse amplitude TENS

Two trials included a comparison between high and low pulse amplitude TENS. Olsén 2007 reported that high intensity (50 mA) high frequency (70 to 100 Hz) TENS produced a larger decrease in the intensity of pain associated with postpartum uterine contractions than low intensity (15 mA) high frequency (70 to 100 Hz) TENS just above sensory detection threshold. The trial authors reported a significantly higher number of participants reported discomfort with the higher pulse amplitudes ($P < 0.01$). Liu 1985 delivered active TENS at a "subjective level of comfort" with a mean ± SD amplitude of 5.86 ± 0.96 mA across the sample. For this analysis we interpret this 'high pulse amplitude'. They also administered 'control' TENS fixed at 2.5 mA as they believed that this was a more valid control than a no stimulus placebo. For the purposes of this Cochrane Review, we treated this as low pulse amplitude TENS rather than placebo TENS. Liu 1985 found no significant differences between these two pulse amplitudes (VAS, WMD -1.53 cm, 95% CI -3.37 to 0.31; $P = 0.1$). In addition, De Angelis 2003 measured pain intensity (VAS) during hysteroscopy in one group of participants and reported that pain was reduced to a greater extent when participants increased pulse amplitude and associated intensity by pressing a 'plus' switch on the device. MD for these latter two trials was -23.47mm (95% CI -29.60 to -17.34) in favour of high TENS using a random-effects model (Analysis 4.1).

Secondary objectives

Insufficient extractable data meant that it was not possible to perform any planned subgroup analysis for any secondary objectives. We were unable to determine whether TENS effectiveness was influenced by the time of recording the outcome measure, i.e. during TENS measurement compared to post TENS measurement, or to compare the duration of TENS treatment or comparisons for different acute pain conditions.

Discussion

Summary of main results

This updated Cochrane Review examined the effectiveness of TENS as a sole intervention for the treatment of acute pain in adults. We retrieved 1065 reports from literature searches for this update, in addition to the 1775 reports identified for the 2011 update. We included seven new trials and 11 studies are awaiting classification. Thus, 19 RCTs involving 1346 participants at entry met the inclusion criteria. We were able to extract data from 13 of the 19 included trials (Amer-Cuenca 2011; Cheing 2005; De Angelis 2003; de Sousa 2014; Ekblom 1987; Hansson 1983; Kim 2012; Limoges 2004; Liu 1985; Olsén 2007; Oncel 2002; Ordog 1987; Roche 1985). Eight of 11 trial reports with a placebo TENS comparison identified a statistically significant improvement in favour of TENS of at least one outcome measures at one or more measurement time point. Pooled data from six trials found a MD of -24.62 mm (95% CI -31.79 to -17.46) on 100mm VAS in favour of TENS. Pooled data from four trials (seven comparisons) found a relative risk of 3.91 (95% CI 2.42 to 6.32), in favour of TENS with a NNTB of 2.49 for the proportion of participants achieving ≥ 50% reduction in pain. The NNTB is remarkably low and most likely to have been exaggerated by the high risk of bias associated with small sample sizes and various other biases as highlighted in the risk of bias analysis. We do not attribute statistical credibility to the effect sizes because of statistical heterogeneity but it is noteworthy that the direction of effect is consistent.

Five of the seven trial reports with a no treatment control identified an improvement in favour of TENS in at least one outcome measure at one or more time point. Pooled data from five studies produced a MD of -19.05mm (95% CI -27.30 to -10.79) in favour of TENS. Three out of four trials that compared TENS with an analgesic drug and one out of two studies that compared TENS with a non-pharmacological treatment found an improvement in favour of TENS of at least one outcome measure at one or more measurement time point. Three trials included a comparison between high and low pulse amplitude and all found that higher pulse amplitudes were superior. This finding is consistent with recent experimental pain studies that indicated high pulse amplitude (irrespective of the applied frequency) is the key parameter for effective TENS applications (Aarskog 2007; Chen 2008; Claydon 2008). Furthermore, a meta-analysis of TENS for postoperative pain by Bjordal 2003 highlighted the relevance of optimal (strong or maximal non-painful) intensity levels for pain relief in this clinical population. There were no differences in the proportion of participants achieving ≥ 50% reduction in pain between conventional and AL-TENS in the two included trials. Three trial reports indicated that there were no adverse effects and seven reports indicated a range of adverse effects that were primarily related to sensations experienced at the electrode site or the muscle contractions associated with low frequency TENS. We judged these as minor. The methodological quality of the trials varied considerably: we judged sequence generation to be adequate in ten trials, allocation concealment was adequate in three trials and only five had adequate assessor blinding. There was a high risk of bias associated with inadequate sample sizes with only two trials having sample sizes ≥ 50 per treatment arm.

Overall completeness and applicability of evidence

The range of acute pain conditions included in this review was limited by eligibility criteria that excluded trials of acute pain during childbirth and primary dysmenorrhoea because these conditions have been covered by previous Cochrane Reviews (Dowswell 2009; Proctor 2002). In addition, we excluded trials that evaluated TENS in combination with any other treatment as part of the formal trial design (e.g. analgesic medication, exercise) on the basis that addition of another treatment would compromise pain relief measures making it impossible to ascertain the contribution of TENS. The highest number of excluded trials were on postoperative pain as they gave analgesic medication in addition to TENS for pain management. The effect of TENS in combination with other treatments for acute pain is the subject for another systematic review. We categorised the 19 included trials into procedural and non-procedural pain but were unable to pool data for subgroup analyses. All trials were in the English language with most based in Europe. Only one trial described the use of TENS by the participants solely at home (Ordog 1987). As TENS can easily be self-applied for most conditions, this limits the evidence for comparison of self-applied versus therapist-applied TENS. The range of outcome measures used provided limited data that could be extracted from the included trials.

The reporting of TENS treatments showed wide variations across the included trials. Several trials failed to report full details of the TENS parameters used or technique of application, thus making replication impossible. Attempts to combine outcomes in a meta-analysis were undermined by substantial heterogeneity, a lack of available data, and a lack of specific information on procedures used to measure pain scores, especially whether scores were taken for present pain or retrospective pain, during or after TENS. This seriously limits the interpretation of the results. Both experimental pain and clinical studies suggest that maximum pain relief is obtained while TENS is switched on (Johnson 1991; Johnson 1999; Tong 2007). Thus the timing of pain measurement is crucial, particularly for procedural pain; some included trials measured pain post procedure but asked participants to record 'during procedure' pain thus relying on recall (De Angelis 2003; Limoges 2004). Often it was impossible to ascertain the exact instruction given to participants about the nature of the pain score required. As TENS has been shown to have maximum pain relieving effects during application, it is important to record pain outcome whilst it is being applied. Few trials continued to record the effect of TENS on pain outcome for more than a few days thus limiting any conclusions regarding the duration of effect of TENS on acute pain.

Quality of the evidence

The 19 included trials involved 1346 participants at entry. In general, the quality of the evidence was weak due to inadequate methods or lack of information on: allocation concealment; blinding of the outcome assessors; incomplete outcome data; and method of analysis (per protocol or ITT). There was a high risk of bias from inadequate sample sizes. Sample sizes ranged from eight to 71 per group and nine trials had fewer than 20 participants in each treatment arm. Only three trials had a prospective sample size calculation. Blinding participants to active TENS is challenging because treatment necessitates a perceptual experience (i.e. TENS sensation) yet investigators should make every attempt to introduce uncertainty about which

treatment arm is active through carefully worded pre-trial instructions. TENS naïvety is an important inclusion criteria in trials attempting to blind participants. Only four of the trials that compared TENS to placebo used participants that were TENS naïve. Typically placebo TENS was administered using a sham TENS device with no electrical output and no perceptual experience and this can be a credible approach to achieve at least partial blinding (Deyo 1990). However, there was no attempt in included trials to monitor the success or otherwise of blinding using an assessment tool, such as that developed by Deyo 1990. Rakel 2010 developed and tested a new sham TENS device that delivered a current for 30 seconds, which then declined in amplitude to 0 mA over 15 seconds. This output allowed the clinician to set the pulse amplitude without knowing if the unit was an active or sham device. Thus, the method of delivery of treatment by the clinician was identical for each participant and this type of sham TENS device may be useful for future trials. Hrobjartsson 2007 highlighted this issue of monitoring blinding in RCTs and analysed a random sample of 1599 blinded RCTs indexed in CENTRAL and found that only 2% of trials included tests for the success of blinding.

Potential biases in the review process

Review authors were not blinded from authors' names, institutions and journal name or trial results at any stage of the review process. However, pairs of review authors undertook each stage of the review process independently and we compared the outcomes.

Agreements and disagreements with other studies or reviews

Cochrane Reviews on TENS for specific types of acute pain have been inconclusive for labour pain (Dowswell 2009) and dysmenorrhoea (Proctor 2002).

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Jump to: included studies | studies awaiting assessment | additional references | other published versions

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Link to article

Characteristics of studies

Characteristics of included studies [ordered by study ID]

Amer-Cuenca 2011

Methods	Type of study: double-blind, placebo controlled RCT. Condition and number of participants randomised: 90 participants attending for unsedated colonoscopy were randomised. Groups: TENS group 30; placebo TENS group 30; no-treatment control group 30.
Participants	Demographics: N = 90, mean age 50.2 years, TENS group mean age 49.5 years ± 2.4, 14F/16M; placebo group mean age 51.3 years ± 2.5, 19 female/11 male; control group mean age 49.9 years ± 2.4, 17 female/13 male. Setting: outpatients. Inclusion: attending unsedated screening colonoscopy, ASA I or II status, age > 18, no visual or hearing impairments, no neuropsychiatric disorders. Exclusion: refusal to consent, non-Spanish speakers, colonic resection or stenosis of the colon, previous experience of TENS, cutaneous damage on application sites, pacemaker or cardiac defibrillator. Withdrawals/dropouts: no withdrawals.

Interventions	Where applied: in hospital. Applied by: not stated. Waveform: not stated. Frequency: 80 to 100 Hz. Pulse duration: 400 µs. Pulse amplitude/Intensity: adjusted to the maximum sensory level without muscle contraction. Placebo Group: procedures identical to those for TENS group, except that a sham unit was used. Internal circuit of the sham TENS unit disconnected but the indicator lamp lit when unit switched on. All participants told that they might or might not feel a tingling sensation during treatment (Rx). Electrodes: 2 rectangular autoadhesive electrodes, 7 cm x 13 cm, applied parallel to the lumbo-sacral spine. Duration and frequency of Rx: for the duration of the procedure. Device/manufacturer: Intellect Advance (Chattanooga) Adverse effects: not detailed.
Outcomes	Pain outcome: VAS, Likert Scale. ITT/per protocol analysis: statistical analysis done according to ITT. Statistical analysis: Intergroup and intragroup differences calculated using one-way ANOVA for continuous variables, followed by Tukey's post-hoc test and Chi^2 test for proportional variables. Mean pain intensity VAS scores were no different from placebo and control groups at 5 minutes. The active TENS group was significantly different at 5 minutes when compared against placebo or control groups ($P < 0.001$). At the end of the procedure the TENS group VAS scores were significantly lower than the other two groups ($P < 0.001$) The differences between the placebo and control groups were not significant at 5 minutes and at the end. Spearman's correlation coefficient between the VAS and Likert scales was performed. There were significant differences when the TENS group was compared with either the placebo or the control groups. The scores were significantly lower in the TENS group compared with the other two groups ($P = 0.009$). There was a strong correlation between VAS and Likert scales in measuring pain at both 5 minutes and at the end of the procedure ($P < 0.001$).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Low risk	Computer-generated block randomisation with stratification for gender.
Allocation concealment (selection bias)	Unclear risk	No details provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Not applicable - no withdrawals or dropouts.
Source of funding bias	Low risk	No funding bias apparent.
Blinding (Participant)	Low risk	TENS and Placebo participants blinded, medics blinded.
Blinding (Outcome Assessor)	Low risk	Blinded assessor.
Sample Size	High risk	N = 30 per treatment arm.

Cheing 2005

Methods	Type of study: double blind, placebo-controlled, parallel RCT. Condition and number of participants randomised: clinical diagnosis of hypersensitive hands due to peripheral nerve injuries (N = 19). Groups: TENS group (N = 10); placebo group (N = 9).

Participants	Demographics: N = 19, mean 35 yrs, range 15 to 58 yrs, 16 male/3 female. TENS group, 32 ± 11 yrs; placebo group, 38 ± 13 yrs (mean ± SD). Setting: outpatients. Inclusion: people who complained of hypersensitive hands within or adjacent to the site of the injury, and who were able to complete the VAS independently. Exclusion: people who had general manifestations of pain as seen in causalgia or shoulder-hand syndrome; people who had received any TENS or undergone a desensitization programme 1 month prior to the trial; cardiac pacemaker or who had experienced sensory loss in their hands prior to the trial. Withdrawals/dropouts: not detailed.
Interventions	Where applied: in hospital. Applied by: presume by clinician. Waveform: square pulses. Frequency: 100 Hz. Pulse duration: 200 μs. Pulse amplitude/Intensity: adjusted to produce a tingling sensation that was strong but tolerable. Placebo Group: procedures identical to those for TENS group, except that a sham unit was used. Internal circuit of the sham TENS unit disconnected but the indicator lamp lit when unit switched on. All participants told that they might or might not feel a tingling sensation during Rx. Electrodes: 2 rectangular carbon rubber electrodes with gel, 2 cm x 3 cm, anode applied directly over the hypersensitive area and cathode placed proximally along the distribution of the same peripheral nerve. Duration and frequency of Rx: 20 mins, 10 Rxs. Device/manufacturer: 120Z TENS unit (ITO, Tokyo). Adverse effects: not detailed.
Outcomes	Pain outcome: pain intensity using VAS for a brush-evoked stimulus with a toothbrush. Recorded before Rx on days 1, 4, 7 and 11. ITT/per protocol analysis: not detailed. Statistical analysis: no evaluable data for this review as mixed age population (adults and children). Significantly lower pain scores were found in the TENS group than in the placebo group by Day 7 and Day 11. Both groups demonstrated significant decreases in VAS scores across treatment sessions.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Subjects were matched by age, history of developing hypersensitivity and baseline VAS scores, and then randomly assigned into either the TENS (n = 10) or placebo group (n = 9) by drawing lots".
Allocation concealment (selection bias)	Unclear risk	No details provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No details provided.
Source of funding bias	Unclear risk	No details provided.
Blinding (Participant)	High risk	It is impossible to adequately blind participants who receive electrical stimulation. "All subjects were blind to group allocation. The placebo group had received no active treatment (just placebo TENS) throughout the trial. The treatment procedures for the placebo group were identical to those for the real TENS group, except that a sham unit was used. The appearance of the sham unit was identical to that of a real TENS unit, but the internal circuit of the sham TENS unit was disconnected. When the machine was switched on, there was no output of current, but the indicator lamp lit up. All subjects were told that they might or might not feel a tingling sensation during the treatment". "People who had received any TENS" was an exclusion criteria.
Blinding (Outcome Assessor)	Low risk	"The blinded assessor repeatedly practiced applying the same brushing force on a digital balance prior to the study".
Sample Size	High risk	TENS (N =10); placebo (N = 9).

Coyne 1995

Methods	Type of study: double blind, placebo-controlled, parallel RCT. Condition and number of participants randomised: procedural IV needlestick pain in blood donors, 71. Groups: TENS group (N = 19); placebo TENS group (N = 21); control group (N = 21), these are numbers after 10 participants were dropped due to not meeting Virginia Blood Service criteria for blood donation.
Participants	Demographics: N = 71 randomised, 26 male/35 female post dropout. TENS group, 36 yrs; placebo TENS group, 37 yrs; control group, 35 yrs (mean). Setting: blood donor clinic. Inclusion: blood donors meeting Virginia Blood Service criteria for donation; previous IV insertion; no previous TENS exposure; upper extremity exposure for electrode placement; appropriate consent obtained; having venipuncture to the right or left antecubital site. Exclusion: not detailed. Withdrawals/dropouts: 10 participants were dropped as they did not meet the Virginia Blood Service criteria for blood donation.
Interventions	Where applied: in clinic. Applied by: clinician. Waveform: balanced and biphasic. Frequency: 160 pulses/s. Pulse duration: 310 to 400 μs on the strength-duration mode. Pulse amplitude/Intensity: below the participant's pain threshold, adjusted during stimulation to maintain this level. Placebo TENS Group: TENS unit without batteries. Control Group: no treatment. Electrodes: 4 carbon electrodes, 4 cm, applied at site of venipuncture in a square fashion. Duration and frequency of Rx: min 12 mins and max 32 mins, 1 Rx. Device/manufacturer: Maxima III TENS unit. Adverse effects: not detailed.

Outcomes	Pain outcome: pain assessed by a subjective and an affective VAS. Recorded before intravenous (IV) insertion, after Rx, and at end of needle insertion phase. ITT/per protocol analysis: per protocol. Statistical analysis: no evaluable data for this review as unable to extract data from paper. No significant difference among groups for sensory or affective VAS scores.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"It was a convenient sample of 71 volunteer donors from the Virginia Blood Service who were randomized into one of the following three groups". Author response "a randomization table was how the participants were selected as participants arrived and consented to the trial".
Allocation concealment (selection bias)	Unclear risk	No details provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	"However, ten subjects were dropped because they did not meet the Virginia Blood Service criteria for blood donation (i.e. low haemoglobin)".
Source of funding bias	Unclear risk	No details provided.
Blinding (Participant)	High risk	It is impossible to adequately blind participants who receive electrical stimulation. "No previous TENS exposure" was an inclusion criteria. Author responded "both were blinded" to the question "who was blinded, was it the patient and person recording VAS?" Author response: "TENS unit without batteries were the sham". Control group received no treatment so these participants could not be blinded.
Blinding (Outcome Assessor)	Low risk	Author responded "both were blinded" to the question "who was blinded, was it the patient and person recording VAS?".
Sample Size	High risk	TENS (N = 19); placebo (N = 21); control (N = 21).

Crompton 1992

Methods	Type of study: parallel RCT. Condition and number of participants randomised: women undergoing cervical laser treatment (N = 100). Two participants were excluded from analysis because they failed to record pain score or found treatment too uncomfortable. Groups: TENS group (N = 34); local anaesthetic group (N = 35); TENS and local anaesthetic group (N = 29). NB 10 more participants recruited than initially intended as researchers lost count of number recruited and failed to stop the trial.
Participants	Demographics: N = 100, all female. TENS group, 31.8 ± 9 yrs; local anaesthetic group, 32.6 ± 9 yrs; TENS and local anaesthetic group, 30.1 ± 8 yrs (mean ± SD). Setting: colposcopy unit. Inclusion: colposcopic diagnosis of cervical intra-epithelial neoplasia (CIN). Exclusion: past history of treatment for CIN; other cervical surgery or pelvic inflammatory disease; postmenopausal women; cardiac pacemakers. Withdrawals/dropouts: 1 woman excluded as she failed to record pain score. Another found treatment too uncomfortable so direct local infiltration was added.
Interventions	Where applied: in hospital. Applied by: clinician. Waveform: not detailed. Frequency: 80 Hz. Pulse duration: 210 µs. Pulse amplitude/Intensity: activated by participants under instruction, told to increase it until it became uncomfortable. Electrodes: 4, conductive silicone polymer electrodes and gel, size not detailed. 2 applied anteriorly to abdominal wall just above symphysis pubis, and 1 on each side of sacrum. Duration and frequency of Rx: participants given approximately 20 min to experiment with TENS until they were called into another room for laser treatment. Duration of TENS during laser treatment not detailed, 1 Rx. Device/manufacturer: Microtens (Neen Pain Management, UK). Adverse effects: not detailed.

Outcomes	Pain outcome: pain assessed by a VAS after the procedure. After procedure, participants asked to complete questionnaire on TENS, one question was "did they find TENS pain relieving?". ITT/per protocol analysis: ITT. Statistical analysis: no evaluable data for this review as data presented as medians and IQ ranges. Median pain score for TENS group was significantly higher than that for local anaesthetic. Combining TENS with local anaesthesia did not further reduce the median pain score. 51 women who used TENS completed questionnaire: of the coherent responses 75% thought it was pain relieving.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Suitable subjects were then allocated to one of the following three groups according to a block randomised code". It is unclear how this code was generated.
Allocation concealment (selection bias)	Unclear risk	"The block randomisation code was held by one investigator who then allocated treatment. The nurses, clerical officers responsible for the computerized appointments, and the laser surgeon did not have access to this code". It is unclear how this code was kept concealed.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	"One woman was excluded because she failed to record pain score. Another found the treatment too uncomfortable and therefore direct local infiltration was added". No indication what group these individuals were randomised to. "Fifty-one women who used TENS completed the questionnaire. Six responses were incoherent and nine women claimed the treatment was not painful and they did not need to turn the TENS on". No indication what group these individuals were randomised to.
Source of funding bias	Low risk	"We are indebted to Roy Sherlock of Neen Pain Management Systems (Old Pharmacy Yard, Church Street, Dereham, Norfolk NR16 1DJ) for lending us the TENS units".
Blinding (Participant)	High risk	"As it is impossible to conceal the use of TENS from the attendants a sham instrument was not used in group 3". Groups were: TENS group; local anaesthetic group; TENS and local anaesthetic group. There was no placebo group.
Blinding (Outcome Assessor)	Unclear risk	No details provided.

Sample Size	High risk	TENS (N = 24); local anaesthetic (N = 35); TENS and local anaesthetic (N = 29).

De Angelis 2003

Methods	Type of study: parallel RCT. Condition and number of participants randomised: participants undergoing office hysteroscopy, N = 142. Groups: TENS group (N = 71); control group (N = 71).
Participants	Demographics: N = 142, all female. TENS group, 47.9 ± 10 yrs; control group, 50 ± 10 yrs (mean ± SD). Setting: gynaecological endoscopy centre. Inclusion: outpatient hysteroscopy. Exclusion: not detailed. Withdrawals/dropouts: not detailed.
Interventions	Where applied: in hospital. Applied by: clinician. Waveform: symmetric rectangular biphasic waveform. Frequency: 100 pulses/s. Pulse duration: 100 µs. Pulse amplitude/Intensity: device set at basal level of stimulation, participant felt mild tickle in area between electrodes. Participant instructed when she felt pain to gently press plus switch once or several times. If feeling was unpleasant she could reduce amplitude by pressing minus switch until discomfort disappeared. Control Group: no TENS applied. Electrodes: 2, type and size not detailed, on abdomen in middle of line joining iliac spine and pubic tubercle. Duration and frequency of Rx: during procedure, 1 Rx. Device/manufacturer: Freelady TENS, Life Care, Tiberias, Israel. Adverse effects: nausea, shoulder pain and dizziness reported in both groups, not specifically linked to TENS.

Outcomes	Pain outcome: pain experienced during procedure assessed by VAS, after procedure. For TENS group, pain at basal level of stimulation was compared with pain felt after participant increased amplitude at least once. ITT/per protocol analysis: not detailed. Statistical analysis: no evaluable data for this review as unclear if SD data are presented. Significantly lower pain experienced during procedure by TENS group vs control group. Within TENS group, pain at basal level of stimulation vs after participants had increased amplitude at least once was significantly higher. Pelvic pain evaluated 5 mins after examination - significant reduction in TENS group vs control group.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"A randomised, computer-generated list was used to divide the subjects into two equal groups (A and B) of 71 patients".
Allocation concealment (selection bias)	Unclear risk	No details provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No details provided.
Source of funding bias	Unclear risk	No details provided.
Blinding (Participant)	High risk	It is impossible to adequately blind participants who receive electrical stimulation. No details provided. Groups were TENS group and no treatment control group. There was no placebo group. As the control group received no treatment, these participants could not be blinded.
Blinding (Outcome Assessor)	Unclear risk	No details provided.
Sample Size	Unclear risk	TENS (N =71); control (N =71).

de Sousa 2014

Methods	Type of study: RCT. Condition and number of participants randomised: 32 post-partum multiparous women were randomised. Groups: TENS group (N = 16); no-treatment control group (N = 16).
Participants	Demographics: N = 32, mean age 26.84 ± 5.14 years. Setting: hospital. Inclusion: aged over 18 years, without post-partum complications, exclusively breastfeeding, who experienced uterine contraction pain while breast-feeding. The women were also literate and able to understand the pain rating scales used. Exclusion: intolerance to the stimulus generated by TENS or complications requiring medical intervention, such as haemorrhage and infection. Withdrawals/dropouts: no withdrawals were reported.
Interventions	Where applied: in hospital. Applied by: not stated. Waveform: asymmetrical. Frequency: 100 Hz. Pulse duration: 75 µs. Pulse amplitude/Intensity: adjusted strong and tolerable sensation without muscular contraction. Control Group: no TENS administered. Electrodes: four 5 x 3 cm silicone and carbon rubber electrodes. Two electrodes were placed in parallel in the T10–L1 region; the other two were placed in the S2–S4 region. Duration and frequency of Rx: 40 mins. Device/manufacturer: KW Indústria Nacional de Tecnologia e Eletrônica, São Paulo, Brazil. Adverse effects: not detailed.

Outcomes	Pain outcome: numerical rating scale (NRS). ITT/per protocol analysis: statistical analysis done according to ITT. Statistical analysis: the Mann–Whitney U-test was used for comparison of pain between the groups before and after application of TENS, and the Wilcoxon rank sum test for intra group analysis. The results showed that the pain intensity of the uterine contraction during breastfeeding in the TENS group showed a reduction of 2.00 compared with 0.69 in the control group. In both groups, the reduction of the intra group pain was significant, as well as the inter group reduction. However, the assessment of the reduction of pain in the TENS group showed clinically relevant pain relief, which was not obtained in the control group. In addition, although the CG showed a significant reduction of pain, it was not clinically significant.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation spreadsheet used - no further detail available.
Allocation concealment (selection bias)	Unclear risk	No details provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No dropouts or withdrawals reported.
Source of funding bias	Unclear risk	No details.
Blinding (Participant)	High risk	Patients would be aware that a no treatment control was being used as comparison.
Blinding (Outcome Assessor)	High risk	No details provided of any attempts to blind assessor to group.
Sample Size	High risk	TENS (N = 16); control (N = 16).

Ekblom 1987

Methods	Type of study: Randomised, placebo-controlled, parallel design. Condition and number of participants randomised: acute pain from teeth or surrounding tissues, N = 40. Groups: 100 Hz Vibration Group (N = 8); placebo vibration group (N = 5); 2 Hz TENS group (N = 11); 100 Hz TENS group (N = 11); placebo TENS group (N = 5).
Participants	Demographics: N = 40, 20 to 58 yrs, 23 male/17 female. Setting: emergency clinic for dental and oral surgery. Inclusion: acute pain from teeth or surrounding tissues, or both. Exclusion: not detailed. Withdrawals/dropouts: not detailed.
Interventions	Where applied: in clinic. Applied by: presume by clinician. Waveform: monopolar square wave pulses. Frequency: high frequency (HF) group, 100 Hz; low frequency (LF) group, 71 Hz pulse train (duration 84 ms) delivered at 2 Hz. Pulse duration: 0.2 ms. Pulse amplitude/Intensity: HF set to produce a tingling sensation. LF set to produce prominent muscular contractions. Placebo TENS Group: electrodes applied to skin but no stimulation transmitted. Participants informed that some people might not experience the stimulation. Electrodes: two 3 cm x 3 cm conducting rubber, skin overlying painful area, anode distal. Duration and frequency of Rx: 30 min, 1 Rx. Device/manufacturer: not detailed. Adverse effects: not detailed.
Outcomes	Pain outcome: VAS and 5 level verbal scale for pain intensity, before and after Rx. Heat pain threshold recorded before, during and after Rx. ITT/per protocol analysis: not detailed. Statistical analysis: no active stimulation was superior to the others re number of participants reporting pain reduction; placebo significantly less effective than active stimulation. No significant effects of Rx on heat pain threshold.

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details provided.
Allocation concealment (selection bias)	Unclear risk	No details provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No details provided.
Source of funding bias	Unclear risk	No details provided.
Blinding (Participant)	Unclear risk	Participants informed that they may or may not experience a sensation associated with treatment.
Blinding (Outcome Assessor)	Unclear risk	No details provided.
Sample Size	High risk	100 Hz Vibration (N = 8); placebo vibration (N = 5); 2 Hz TENS (N = 11); 100Hz TENS (N = 11); placebo TENS (N = 5).

Gregorini 2010

Methods	Type of study: placebo-controlled, parallel RCT. Condition and number of participants randomised: postoperative period of cardiac surgery (N = 25). Groups: placebo group (N = 12); TENS group (N = 13).

Participants	Demographics: N = 25, 59.9 ± 10.3 yrs (mean ± ?SD), 18 male/7 female. Setting: inpatient. Inclusion: patients aged between 35 to 80 years who had undergone elective cardiac surgery via longitudinal median sternotomy. Exclusion: patients with pacemaker; pregnant women; cognitive or intellectual impairment; absence of pain in the postoperative period; sensitivity disorders; and patients undergoing any type of analgesia in the eight-hour period preceding the beginning of the protocol. Withdrawals/dropouts: not detailed.
Interventions	Where applied: in hospital. Applied by: participant. Waveform: not detailed. Frequency: 80 Hz. Pulse duration: 150 µs. Pulse amplitude/intensity: participants adjusted the intensity of stimulation at the point at which they felt a strong, although yet comfortable, prickling sensation, and were told to reduce the intensity if they felt uncomfortable. Electrodes: 2 pairs of adhesive electrodes, 10 x 3.5 cm. Placed one on each side of the surgical wound in the subclavian region. Duration and frequency of Rx: 4 hrs, 1 Rx. Device/manufacturer: TENS Device, KLD, Amparo, São Paulo, Brazil. Adverse effects: not detailed.
Outcomes	Pain outcome: numerical VAS for pain intensity at rest and with cough, before and after Rx. ITT/per protocol analysis: not detailed. Statistical analysis: data were analysed using means and SDs and non-parametric data was analysed as medians and quartiles. Categorical data was expressed as absolute numbers and relative (%) frequency). TENS significantly reduced pain in the postoperative period with an improvement of 40% at rest and 42.9% with cough compared with the placebo group. No statistical differences were found in the placebo group.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Unclear risk	Use of "sealed box" for randomisation but specific details not given.
Allocation concealment (selection bias)	Unclear risk	No details provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No details provided.
Source of funding bias	Low risk	No apparent funding bias.
Blinding (Participant)	Unclear risk	No details provided.
Blinding (Outcome Assessor)	Unclear risk	No details provided.
Sample Size	High risk	TENS (N =13); placebo (N = 12).

Hansson 1983

Methods	Type of study: randomised, placebo-controlled, parallel design. Condition and number of participants randomised: acute oro-facial pain (N = 62). Groups: HF TENS group (N = 22); LF TENS group (N = 20); placebo TENS group (N = 20).
Participants	Demographics: N = 62, 19 to 54 yrs, 26 male/36 female. Setting: emergency clinic for dental surgery. Inclusion: acute oro-facial pain. Exclusion: not detailed. Withdrawals/dropouts: not detailed.

Interventions	Where applied: in clinic. Applied by: presume by clinician. Waveform: monopolar square wave pulses. Frequency: HF Group, 100 Hz; LF Group, 2 Hz, 71 Hz pulse train with total duration of 84 ms delivered at 2 /sec. Pulse duration: 0.2 ms. Pulse amplitude/Intensity: HF, adjusted to 2 to 3 times perception threshold to produce a tingling non-painful sensation from the stimulated area. Output adjusted during TENS in order to maintain a constant tingling sensation. LF, adjusted to 3 to 5 times perception threshold which produced non-painful muscular contractions in the stimulated area. Placebo TENS Group: same as for other TENS groups except no batteries in units and participants told some people may not experience the stimulation. Electrodes: two, 2 cm x 3 cm conducting rubber, skin overlying painful area. Duration and frequency of Rx: 30 min, 1 Rx. Device/manufacturer: CEFAR SIII, Lund, Sweden. Adverse effects: most participants found the muscle twitches produced by LF TENS uncomfortable.
Outcomes	Pain outcome: 5-graded verbal scale for pain intensity before Rx. VAS for pain intensity before and after Rx. During Rx pain rated continuously using a graphic rating scale- consistent results obtained with both methods. Time until first report of subjective pain reduction and maximal pain reduction recorded. ITT/per protocol analysis: not detailed. Statistical analysis: HF TENS: 7/22 reported pain reduction > 50%, includes 2 who had total pain reduction. LF TENS: 9/20 reported pain reduction > 50%, includes 2 who had total pain reduction. Placebo TENS: 8/20 reported some degree of pain relief, includes 2 who had pain reduction > 50%. In the two active TENS groups, approx 80% reported a reduction of pain within less than 5 mins after onset of stimulation.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"The patients were assigned randomly to one of the three groups".

Allocation concealment (selection bias)	Unclear risk	No details provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No details provided.
Source of funding bias	Low risk	"This work has been supported by grants from Magnus Bergwalls Stiftelse". This is a research foundation.
Blinding (Participant)	High risk	It is impossible to adequately blind participants who receive electrical stimulation. "For practical reasons a double-blind technique could not be used." For the placebo TENS group: "Twenty patients received in all ways, except two, the same treatment as the two groups receiving TENS. One difference was that the TENS stimulators used were not equipped with batteries; and the other difference was that these patients were told that some people may not experience the stimulation". The exclusion criteria were not provided so we do not know if participants had to be TENS naïve.
Blinding (Outcome Assessor)	High risk	Study appears to be designed as single blind (i.e. participants blind).
Sample Size	High risk	HF TENS (N = 22); LF TENS (N = 20); placebo TENS (N =20).

Hruby 2006

Methods	Type of study: double blind, placebo-controlled, parallel RCT. Condition and number of participants randomised: participants undergoing flexible cystoscopy (N = 148). Groups: active TENS group (N = 48); placebo TENS group (N = 49); control group (N = 51).

Participants	Demographics: N = 148, 108 male/40 female. Active TENS Group, 62.23 yrs; placebo TENS Group, 61.53 yrs; control group, 60.98 yrs (? mean). Setting: office-based. Inclusion: flexible cystoscopy for surveillance of transitional cell carcinoma; voiding symptoms; hematuria, or stent removal. Exclusion: participants with a neobladder; cystoscopy with biopsy or with dilation of strictures; participants taking chronic analgesics or with pain syndromes; and participants who required post procedure catheterization. Withdrawals/dropouts: not detailed.
Interventions	Where applied: in hospital. Applied by: clinician. Waveform: symmetric rectangular biphasic. Frequency: 100 pulses/s. Pulse duration: 180 µs. Pulse amplitude/Intensity: at the initial settings, the participant typically felt a slight tickle at the site of the electrodes. The tickling sensation is greater than the sensory threshold but less than the pain threshold. The starting point for pulse amplitude was 20 mA. During flexible cystoscopy, participants were able to change the amplitude on the TENS device at will. Placebo TENS Group: unit identical to active unit but without any nerve stimulation. Control Group: no analgesia. Electrodes: 2, type and size not detailed, each electrode was placed halfway along an imaginary line drawn from the ASIS to pubis. Duration and frequency of Rx: duration not detailed, 1 Rx. Device/manufacturer: Prometheus Group, Dover, NH. Adverse effects: 2 participants in the Active TENS group could not tolerate the TENS unit as the amplitude was gradually increased to the starting point of 20 mA; 1 participant in the Placebo TENS group reported severe abdominal pain several hours after the procedure.
Outcomes	Pain outcome: VAS, 30 seconds and 1 min into the procedure, 5 mins after procedure finished. ITT/per protocol analysis: not detailed. Statistical analysis: no evaluable data for this review as unclear if SD data are presented. No significant changes in VAS between groups at each of the 3 time points.
Notes	Abbreviation: ASIS-anterior superior iliac spine

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"A total of 148 patients were prospectively randomised into one of three groups."
Allocation concealment (selection bias)	Unclear risk	No details provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No details provided.
Source of funding bias	Unclear risk	No details provided.
Blinding (Participant)	High risk	It is impossible to adequately blind participants who receive electrical stimulation. Text says it was a double-blind study but no details provided - assume they intended to blind the participants. The placebo TENS group was described as "a control group with a placebo TENS unit (unit identical to active unit but without any nerve stimulation)". The inclusion/exclusion criteria did not state that participants had to be TENS naïve. Control group received no treatment so these participants could not be blinded.
Blinding (Outcome Assessor)	Unclear risk	Text states that it was a double-blind study but no details provided if the outcome assessor was blinded.
Sample Size	High risk	TENS (N = 48); placebo TENS (N = 49); control (N = 51).

Keskin 2012

Methods	Type of study: prospective RCT. Condition and number of participants randomised: 88 pregnant women suffering from LBP with no previous history of LBP or lumbar pathology. Groups: active TENS (N = 22); exercise (N = 22); acetaminophen (N = 22); no-Rx control (N = 22).

Participants	Demographics: N = 88, all female. Age: TENS group 29.1yrs ± 5.0; exercise group 30.7 ±4.3; acetaminophen 29.7 ± 4.2, control 29.2 ± 4.0. Setting: outpatient antenatal care unit, Turkey. Inclusion: uncomplicated pregnancy with LBP. Exclusion: history of Lumbar pathology pre-pregnancy or pathology detected during physical examination; pain due to non-musculoskeletal factors; declined to take part. Withdrawals/dropouts: TENS (N = 2); exercise (N = 3); acetaminophen (N = 3); control (N = 1).
Interventions	Where applied: on the painful lumbar region. Applied by: not stated. Waveform: not stated. Frequency: 120 Hz Pulse duration: 100 µs Pulse amplitude/Intensity: adjusted to produce a tingling sensation approx 2 to 3 times above the sensory threshold. Placebo TENS Group: N/A. Exercise group: completed a home exercise programme set by a physical therapist and including pelvic tilting, stretching for the lower extremity and mild isometric abdominal contractions x 10 of each per session, twice daily for 3 weeks. Acetaminophen group: one 500 mg paracetamol tablet 2 x daily for 3 weeks. Control Group: no Rx administered Electrodes: 4 surface electrodes 5 cm^2 Duration and frequency of Rx: duration not stated. 2 sessions weekly for 3 weeks. Device/manufacturer: Intelect TENS, Chattanooga Medical Supplies Inc., Taiwan). Adverse effects: discomfort using TENS and gastric effect with medication.

Outcomes	Pain outcome: VAS scores and Roland-Morris Disability Questionnaire (RMDQ). ITT/per protocol analysis: not stated. Statistical analysis: median pre-treatment VAS scores differed significantly between groups (P = 0.004; Kruskal-Wallis test). These scores were significantly higher in the TENS group (P = 0.002; post-hoc Mann-Whitney) and acetaminophen groups (P = 0.009). Median pre-treatment RMDQ scores were similar across all groups. At the end of the trial pain intensity had increased in control group (57%), and decreased in exercise group(95%). In acetaminophen and TENS groups 100% had a decrease in pain. All treatment groups showed a significant improvement in both VAS and RMDQ scores (P < 0.0001) using the Wilcoxon test. Differences in pre and post-Rx VAS and RMDQ scores were significant in all treatment groups using Kruskal Wallis (VAS; P < 0.001; RMDQ, P < 0.001). This difference was caused by markedly higher scores in the TENS group (P < 0.001 for both comparisons; Mann-Whitney test).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation using sealed envelopes.
Allocation concealment (selection bias)	Low risk	Use of sealed envelopes.
Incomplete outcome data (attrition bias) All outcomes	High risk	Withdrawals and dropouts were reported but no information was included as to how the data was dealt with.
Source of funding bias	Low risk	No apparent funding bias.
Blinding (Participant)	High risk	No TENS placebo group so not possible to blind participants as to which group they were allocated to.
Blinding (Outcome Assessor)	Unclear risk	No details provided.

Sample Size	High risk	TENS (N = 22); exercise (N = 22); acetaminophen (N = 22); control (N = 22).

Kim 2012

Methods	Type of study: single-blind, placebo-controlled RCT. Condition and number of participants randomised: 100 patients undergoing plastic surgery. Groups: 2 groups: active TENS (N = 50); placebo TENS (N = 50).
Participants	Demographics: N = 100; TENS group 21 male/29 female; age 48.2 yrs ± 13.0; placebo group 19 male/31 female; age 51.2 yrs ± 11.7. Setting: Hospital outpatient, Korea. Inclusion: patients undergoing plastic surgery. Exclusion: concomitant sedative or analgesic medication and neurological disease, or potentially serious internal diseases (ASA physical status > 3). Withdrawals/dropouts: none.
Interventions	Where applied: radial side of the dominant forearm - cathode over cephalic vein 1cm proximal to radial styloid process; anode 3 cm away proximal to cathode. Applied by: anaesthesiologist. Waveform: not stated. Frequency: 80Hz. Pulse duration: 200 μs. Pulse amplitude/Intensity: maximum tolerable level below pain threshold without noticeable muscle contraction. Placebo TENS Group: TENS device without current output but with power indicator light illuminated. Control Group: none. Electrodes: 2 TensCare electrodes, 5 cm^2 Duration and frequency of Rx: 20 minutes immediately prior to venous cannulation. 1 single Rx. Device/manufacturer: select TENS unit (Empi, St Paul, Minnesota). Adverse effects: itching and erythema reported.

Outcomes	Pain outcome: pain incidence; VAS scores. ITT/per protocol analysis: not stated. Statistical analysis: pain incidence was similar between the 2 groups (P > 0.05); 45 (90%) in the TENS group experienced pain against 50 (100%) in the placebo group using the X^2 test or Fisher exact test. Pain intensity (VAS) in TENS group was significantly lower than placebo, with TENS VAS scores 1.9 ± 1.2 (P < 0.01) against placebo VAS scores 4.8 ± 1.5 using Wlcoxon rank sum test with continuity correction.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details provided.
Allocation concealment (selection bias)	Unclear risk	No details provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not stated but no withdrawals/dropouts reported.
Source of funding bias	Low risk	No apparent funding bias.
Blinding (Participant)	Low risk	Placebo tens applied to blind participants.
Blinding (Outcome Assessor)	Low risk	"study-blinded anaesthesiologist".
Sample Size	Unclear risk	TENS (N = 50); placebo TENS (N = 50).

Limoges 2004

Methods	Type of study: double blind, placebo-controlled, parallel RCT. Condition and number of participants randomised: participants undergoing screening flexible sigmoidoscopy (N = 90). Groups: TENS group (N = 30); placebo TENS group (N = 30); control group (N = 30).
Participants	Demographics: N = 90, 51 male/39 female. TENS group, 57.18 ± 7.787 yrs; placebo TENS group, 55.97 ± 5.411 yrs; control group, 58.6 ± 9.073 yrs (mean ± SD). Setting: screening flexible sigmoidoscopy (SFS) speciality clinic. Inclusion: over 50 yrs; presenting for screening flexible sigmoidoscopy. Exclusion: cardiac pacemakers; automated implanted cardiac defibrillators; pre procedural skin irritation at electrode placement site; pre procedural sedation or analgesia. Withdrawals/dropouts: not detailed.
Interventions	Where applied: in clinic. Applied by: clinician. Waveform: biphasic waveform and asymmetric pulse pattern. Frequency: 100 Hz. Pulse duration: 190 μs. Pulse amplitude/Intensity: 30 mA, setting chosen after progressively increasing amplitude and testing tolerability of each level on volunteers. Same intensity used for all participants. Placebo TENS Group: unit same as active group, attached to participant but not turned on. All participants told they may or may not feel tingling sensation at electrode site. Control Group: received only verbal encouragement. Electrodes: 4 self-adhesive, 2 x 5 inch rectangular, 2 on left upper and lower quadrants of abdomen and 2 parallel to spinal cord at L1-S3 level. Duration and frequency of Rx: varied 5 to 15 mins, 1 Rx. Device/manufacturer: Empi EPIX VT TENS. Adverse effects: 29 participants in TENS group and 6 participants in placebo TENS group reported pain/burning/tingling at electrode site.

Outcomes	Pain outcome: pain experienced during procedure assessed by a NRS of 1 to 5 for pain intensity after procedure finished. ITT/per protocol analysis: not detailed. Statistical analysis: no significant difference between groups for pain experienced during the procedure.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Author response: "Randomization was done by drawing numbers out of a hat. We picked a number out of the hat after the patient arrived and consented to participate".
Allocation concealment (selection bias)	High risk	Author response: "Randomization was done by drawing numbers out of a hat. We picked a number out of the hat after the patient arrived and consented to participate".
Incomplete outcome data (attrition bias) All outcomes	Low risk	"Ninety subjects were enrolled and completed the study".
Source of funding bias	Low risk	"Funding for this study was provided by the Innovative Pilot Project Grant Program at the University of California Davis Medical Center. The TENS unit was provided by EMPI, Inc."
Blinding (Participant)	High risk	It is impossible to adequately blind participants who receive electrical stimulation. "Subjects in the sham TENS group were connected to the TENS unit exactly the same as subjects in the TENS group. The research assistant manipulated the programming buttons on the TENS unit exactly as with the TENS group, but without actually turning the TENS units on beforehand. This step was performed in an effort to maintain blinding of both the endoscopist and subject. Subjects in the control group received only verbal encouragement." The inclusion/exclusion criteria did not state that participants had to be TENS naïve. Control group received no active treatment so these participants could not be blinded.

Blinding (Outcome Assessor)	High risk	Author response regarding the placebo TENS group: "the TENS unit was attached to the subject but never turned on by the RA (I and the subject were blinded to this)". "My RA administered the questionnaires".
Sample Size	High risk	TENS (N = 30); placebo TENS (N = 30); control (N = 30).

Liu 1985

Methods	Type of study: randomised, double blind, controlled, parallel design. Condition and number of participants randomised: post thoracotomy, 30. Groups: TENS group, 15; control group, 15.
Participants	Demographics: N = 30, 18 to 72 yrs, 22 male/8 female. TENS group, 51.73 yrs; control group, 52.73 yrs (mean). Setting: hospital. Inclusion: post thoracotomy. Exclusion: participants who had cardiac surgery. Withdrawals/dropouts: not detailed.
Interventions	Where applied: in hospital. Applied by: clinician. Waveform: not detailed. Frequency: mean was 75.75 Hz for TENS Group, 51 Hz for Control Group. Pulse duration: 0.1 ms. Pulse amplitude/Intensity: set at a subjective level of comfort, not adjusted during treatment, mean pulse amplitude was 7.33 mA for TENS Group. Control Group: TENS applied at fixed pulse amplitude of 2.5 mA. All participants told how TENS worked to control pain and what to expect from TENS after surgery. Electrodes: 2 carbon rubber and gel, size not detailed, placed on most painful area along incision wound. Duration and frequency of Rx: 20 min, daily treatment from 1st post-op day until pain disappeared or participant discharged or Rx rejected by participant. Device/manufacturer: HRS Neuro-Pulse Model HME-12. Adverse effects: not detailed.

Outcomes	Pain outcome: overall impression with TENS rated using 4 categories, after TENS discontinued. Pain rated using a 0 to 10 scale before and after each TENS Rx. Recorded daily (for 10 days) until pain disappeared, or patient discharged or treatment rejected by the patient. ITT/per protocol analysis: not detailed. Statistical analysis: significant alleviation of pain after TENS every day in the TENS group. No significant change in the Control group except on days 4 and 6. Significant difference between groups for post TENS pain scores on days 2/5/6/7/8.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Author response: "The patients were enrolled to the study consecutively before the surgery, divided into experimental and control groups alternatively". "Males and females were counted separately".
Allocation concealment (selection bias)	High risk	See under randomisation.
Incomplete outcome data (attrition bias) All outcomes	High risk	Table 2 gives pain scores on days 1 to 10. The table details the number of participants from whom data were recorded on each day - shows a decline as the days progress. The text says that stimulation was given everyday from first postop day until pain disappeared, or the participant was discharged or the treatment was rejected by the participant. Table shows data collected for all participants (N = 15/group) for days 1 and 2 only. Figure 1 shows number of participants in each group that continued with TENS for each postop day. Specific reasons for each participant not recording pain scores was not given.
Source of funding bias	Unclear risk	No funding source detailed.
Blinding (Participant)	High risk	It is impossible to adequately blind participants who receive electrical stimulation. Author response: "The study design was double blinded. The patients and I (the evaluator) were blinded. All patients were explained how TENS worked to control pain and what the patient should expect from TENS after operation". The control group received low intensity TENS. The exclusion criteria were not provided so we do not know if participants had to be TENS naïve.

Blinding (Outcome Assessor)	Low risk	Author response: "The study design was double blinded. The patients and I (the evaluator) were blinded".
Sample Size	High risk	TENS (N = 15); control (N = 15)

Olsén 2007

Methods	Type of study: parallel RCT. Condition and number of participants randomised: newly delivered women with pain from postpartum uterine contractions (N = 21). Groups: HI TENS group (N = 13); LI TENS group (N = 8).
Participants	Demographics: N = 21, all female, 31 yrs (mean). HI TENS Group, 31 ± 4.2 yrs; LI TENS Group, 31 ± 4.8 yrs (mean ± SD). Setting: Department of Obstetrics and Gynecology. Inclusion: newly delivered healthy women; well integrated in the Swedish language with uncomplicated vaginal delivery; painful postpartum uterine contractions that required pain relief. Exclusion: systemic disorders; abnormal pregnancy; operative delivery; other treatments for the pain should not have been initiated. Withdrawals/dropouts: 1 in HI TENS group dropped out due to discomfort of stimulation.
Interventions	Where applied: in hospital. Applied by: clinician. Waveform: not detailed. Frequency: 80 Hz. Pulse duration: 0.2 ms. Pulse amplitude/Intensity: HI, set at 50 mA. LI, set at just above the sensory threshold (10 to 15 mA). Electrodes: 2 carbon rubber and gel, 53 x 34 mm, placed on the lower part of the abdomen, bilaterally over the uterus. Duration and frequency of Rx: 1 minute, 1 Rx repeated twice if no effect occurred. Device/manufacturer: Cefar AB, Lund, Sweden. Adverse effects: no adverse effects except for discomfort during stimulation were recorded.

Outcomes	Pain outcome: measurement of discomfort on a 5-point verbal scale, before and after Rx. VAS for present pain intensity, before and after Rx. Discomfort of Rx recorded on a 5-point verbal scale. ITT/per protocol analysis: not detailed. Statistical analysis: median decrease in VAS pain ratings before and after treatment was larger in the HI TENS group than in the LI TENS group. Post Rx, women in the HI TENS group had less pain from the uterine contractions than the women in the LI TENS group. HI TENS group experienced significantly less discomfort from uterine contractions after treatment compared with the LI TENS group. Discomfort from TENS itself was significantly greater in HI group than in LI group.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"After informed written consent, the women were randomised to either high-intensity (HI) or low intensity (LI) high-frequency (80 Hz) TENS. The allocation sequence was determined before the study by a research assistant using a computer generated random table."
Allocation concealment (selection bias)	Low risk	"Groups were coded and the allocation transferred to a series of pre-sealed opaque envelopes."
Incomplete outcome data (attrition bias) All outcomes	Low risk	"One patient in the HI TENS group dropped out from the study immediately after commencing TENS treatment because of discomfort of the stimulation."
Source of funding bias	Unclear risk	No details provided.
Blinding (Participant)	Low risk	Study described as single-blind. Groups were high-intensity (HI) or low intensity (LI) high-frequency (80 Hz) TENS. There was no placebo TENS group. "Before treatment the women were informed that they might experience pain or discomfort from the electrical stimulation." Author response: "it was the participants who were blinded to the treatment". Author response: "The patients had no previous experience of TENS".

Blinding (Outcome Assessor)	High risk	Study was designed as single blind.
Sample Size	High risk	HI TENS (N = 13); LI TENS (N = 8).

Oncel 2002

Methods	Type of study: randomised, placebo-controlled, parallel design. Condition and number of participants randomised: minor rib fractures, 100. Groups: NSAID group, 25; TENS group, 25; NSAID and placebo TENS group, 25; placebo tablets group, 25.
Participants	Demographics: N = 100, 11 to 81 yrs, 41 female/59 male, 40 ± 16 yrs (mean ± SD). NSAID group, 35 ± 19 yrs; TENS group, 44 ± 15 yrs; NSAID and placebo TENS group, 41 ± 14 yrs; Placebo tablets group, 40 ± 16 yrs. Setting: hospital emergency service. Inclusion: minor rib fractures. Exclusion: 1st or 2nd rib fracture; more than 3 rib fractures or flail chest; requiring hospitalisation for cranial or abdominal trauma; patient refusal; undergoing any kind of surgery (including tube thoracostomy); cardiac or psychiatric illness; < 10 yrs; history of gastrointestinal bleeding or ulcer or other contraindications for NSAIDS; being pregnant. Withdrawals/dropouts: 8 participants were excluded because of complications and they were replaced. 7 had respiratory distress during the hospitalisation period; 3 had haemothorax and 4 had pneumothorax. All were treated with tube thoracostomy. Right haemothorax was diagnosed on the eighth patient the day after he had been discharged. He was re-hospitalised and underwent a tube thoracostomy procedure.

Interventions	Where applied: in hospital and at home. Applied by: clinician in hospital and by participant at home. Waveform: not detailed. Frequency: 80 Hz. Pulse duration: 50 µs. Pulse amplitude/Intensity: participants asked to turn up to the highest level that did not make them uncomfortable. Placebo TENS Group: TENS unit without batteries and no sign on unit that showed it was on. Participants in the TENS and NSAID and Inactive TENS group told they might or might not feel a sensation of tingling. Electrodes: 2 or 4 carbon rubber electrodes with adhesive gel, 3.4 x 4.2 cm, placed on both sides of fractures along lines of intercostal nerves. Duration and frequency of Rx: 30 mins, 6 Rxs. 2 treatments in hospital: within 2 hrs after admission and 12 hrs later. On discharge, home TENS twice a day for 2 days. Device/manufacturer: dual channel TENS, Biotens Inc Istanbul, Turkey. Adverse effects: no complications seen during trial.
Outcomes	Pain outcome: pain assessed by 0 to 10 scoring system. Recorded when hospitalised -pre Rx, next day before they were discharged (after 2 phases of Rx) and third day after therapy had ended. ITT/per protocol analysis: no. Statistical analysis: no evaluable data for this review as mixed age population (adults and children). Day 0: no significant difference between groups. Day 1: pain in placebo group significantly higher than other groups. Pain in TENS group significantly less than NSAID and NSAID and inactive TENS groups. Day 3: pain in TENS group significantly less than all other groups and no significant difference between these 3 groups. All participants except the placebo group had significantly less pain on days 1 and 3 than day 0. In the placebo group, pain was significantly less on day 3 than 0 but no difference between pain levels on day 0 and 1.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"One hundred consecutive patients admitted to Kartal Education and Research Hospital Emergency Service, were randomized into four groups". Author response: "A computerized randomization protocol had been received prior to the beginning of the trial, and the randomization of the patients was done accordingly".

Allocation concealment (selection bias)	Unclear risk	No details provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	"Eight patients were excluded because of complications and they were replaced. Seven had respiratory distress during the hospitalisation period; three had haemothorax and four had pneumothorax. All were treated with tube thoracostomy. Right haemothorax was diagnosed on the eighth patient the day after he had been discharged. He was re-hospitalized and underwent a tube thoracostomy procedure". No indication which group these individuals were randomised to.
Source of funding bias	Unclear risk	No details provided.
Blinding (Participant)	High risk	It is impossible to adequately blind participants who receive electrical stimulation. "These patients were told that they might or might not feel a sensation of tingling, and this instruction was carefully standardized. The same blinded nurses performed two phases of TENS therapy during the hospitalisation period and instructed the patients how to use the machine at home. These nurses were told that every patient would be treated with active TENS units and that they were not to know about the content of the trial. Inactive TENS units were out of battery and there were no signs on the machines that showed they were 'on'.' Author response ‘As mentioned in the paper, the patients were completely unaware that the cases in the control group would not feel a sensation, and both the patients and the nurses assumed that all cases would have a TENS treatment." The inclusion/exclusion criteria did not state that participants had to be TENS naïve.
Blinding (Outcome Assessor)	High risk	Author response: "The pain scores were recorded by one of the authors (HY) or by educated nurses. The nurses were blinded to the randomisation but the author was not". Not all of the outcome assessors were blind to group allocation.
Sample Size	High risk	NSAID (N = 25); TENS (N = 25); NSAID and placebo TENS (N = 25); placebo tablets (N = 25).

Ordog 1987

Methods	Type of study: randomised, double blind, placebo-controlled, parallel design. Condition and number of participants randomised: acute trauma outpatients, 100. Groups: functioning TENS group (N = 25); placebo TENS group (N = 25); functioning TENS plus Tylenol (N = 25); placebo TENS plus Tylenol (N = 25).

Participants	Demographics: N = 100, age/gender not detailed. Setting: outpatients. Inclusion: acute trauma outpatients. Exclusion: < 21 yrs; hx cardiac disease or pacemaker; insufficient aptitude or personality for operation of apparatus; allergies to acetaminophen or codeine; pregnancy. Withdrawals/dropouts: not detailed.
Interventions	Where applied: at home by participant. Applied by: participant. Waveform: not detailed. Frequency: not detailed. Pulse duration: not detailed. Pulse amplitude/Intensity: instructed to adjust energy knob to level at which pain disappeared or until they felt a mild electric shock from the unit. Placebo TENS group: unit appeared like active but no electrical current transmitted to the skin. It produced the slight hum and vibration that active unit produced. Participants were not told that the functioning units could produce a mild electrical shock by turning up the unit. Electrodes: 2 metal electrodes and a disposable sterile skin pad, size not detailed. Applied over area of injury or as close to it as practical. Duration and frequency of Rx: could be worn at all times or as often as required for pain control. Device/manufacturer: disposable TENS-PAC unit measures ½ x 3 x 4 inches. Dow Corning, Arlington, Tennessee. Adverse effects: no complications and no side effects except a mild tingling sensation at higher output levels, 20% of participants reported this effect.
Outcomes	Pain outcome: 11 point VAS for pain intensity, administered pre Rx, after two days of Rx, and a month after initial injury. ITT/per protocol analysis: not detailed. Statistical analysis: statistically significant reduction in pain severity in functioning TENS vs placebo group at day 2, not at 1 month. No significant difference between functioning TENS unit and Tylenol group when either the subjective levels of pain versus time or pre-Rx and post-Rx pain levels at 2 days and 1 month were compared. Mean length of use of TENS in all groups was 3 days versus a mean of 5 days for the oral analgesics in the 2 Tylenol groups.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"One hundred consecutive consenting acute trauma outpatients seen by the researcher were randomly assigned to four pain treatment groups. Randomization of the TENS-PAC units was achieved by mixing the two boxes of 50 functioning and 50 placebo units together. A decoding process was released when all of the TENS-PAC units were returned after the trial was completed. All of the units were returned to the researcher following the trial to determine which units the patient had and also to assure their function".
Allocation concealment (selection bias)	Low risk	"A decoding process was released when all of the TENS-PAC units were returned after the trial was completed. All of the units were returned to the researcher following the trial to determine which units the patient had and also to assure their function".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No details provided.
Source of funding bias	Unclear risk	No details provided.
Blinding (Participant)	High risk	It is impossible to adequately blind participants who receive electrical stimulation. "In the study, 50% of the patients received a functioning TENS-PAC, and the other 50% received a 'placebo' unit, which appeared and operated in all ways similar to the functioning unit except that no electrical current was transmitted to the skin. This 'placebo' unit was originally a functioning TENS-PAC, but in this unit, an internal wire that supplied the electrical current to the skin was cut. The TENS-PAC produces a slight hum and vibration that the 'placebo' unit also produced. The 'placebo' units were prepared by an independent source, and neither the researcher nor the patient was able to identify which unit was given until the trial was completed. The possibility that the patients might have figured out whether they had the placebo units seems remote, as patients were not told that the functioning units can produce a mild electrical shock by turning up the unit. As none of the patients had used TENS previously, it is unlikely that they would have known that an electrical shock could be produced only by the functioning units".
Blinding (Outcome Assessor)	Low risk	"The 'placebo' units were prepared by an independent source, and neither the researcher nor the patient was able to identify which unit was given until the study was completed".
Sample Size	High risk	TENS (N = 25); placebo TENS (N = 25); TENS plus Tylenol (N = 25); placebo TENS plus Tylenol (N = 25).

Pitangui 2012

Methods	Type of study: RCT. Condition and number of participants randomised: 40 primiparous women who had experienced spontaneous vaginal delivery were randomised. Groups: N = 40, all female. HF TENS (N = 20), no-Rx control (N = 20).
Participants	Demographics: all female (N = 40). Age 18 to 31 years (median 20.5 years) with no statistical differences in age, education or colour between groups. Setting: hospital maternity ward, Brazil. Inclusion: low-risk, primiparous pregnancy, older than 18 years of age, literate and understanding of Portuguese language,aware of time and space, post-vaginal spontaneous delivery, experienced an episiotomy with stitches, presenting with pain in the episiotomy area, absence of any genitourinary pathology. Exclusion: contraindications to TENS, puerperal complications, previous exposure to TENS, morbid obesity, instrumental delivery (e.g. use of forceps). Withdrawals/dropouts: none reported
Interventions	Where applied: parallel to the episiotomy site. Applied by: not stated. Waveform: biphasic, asymmetrical. Frequency: 100 Hz. Pulse duration: 75 µs. Pulse amplitude/Intensity: strong numbing sensation but no muscle contractions. Placebo TENS Group: N/A. Control Group: no intervention received. Electrodes: 4 silicone-carbon electrodes 5.5 cm x 3 cm. Duration and frequency of Rx: 60 mins, single-session. Device/manufacturer: Tens KW Compact, KW Industria Nacional Tecnologia e Electronica, San Paulo, Brazil. Adverse effects: none reported.

Outcomes	Pain outcome: numerical rating scale (NRS) 11 point (0 to 10) carried out at the beginning of the trial (1st evaluation), at 60 mins (2nd evaluation) and 120 mins (3rd evaluation). Pain was measured during resting, sitting and ambulation at each evaluation. McGill pain questionnaire used to obtain pain descriptors. ITT/per protocol analysis: not stated. Statistical analysis: data for the groups were compared using the unpaired t-test and intragroup differences analysed using a repeated-measures ANOVA with a post-hoc Tukey test. Mann-Whitney test was used for analysing continuous variables such as neonatal or obstetric data and Pearson's Chi^2 test or Fisher's exact test was used for categorical variables. Groups presented similar pain scores at baseline. The application of TENS significantly reduced pain intensity in resting, sitting and ambulating ($P > 0.001$) immediately after TENS and 60 mins later compared with the control group. Comparing the 1st evaluation with the 3rd there was only a significant difference in the TENS group. On the McGill pain questionnaire at baseline there were no significant differences. After TENS there was a decrease in NWC ($P > 0.001$) in the TENS group and PRI for the sensory, affective, evaluative, miscellaneous and total categories ($P > 0.001$). The TENS group also showed a reduction in the NWC. The control group did not show a similar alteration in the PRI or NWC.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated block randomisation method.
Allocation concealment (selection bias)	Unclear risk	No details provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No withdrawals reported.
Source of funding bias	Low risk	No apparent funding bias.
Blinding (Participant)	High risk	No blinding.

Blinding (Outcome Assessor)	Unclear risk	No details provided.
Sample Size	High risk	HF TENS (N = 20); control (N = 20).

Roche 1985

Methods	Type of study: placebo-controlled, parallel RCT. Condition and number of participants randomised: haemophiliac participants (N = 36). Groups: active TENS group (N = 28); placebo TENS group (N = 8).
Participants	Demographics: N = 36, 35 ± 12 yrs (mean ± ?SD), gender not detailed. Setting: specialised outpatient clinic at hospital. Inclusion: haemophiliac participants suffering from unilateral haemorrhage into a joint. Exclusion: participants attending for dental care or for treatment to haemorrhage in the region of the face, abdomen or cranium. Withdrawals/dropouts: none.

Interventions	Where applied: in hospital. Applied by: clinician. Waveform: square wave pulses. Frequency: internal pulse frequency of trains was 100 Hz and repetition rate of trains was 5 Hz. In initial stage of trial, trains of pulses rather than continuous TENS reported by participants as being more tolerable, consequently this form of TENS was adopted throughout the trial. Pulse duration: 1 ms pulses, 100 ms train duration. Pulse amplitude/Intensity: raised to a level of definite but comfortable perception with no presence of muscle activation. Placebo TENS Group: as for active group but no stimulation applied. Participants informed that a very high frequency of stimulation was being used which they might or might not feel. Electrodes: 2 or 4, flexible carbon electrodes layered with electrode gel, 2x2 cm, over the major sensory nerves supplying affected area or as close as possible to area of bleed. Duration and frequency of Rx: 25 min, 1 Rx. Device/manufacturer: Digitimer Ltd, Model DS2. Adverse effects: none.
Outcomes	Pain outcome: MPQ (PRI, PPI, group scores for each category) before and after Rx for current pain. ITT/per protocol analysis: no. Statistical analysis: over 71% of participants receiving TENS reported changes in MPQ scores which represented pain relief > 50%. Only 2 placebo participants (25%) reported this amount of pain relief. The difference between participants reporting at least 50% relief was significantly different between groups using PRI and PPI. 9 TENS participants reported > 80% pain relief, 4 of these reported 100% pain relief. 2 placebo participants reported > 50% pain relief, neither reported 100%. Pre Rx PRI data divided into mild-medium (PRI score of 0 to 25) and medium-severe (PRI score of 26 to 50) based on highest recorded PRI score of 50. For TENS participants, difference between these 2 groups of scores was not significant.
Notes	Abbreviation: MPQ- McGill pain questionnaire; PPI- present pain index; PRI- pain rating index.

Risk of bias

Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Unclear risk	"The subjects were randomly assigned to one of two groups".
Allocation concealment (selection bias)	Unclear risk	No details provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Trial author responded "no" to question "Were there any dropouts/withdrawals?".
Source of funding bias	Low risk	"The research was supported by a grant from The British Medical Research Council (Grant No. 0979/723/N) awarded to K. Gijsbers".
Blinding (Participant)	High risk	It is impossible to adequately blind participants who receive electrical stimulation. Author response "The study was single blind. The same researcher took measures and applied TENS. Specific TENS settings were screened from participants". "The same apparatus and electrodes were used for the placebo group, but no stimulation was applied. These subjects were informed that a very high frequency of stimulation was being used which they might or might not feel". The exclusion criteria were not provided so we do not know if participants had to be TENS naïve.
Blinding (Outcome Assessor)	High risk	Author response: "The study was single blind. The same researcher took measures and applied TENS. Specific TENS settings were screened from participants".
Sample Size	High risk	N = 28 TENS; N = 8 placebo TENS

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Akhmadeeva 2010	RCT but chronic pain.
Andersen 2009a	RCT but not a standard TENS device.

Study	Reason for exclusion
Andersen 2009b	RCT but not a standard TENS device.
Barbarisi 2010	RCT but chronic pain.
Barker 2006	RCT but intensity too low.
Baskurt 2006	RCT but chronic pain.
Bertalanffy 2005	RCT but intensity too low.
Celik 2013	RCT but chronic pain.
Chee 1986	RCT but microcurrent used.
Coletta 1988	RCT but intensity too low.
Doğu 2009	RCT but chronic pain.
Durmus 2009	RCT but chronic pain.
Ekblom 1985	RCT but TENS delivered at distal acupuncture point.
Eyigor 2012	RCT but chronic pain.
Fengler 2007	RCT but microcurrent used/chronic condition.
Gemmell 2011	RCT but 'latent' myofascial trigger points used on otherwise asymptomatic adults.
Gupta 2002	RCT but concurrent 'rescue' medication given.
Gül 2009	RCT but chronic pain.
Herman 1994	RCT but not a standard TENS device.
Izadpanah 2005	RCT but needle electrode used/not standard TENS device.
Korkmaz 2010	RCT but chronic pain.
Kumar 2014	RCT but chronic pain.
Lang 2007	RCT but intensity too low.
Lee 1997	RCT but not a standard TENS device.
Lee 2012	RCT but concurrent pain medication.
Leo 1986	RCT but mixed acute and chronic pain.
Mora 2006	RCT but intensity too low.

Study	Reason for exclusion
Murina 2008	RCT but chronic pain.
Myśliwiec 2011	RCT but chronic pain.
Peng-fei 2011	This is a letter a letter in response to study by Korkmaz et al which was excluded in first screening because chronic pain.
Pope 1994	RCT but not acute pain.
Reichstein 2005	RCT but H-wave device used.
Rodarti 2012	Duplicate of another study. Pitangui 2012
Rodríguez-Fernández 2011	Use of 'latent' myofascial trigger points on otherwise asymptomatic individuals.
Sahin 2011	RCT but chronic pain.
Solomon 1985	RCT but not a standard TENS device.
Stratton 2009	RCT but chronic pain.
Sunshine 1996	RCT but APS therapy used/chronic condition.
Taskaynatan 2007	RCT but IFT used.
Tsai 2010	RCT but chronic pain.
Tulgar 1991a	RCT but chronic conditions included.
Tulgar 1991b	RCT but chronic conditions included.
Wang 2009	RCT but chronic pain.

Characteristics of studies awaiting assessment [ordered by study ID]

Cambiaghi 2013

Methods	Type of study: RCT. Condition and number of participants randomised: 40 females submitted for office diagnostic hysteroscopy and endometrial biopsy. Groups: active TENS with Tanyx and no-treatment control.

Participants	Demographics: N = 40, female participants. Age not available. Setting: Brazil. Inclusion: information not available. Exclusion: information not available. Withdrawals/dropouts: information not available.
Interventions	Where applied: infra-umbilical area. Applied by: information not available. Waveform: information not available. Frequency: information not available. Pulse duration: information not available. Pulse amplitude/Intensity: information not available. Electrodes: information not available. Duration and frequency of Rx: information not available. Device/manufacturer: information not available. Adverse effects: information not available.
Outcomes	Pain outcome: VAS for pain intensity, during Rx. ITT/per protocol analysis: not detailed. Statistical analysis: statistically significant reduction in VAS scores during both procedures in the TENS group.
Notes	

de Paiva Tosato 2007

Methods	Type of study: parallel RCT. Condition and number of participants randomised: temporomandibular pain (? acute pain), 20. Groups: massage group, 10; TENS group, 10.

Participants	Demographics: N = 20, 22 to 46 yrs, 31.75 ± 8.71 (mean ± SD), all female. Setting: not detailed. Inclusion: signs and symptoms of temporomandibular disorders; females. Exclusion: no temporomandibular pain; males; dental problems; systemic disease; patients having other treatment (dental treatment, physiotherapy, medication). Withdrawals/dropouts: not detailed.
Interventions	Where applied: not detailed. Applied by: not detailed. Waveform: not detailed. Frequency: not detailed. Pulse duration: not detailed. Pulse amplitude/Intensity: participants told the sensation should be pleasant and were told to report whenever the intensity of the current decreased. Electrodes: not detailed. Placed over masseter muscle, anterior portion of temporal muscle. Duration and frequency of Rx: 30 min, 1 Rx. Device/manufacturer: Quark. Adverse effects: not detailed.
Outcomes	Pain outcome: VAS for pain intensity, before and after Rx. ITT/per protocol analysis: not detailed. Statistical analysis: statistically significant reduction in VAS scores post Rx in both groups.
Notes	

França 2012

Methods	Type of study: RCT. Condition and number of participants randomised: 23 patients randomized into two groups. Groups: TENS group, stabilization group (received exercises of lumbar segmental stabilization - transversus abdominis and lumbar multifidus muscles exercises).

Participants	Demographics: N = 23. Stabilization group (SG N = 12; age 43.58 + 7.17; BMI 26.47 + 3.39). TENS group (TG N = 11; age 46.45 + 5.14; BMI 26.92 + 3.02). Setting: information not available. Inclusion: information not available. Exclusion: information not available. Withdrawals/dropouts: information not available.
Interventions	Both groups received 16 sessions, lasting 60 minutes, twice a week and evaluated before and after 8 weeks. TENS Group Where applied: Information not available. Applied by: information not available. Waveform: information not available. Frequency: information not available. Pulse duration: information not available. Pulse amplitude/intensity: information not available. Electrodes: information not available. Duration and frequency of Rx: 16 sessions, lasting 60 minutes, twice a week. Device/manufacturer: information not available. Adverse effects: information not available.
Outcomes	Pain outcome: Visual Analog Pain Scale, Oswestry disability questionnaire for functional disability and pressure biofeedback unit for the ability to contract the TrA muscle. ITT/per protocol analysis: information not available. Statistical analysis: intragroup statistical analysis using t-test and Wilcoxon Signed Rank tests. "After eight weeks, Stabilization Group showed statistically significant improvement in pain (6.16+1.26; 1.58+1.24; p<0.001), functional disability (15.50+3.77; 4.83+2.94; p<0,001) and the ability to contract the TrA muscle (-0.83+1.49;-3.16+0.77; p<0,001). There was no statistically significant difference in TENS Group for functional disability (18.09+4.27;17.09+7.96; p=0.569) and ability to contract the TrA muscle (-1.40+0.83; -1.54+0.93; p=0.557), however it demonstrated improvement in pain (6.90+2.30;4.81+2.52; p=0.004)".
Notes	.

Hsueh 1997

Methods	Type of study: randomised, double blind, placebo-controlled, parallel design. Condition and number of participants randomised: myofascial trigger points of upper trapezius muscle (? acute pain), N = 60. Groups: placebo group (N = 18); ENS group (N = 20); EMS therapy (N = 22).
Participants	Demographics: N = 60, 44.4 ± 13.9 yrs (mean ± ?SD), 25 male/35 female. Placebo group, 41.4 ± 13.0 yrs; ENS group, 42.7 ± 13.8 yrs; EMS therapy, 44.4 ± 14.5 yrs (mean ± ?SD). Setting: outpatient clinic at hospital. Inclusion: myofascial trigger points in one side of upper trapezius muscles. Exclusion: < 18 yrs or > 80 yrs; acute or serious illness; mental retardation; neurologic deficits involving the investigated upper limb; advanced osteopathic or arthropathic disorder of the cervical spine or the shoulder of the investigated side; participants should have had no therapy, such as physical therapy or injection therapy, within the last 2 months on MTrPs selected for this trial. Withdrawals/dropouts: not detailed.
Interventions	Where applied: in clinic. Applied by: presume by clinician. Waveform: not detailed. Frequency: 60 Hz. Pulse duration: not detailed. Pulse amplitude/Intensity: at a level that the participant could feel but was not strong enough to induce muscle contraction. Placebo Group: participant told that a certain type of therapy would be given to treat MTrPs, but was not told what treatment was to be given. Electrodes were applied on the upper trapezius muscle as in other groups, 0 mA current intensity. Electrodes: 2, type and number not detailed, negative electrode placed on MTrP of upper trapezius muscle and positive one on its acromial tendon insertional site. Duration and frequency of Rx: 20 min, 1 Rx. Device/manufacturer: not detailed. Adverse effects: not detailed.

Outcomes	Pain outcome: VAS for pain intensity, before and after Rx. PT of MTrP of the upper trapezius muscle before and after Rx. ITT/per protocol analysis: not detailed. Statistical analysis: improvement in PI and PT was significantly greater in the ENS Group than the other 2 groups.
Notes	ENS- electrical nerve stimulation; EMS- electrical muscle stimulation; MTrPs- myofascial trigger points; PI- pain intensity; PT- pain threshold.

Liebano 2013

Methods	Type of study: information not available. Condition and number of participants randomised: information not available. Groups: information not available.
Participants	Demographics: N =74; gender and age not known. Setting: information not available. Inclusion: information not available. Exclusion: information not available. Withdrawals/dropouts: information not available.
Interventions	Where applied: information not available. Applied by: information not available. Waveform: information not available. Frequency: information not available. Pulse duration: information not available. Pulse amplitude/Intensity: information not available. Electrodes: information not available. Duration and frequency of Rx: information not available. Device/manufacturer: information not available. Adverse effects: information not available.

Outcomes	Pain outcome: VAS for pain intensity, before and after Rx. ITT/per protocol analysis: information not available. Statistical analysis: information not available.
Notes	

Park 2014

Methods	Type of study: RCT. Condition and number of participants randomised: 20 to 60 year-old women undergoing thyroidectomy. Groups: control or TENS.
Participants	Demographics: 20 to 60 year-old women undergoing thyroidectomy without history of headache or neck pain within six months. Setting: information not available. Inclusion: information not available. Exclusion: information not available. Withdrawals/dropouts: information not available.
Interventions	TENS group Intraoperative TENS. Where applied: in the upper trapezius during thyroidectomy. Applied by: information not available. Waveform: information not available. Frequency: information not available. Pulse duration: information not available. Pulse amplitude/Intensity: information not available. Electrodes: information not available. Duration and frequency of Rx: information not available. Device/manufacturer: information not available. Adverse effects: information not available.

Outcomes	Pain outcome: numerical rating scale of posterior neck pain and wound pain at 30 minutes, 6, 24 and 48 hours after surgery. ITT/per protocol analysis: information not available. Statistical analysis: information not available.
Notes	

Rajpurohit 2010

Methods	Type of study: randomised, controlled, parallel design. Condition and number of participants randomised: bruxism with masticatory muscle pain (? acute pain), 60. Groups: MENS group (N = 30); TENS group (N = 30).
Participants	Demographics: N = 60, age not detailed, 36 male/24 female. Setting: physiotherapy department in a hospital. Inclusion: clinical diagnosis of bruxism; muscle tenderness over masseter muscle; early morning temporomandibular joint stiffness and pain; duration of pain more than three weeks; and, age ranged from 19 to 60 years. Exclusion: wearing any removable restoration; treated with analgesic and antiinflammatory drugs; having muscle pain without bruxism; presence of any tumour or cancer around jaws or infection. Withdrawals/dropouts: not detailed.
Interventions	Where applied: in hospital. Applied by: not detailed. Waveform: not detailed. Frequency: 50 Hz. Pulse duration: 0.5 ms. Pulse amplitude/Intensity: intensity was as per the participant's tolerance. Electrodes: carbon electrodes, number not detailed, 40 x 54 mm^2. Placed over the affected side of masseter muscle. Duration and frequency of Rx: 20 minutes, 1 Rx daily for 7 days. Device/manufacturer: not detailed. Adverse effects: not detailed.

Outcomes	Pain outcome: VAS for pain intensity, pre-TENS and post-TENS at the end of the 7th day of treatment. Tenderness by using digital pressometer of 2 KgF, pre-TENS and post-TENS at the end of the seventh day of treatment. ITT/per protocol analysis: not detailed. Statistical analysis: statistically significant pain relief and decrease in tenderness in MENS group compared to TENS group.
Notes	

Salvador 2005

Methods	Type of study: Randomised, blinded, controlled, parallel design. Condition and number of participants randomised: acute LBP, 28. Groups: muscle energy technique group (N = 14); TENS group (N = 14).
Participants	Demographics: N = 28, age not detailed, all male. Setting: clinic. Inclusion: acute LBP (constant pain present for no more than 3 weeks); shortening of at least one of the muscle groups assessed; no treatment (physiotherapy or tablets) in the last 2 weeks for the LBP. Exclusion: chronic LBP; rheumatological problems (arthritis, osteoporosis); no muscle shortening; positive Valsalva. Withdrawals/dropouts: not detailed.
Interventions	Where applied: in clinic. Applied by: clinician. Waveform: not detailed. Frequency: not detailed. Pulse duration: not detailed. Pulse amplitude/Intensity: not detailed. Electrodes: not detailed. Duration and frequency of Rx: 5 min, 1 Rx. Device/manufacturer: Quark. Adverse effects: not detailed.

Outcomes	Pain outcome: VAS for pain intensity, before and after Rx. ITT/per protocol analysis: not detailed. Statistical analysis: significant reduction in pain intensity after treatment in TENS group when compared to muscle energy technique group.
Notes	

Salvino 2013

Methods	Type of study: randomised, placebo controlled. Condition and number of participants randomised: 145 consecutive headache sufferers grouped in 2 groups according to cutaneous allodynia total score. Groups: real or sham TENS.
Participants	Demographics: information not available. Setting: information not available. Inclusion: information not available. Exclusion: information not available. Withdrawals/dropouts: information not available.
Interventions	TENS group Where applied: at the back of the head bilaterally. Applied by: information not available. Waveform: information not available. Frequency: information not available. Pulse duration: information not available. Pulse amplitude/Intensity: information not available. Electrodes: information not available. Duration and frequency of Rx: 30 minutes, three times a day for two consecutive weeks. Device/manufacturer: information not available. Adverse effects: information not available. Sham TENS group: information not available.

Outcomes	Pain outcome: number of headache free-days (> 50%) at 15, 30 and 60 days. ITT/per protocol analysis: information not available. Statistical analysis: information not available. "A significant change in number of headache free-days above 50% was observed in 53 (49%) out of l08 patients treated with real TENS. Of these patients thirty-seven respondents (82%) were non allodynic. While 47 (75%) out of the 63 non respondents were allodynic patients. Only 2 (5%) out of the 37 patients were responsive to sham TENS therapy."
Notes	Objectives: to test if cutaneous allodynia influences the response to treatment with TENS in headache sufferers.

Silva 2012

Methods	Type of study: single-blind, randomised design. Condition and number of participants randomised: patients post-laparoscopic cholecystectomy (N = ?). Groups: active TENS and placebo TENS.
Participants	Demographics: N = ? Age and gender not available. Setting: not available. Inclusion: not available. Exclusion: not available. Withdrawals/dropouts: not available.
Interventions	Where applied: information not available. Applied by: information not available. Waveform: biphasic square pulse TENS current. Frequency: 150 Hz. Pulse duration: 75 µs. Pulse amplitude/Intensity: information not available. Electrodes: information not available. Duration and frequency of Rx: information not available. Device/manufacturer: information not available. Adverse effects: information not available.

Outcomes	Pain outcome: VAS for pain intensity, post Rx. ITT/per protocol analysis: information not available. Statistical analysis: statistically significant reduction in VAS scores post Rx in active TENS group.
Notes	

Treacy 2011

Methods	Type of study: randomised, placebo controlled design (pilot study). Condition and number of participants randomised: 12 adults admitted for IV antibiotics with acute lung pain (VAS score > 4/10) Groups: active TENS and placebo TENS
Participants	Demographics: N = 12; age and gender information not available. Setting: Northern Ireland; hospital inpatient setting. Inclusion: TENS naive. Exclusion: information not available. Withdrawals/dropouts: information not available.
Interventions	Where applied: information not available. Applied by: information not available. Waveform: information not available. Frequency: 150 Hz. Pulse duration: 200 ms. Pulse amplitude/Intensity: information not available. Electrodes: Information not available. Duration and frequency of Rx: the duration of the lung pain. Device/manufacturer: information not available. Adverse effects: information not available.

Outcomes	Pain outcome: VAS for pain intensity, before and after Rx. ITT/per protocol analysis: not detailed. Statistical analysis: statistically significant reduction in VAS scores post Rx in both groups.
Notes	

Data and analyses

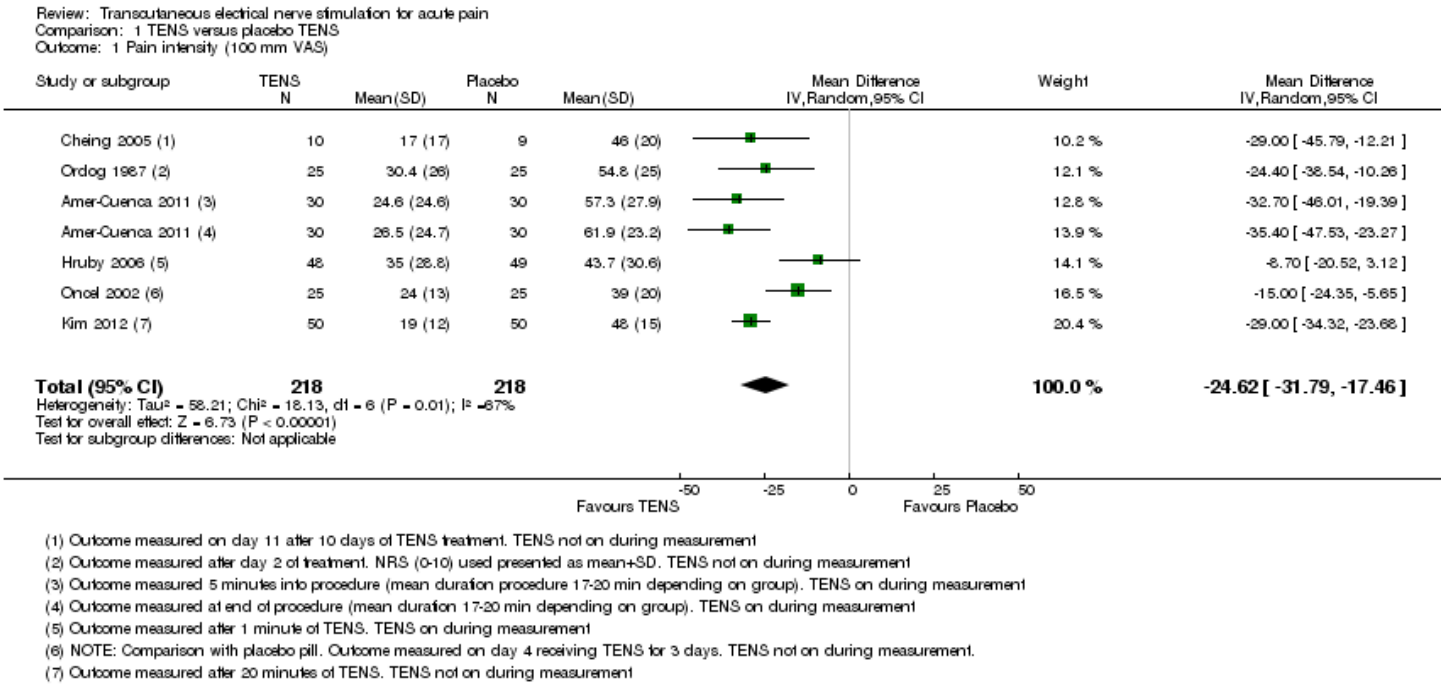
Comparison 1. TENS versus placebo TENS **Open in table viewer**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain intensity (100 mm VAS) **Show forest plot**	6	436	Mean Difference (IV, Random, 95% CI)	-24.62 [-31.79, -17.46]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 1.1

Open in figure viewer | Download as PowerPoint



(1) Outcome measured on day 11 after 10 days of TENS treatment. TENS not on during measurement
(2) Outcome measured after day 2 of treatment. NRS (0-10) used presented as mean+SD. TENS not on during measurement
(3) Outcome measured 5 minutes into procedure (mean duration procedure 17-20 min depending on group). TENS on during measurement
(4) Outcome measured at end of procedure (mean duration 17-20 min depending on group). TENS on during measurement
(5) Outcome measured after 1 minute of TENS. TENS on during measurement
(6) NOTE: Comparison with placebo pill. Outcome measured on day 4 receiving TENS for 3 days. TENS not on during measurement.
(7) Outcome measured after 20 minutes of TENS. TENS not on during measurement

Comparison 1 TENS versus placebo TENS, Outcome 1 Pain intensity (100 mm VAS).

2 > 50% reduction in pain Show forest plot	4	280	Risk Ratio (M-H, Fixed, 95% CI)	3.91 [2.42, 6.32]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 1.2

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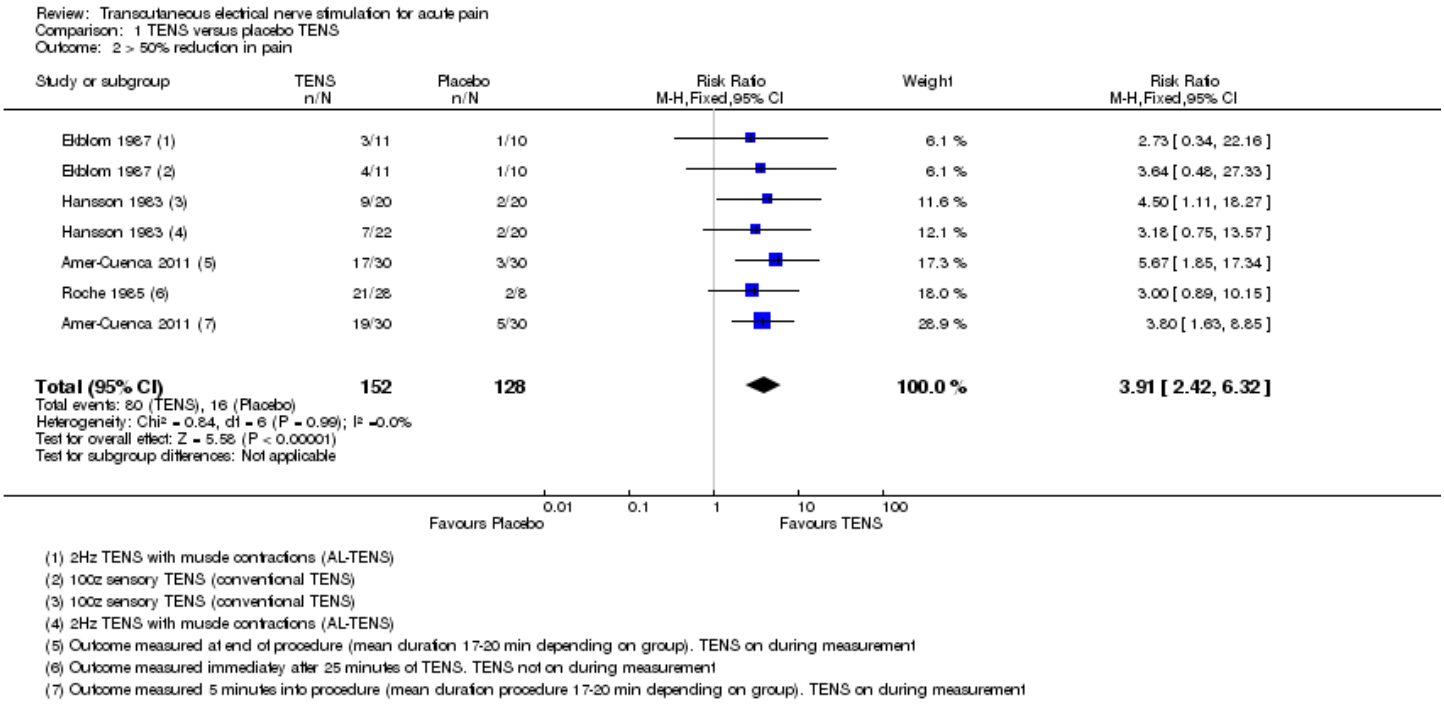


(1) 2Hz TENS with muscle contractions (AL-TENS)
(2) 100z sensory TENS (conventional TENS)
(3) 100z sensory TENS (conventional TENS)
(4) 2Hz TENS with muscle contractions (AL-TENS)
(5) Outcome measured at end of procedure (mean duration 17-20 min depending on group). TENS on during measurement
(6) Outcome measured immediatley after 25 minutes of TENS. TENS not on during measurement
(7) Outcome measured 5 minutes into procedure (mean duration procedure 17-20 min depending on group). TENS on during measurement

Comparison 1 TENS versus placebo TENS, Outcome 2 > 50% reduction in pain.

Comparison 2. TENS versus no treatment control

Open in table viewer

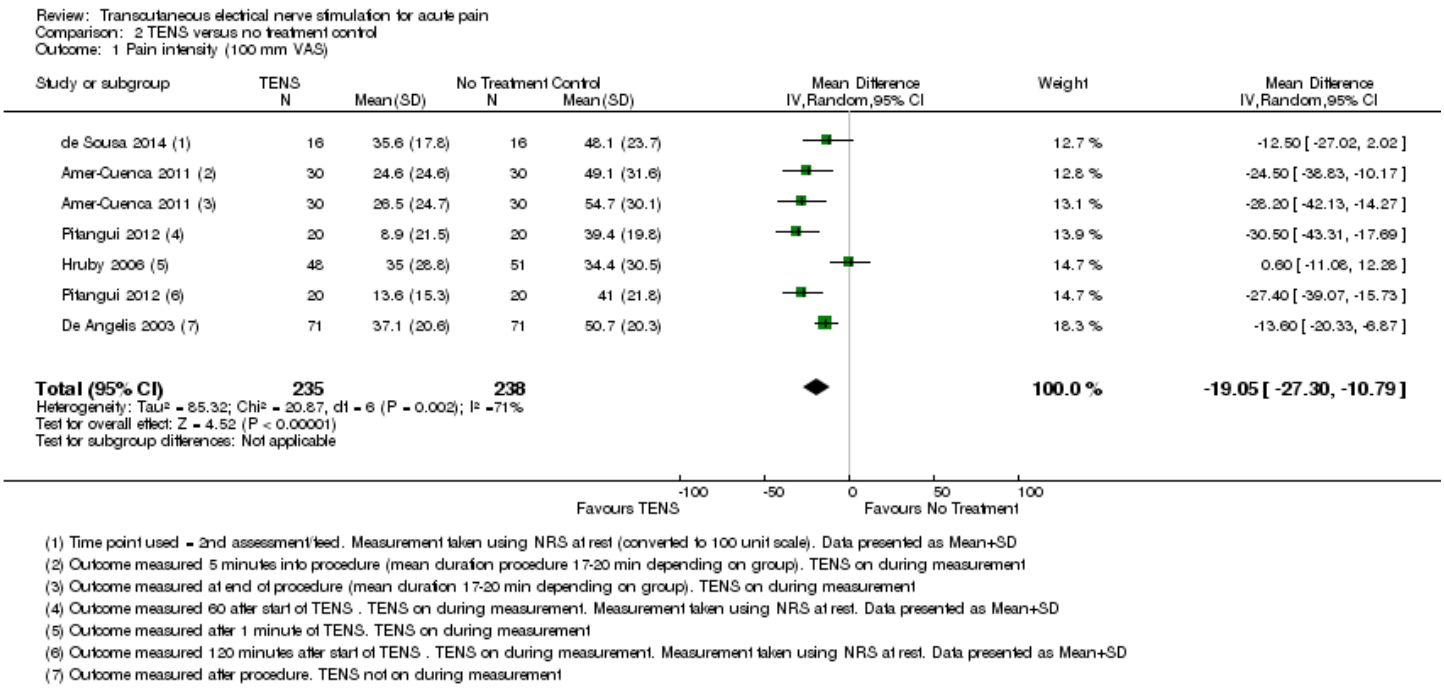
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain intensity (100 mm VAS)	5	473	Mean Difference (IV, Random, 95% CI)	-19.05 [-27.30, -10.79]

Show forest plot

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 2.1

Open in figure viewer | Download as PowerPoint



(1) Time point used = 2nd assessment/feed. Measurement taken using NRS at rest (converted to 100 unit scale). Data presented as Mean+SD
(2) Outcome measured 5 minutes into procedure (mean duration procedure 17-20 min depending on group). TENS on during measurement
(3) Outcome measured at end of procedure (mean duration 17-20 min depending on group). TENS on during measurement
(4) Outcome measured 60 after start of TENS . TENS on during measurement. Measurement taken using NRS at rest. Data presented as Mean+SD
(5) Outcome measured after 1 minute of TENS. TENS on during measurement
(6) Outcome measured 120 minutes after start of TENS . TENS on during measurement. Measurement taken using NRS at rest. Data presented as Mean+SD
(7) Outcome measured after procedure. TENS not on during measurement

Comparison 2 TENS versus no treatment control, Outcome 1 Pain intensity (100 mm VAS).

Comparison 3. Conventional TENS versus AL-TENS

Open in table viewer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 > 50% reduction in pain Show forest plot	2	64	Risk Ratio (M-H, Fixed, 95% CI)	0.72 [0.37, 1.39]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 3.1

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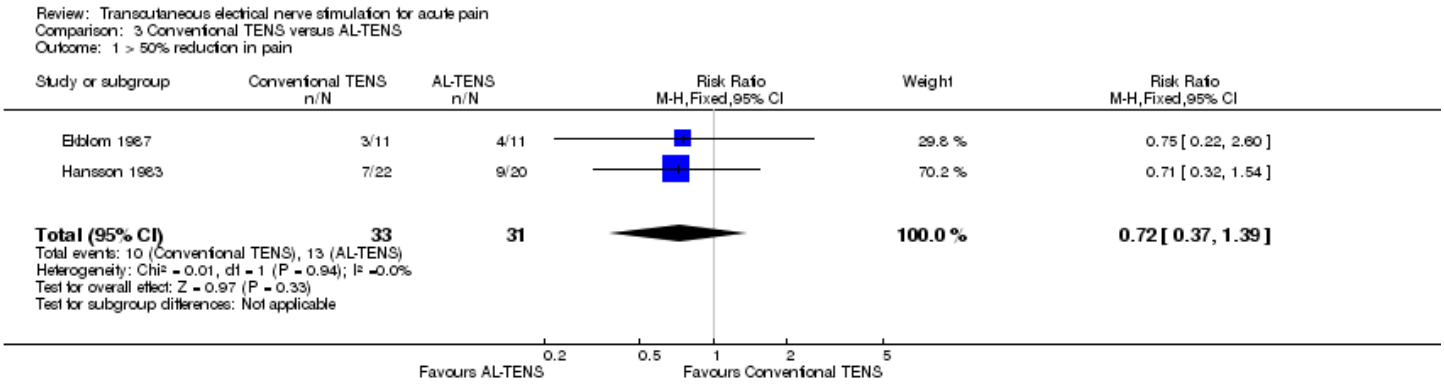


Comparison 3 Conventional TENS versus AL-TENS, Outcome 1 > 50% reduction in pain.

Comparison 4. High pulse amplitude TENS versus low pulse amplitude TENS

Open in table viewer

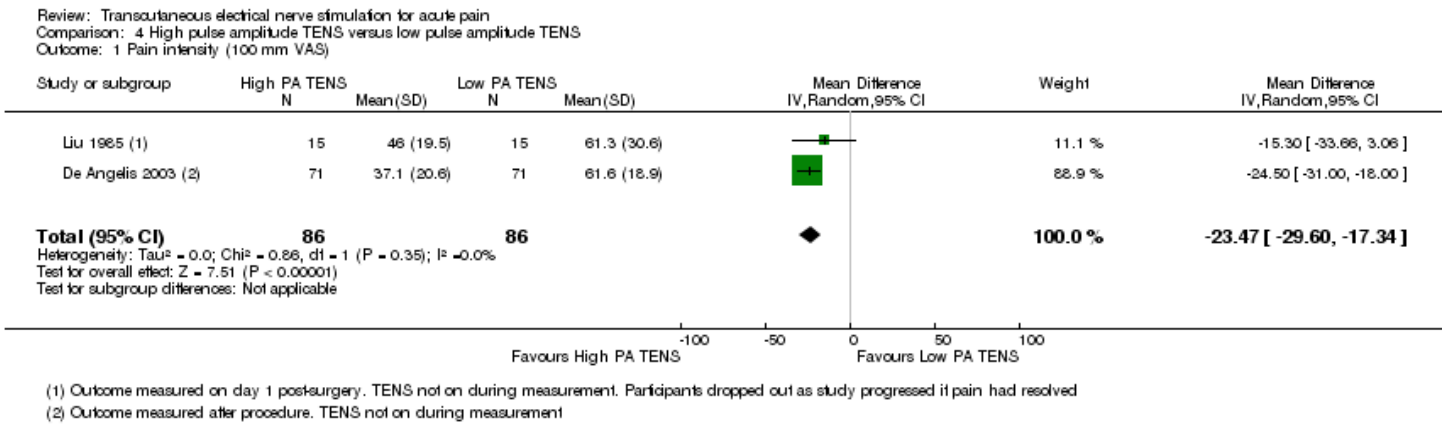
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain intensity (100 mm VAS)	2	172	Mean Difference (IV, Random, 95% CI)	-23.47 [-29.60, -17.34]

Show forest plot

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 4.1

Open in figure viewer | Download as PowerPoint



(1) Outcome measured on day 1 post-surgery. TENS not on during measurement. Participants dropped out as study progressed if pain had resolved
(2) Outcome measured after procedure. TENS not on during measurement

Comparison 4 High pulse amplitude TENS versus low pulse amplitude TENS, Outcome 1 Pain intensity (100 mm VAS).

Information

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Cochrane Database of Systematic Reviews

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15 June 2015 see what's new

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Declarations of interest

Mark I Johnson has no conflicts of interest to declare.
Carole A Paley has no conflicts of interest to declare.
Tracey E Howe has no conflicts of interest to declare.
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What's new

Last assessed as up-to-date: 3 December 2014.

Date	Event	Description
12 June 2015	Review declared as stable	At 2015, the authors and editors agreed to reassess this review for further updating in 2020.

History

Protocol first published: Issue 3, 2006
Review first published: Issue 2, 2009

Date	Event	Description
20 November 2014	New search has been performed	We updated the review using a search conducted up to 3 December 2014.
17 January 2014	New citation required but conclusions have not changed	We included seven new trials in this update. In total, there were 19 included RCTs with 1346 participants at entry, and 11 trials awaiting classification. The analysis provides tentative evidence that TENS reduces pain intensity over and above that seen with placebo (no current) TENS when administered as a stand-alone treatment for acute pain in adults. However, there is high risk of bias associated with inadequate sample sizes in treatment arms and unsuccessful blinding of treatment interventions. This makes definitive conclusions impossible.
7 January 2011	New search has been performed	Updated search done in January 2011. No new included studies but two new studies are awaiting classification (Gregorini 2010; Rajpurohit 2010) and an additional 12 studies were assessed and excluded from this review (Akhmadeeva 2010; Andersen 2009a; Andersen 2009b; Barbarisi 2010; Dogu 2009; Durmus 2009; Gul 2009; Korkmaz 2010; Murina 2008; Stratton 2009; Tsai 2010; Wang 2009). A further 17 studies were excluded as TENS was given with another treatment (see Table 1).

Date	Event	Description
1 May 2008	Amended	Protocol converted to new review format

Version history

Title	Stage	Authors	Version	Publication Date
Transcutaneous electrical nerve stimulation for acute pain	Review	Mark I Johnson, Carole A Paley, Tracey E Howe, Kathleen A Sluka	https://doi.org/10.1002/14651858.CD006142.pub3	15 June 2015
Transcutaneous electrical nerve stimulation for acute pain	Review	Deirdre M Walsh, Tracey E Howe, Mark I Johnson, Fidelma Moran, Kathleen A Sluka	https://doi.org/10.1002/14651858.CD006142.pub2	15 April 2009
Transcutaneous electrical nerve stimulation for acute pain	Protocol	Deirdre M Walsh, Tracey E Howe, Mark I Johnson, Kathleen A Sluka	https://doi.org/10.1002/14651858.CD006142	19 July 2006

Differences between protocol and review

In the 2011 update we decided to use the Cochrane Collaboration's 'Risk of bias' assessment tool to ascertain the methodological quality of trials (instead of Jadad's scale) as this is now the Cochrane Collaboration's recommended tool for all Cochrane Reviews. We excluded trials if TENS was given in combination with any other treatment, either pharmacological or non-pharmacological. We have listed the trials we excluded for this reason in Table 1.

What's new

Last assessed as up-to-date: 3 December 2014.

Date	Event	Description
12 June 2015	Review declared as stable	At 2015, the authors and editors agreed to reassess this review for further updating in 2020.

Appendices

Appendix 1. Ovid MEDLINE search strategy

1. exp Pain/

2. Pain Measurement/

3. Pain Threshold/

4. Pain Clinics/

5. Myofascial Pain Syndromes/

6. Hyperalgesia/

7. exp Headache Disorders/

8. (toothache$ or tooth-ache$ or ear-ache$ or earache$ or sciatic$ or neuralgi$ or migraine$ or headache$ or neuralgi$ or cephalalgi$ or metatarsalgia$ or bursitis or hyperalg$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]

9. pain$.ti.

10. pain$.ab.

11. exp Angina Pectoris/

12. angina.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]

13. Metatarsalgia/

14. or/1-13

15. exp Transcutaneous Electric Nerve Stimulation/

16. "TENS".ti.

17. "TENS".ab.

18. "TNS".ti.

19. "TNS".ab.

20. "ENS".ti.

21. "ENS".ab.

22. ("transcutaneous electric$ nerve stimulation" or "transcutaneous nerve stimulation").mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]

23. ("electric$ nerve stimulation" or "electrostimulation therap$" or "electro-stimulation therap$").mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]

24. ("electric$ nerve therap$" or electroanalgesi$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]

25. transcutaneous electric$ stimulation.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]

26. TES.ti,ab.

27. or/15-26

28. 14 and 27

29. RANDOMIZED CONTROLLED TRIAL.pt.

30. CONTROLLED CLINICAL TRIAL.pt.

31. RANDOMIZED CONTROLLED TRIALS.sh.

32. RANDOM ALLOCATION.sh.

33. DOUBLE BLIND METHOD.sh.

34. SINGLE BLIND METHOD.sh.

35. or/29-34

36. (ANIMALS not HUMAN).sh.

37. 35 not 36

38. CLINICAL TRIAL.pt.

39. exp CLINICAL TRIALS/

40. (clin$ adj25 trial$).ti,ab.

41. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.

42. PLACEBOS.sh.

43. placebo$.ti,ab.

44. random$.ti,ab.

45. RESEARCH DESIGN.sh.

46. or/38-45

47. 46 not 36

48. 47 not 37

49. 37 or 48

50. 28 and 49

Appendix 2. PaPaS Specialized Register search strategy

((pain* or hyperalgesi* or headache* or migrain* or toothache or "tooth ache*" or earache or "ear ache*" or sciatic* or neuralgi* or cephalgi* or metatarsalg* or bursitis or angina) AND ("transcutaneous electric* nerve stimulation" or "transcutaneous nerve stimulation" or "electric* nerve stimulation" or "electrostimulation therap*" or electroanalgesi* or TENS))

Appendix 3. CENTRAL (the Cochrane Library) search strategy

1. MeSH descriptor Pain explode all trees in MeSH products
2. MeSH descriptor Pain Measurement, this term only in MeSH products
3. MeSH descriptor Pain Threshold, this term only in MeSH products
4. MeSH descriptor Pain Clinics, this term only in MeSH products
5. MeSH descriptor Myofascial Pain Syndromes, this term only in MeSH products
6. MeSH descriptor Hyperalgesia, this term only in MeSH products
7. MeSH descriptor Headache Disorders explode all trees in MeSH products
8. (Toothache* or tooth-ache* or ear-ache* or earache* or sciatic* or neuralgi* or migrain* or headache* or neuralgi* or cephalalgia or metatarsalgia* or bursitis or hyperalg*) in All Fields in all products
9. pain* in Record Title in all products

10. pain* in Abstract in all products
11. MeSH descriptor Angina Pectoris explode all trees in MeSH products
12. angina in All Fields in all products
13. MeSH descriptor Metatarsalgia, this term only in MeSH products
14. (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13)
15. MeSH descriptor Transcutaneous Electric Nerve Stimulation explode all trees in MeSH products
16. "TENS" in Record Title in all products
17. "TENS" in Abstract in all products
18. "TNS" in Record Title in all products
19. "TNS" in Abstract in all products
20. "ENS" in Record Title in all products
21. "ENS" in Abstract in all products
22. (transcutaneous next electric* next nerve next stimulation or "transcutaneous nerve stimulation") in All Fields in all products
23. ("electric* nerve stimulation" or "electrostimulation therap*") in All Fields in all products
24. ("electric* nerve therap*" or electroanalgesi*) in All Fields in all products
25. "TES" in Record Title in all products
26. "TES" in Abstract in all products
27. (transcutaneous next electric* next stimulation) in All Fields in all products
28. (#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27)
29. (#14 AND #28)

Appendix 4. Ovid EMBASE search strategy

1. exp PAIN/
2. Pain Assessment/
3. Pain Threshold/
4. Pain Clinic/
5. Myofascial Pain/

6. HYPERALGESIA/

7. exp "Headache and Facial Pain"/

8. (toothache$ or tooth-ache$ or ear-ache$ or earache$ or sciatic$ or neuralgi$ or migraine$ or headache$ or neuralgi$ or cephalalgi$ or metatarsalgia$ or bursitis or hyperalg$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]

9. pain$.ti.

10. pain$.ab.

11. exp Angina Pectoris/

12. angina.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]

13. METATARSALGIA/

14. or/1-13

15. exp Transcutaneous Nerve Stimulation/

16. "TENS".ti.

17. "TENS".ab.

18. "TNS".ti.

19. "TNS".ab.

20. "ENS".ti.

21. "ENS".ab.

22. ("transcutaneous electric$ nerve stimulation" or "transcutaneous nerve stimulation").mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]

23. ("electric$ nerve stimulation" or "electrostimulation therap$" or "electro-stimulation therap$").mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]

24. ("electric$ nerve therap$" or electroanalgesi$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]

25. transcutaneous electric$ stimulation.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]

26. TES.ti,ab.

27. or/15-26

28. 14 and 27

29. random$.ti,ab.

30. factorial$.ti,ab.

31. (crossover$ or cross over$ or cross-over$).ti,ab.

32. placebo$.ti,ab.

33. (doubl$ adj blind$).ti,ab.

34. (singl$ adj blind$).ti,ab.

35. assign$.ti,ab.

36. allocat$.ti,ab.

37. volunteer$.ti,ab.

38. CROSSOVER PROCEDURE.sh.

39. DOUBLE-BLIND PROCEDURE.sh.

40. RANDOMIZED CONTROLLED TRIAL.sh.

41. SINGLE BLIND PROCEDURE.sh.

42. or/29-41

43. ANIMAL/ or NONHUMAN/ or ANIMAL EXPERIMENT/

44. HUMAN/

45. 44 and 43

46. 43 not 45

47. 42 not 46

48. 28 and 47

Appendix 5. EBSCO CINAHL search strategy

1 exp PAIN/

2 PAIN MEASUREMENT/

3 PAIN CLINICS/

4 MYOFASCIAL PAIN SYNDROMES/

5 HYPERALGESIA/

6 exp HEADACHE/

7 (toothache* OR tooth-ache* OR ear-ache* OR earache* OR sciatic* OR neuralgi* OR migraine* OR headache* OR neuralgi* OR cephalalgi* OR metatarsalgia* OR bursitis OR hyperalg*).ti,ab

8 pain*.ti,ab

9 exp ANGINA PECTORIS/

10 angina.ti,ab

11 PAIN THRESHOLD/

12 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11

13 exp TRANSCUTANEOUS ELECTRIC NERVE STIMULATION/

14 (TENS OR TNS OR ENS).ti,ab

15 (transcutaneous AND stimulation).ti,ab

16 TES.ti,ab

17 ((electric* AND stimulation) OR electrostimulation OR electro-stimulation).ti,ab

18 ((electric* nerve therap*) OR electroanalgesi*).ti,ab

19 13 OR 14 OR 15 OR 16 OR 17 OR 18

20 12 AND 19

21 RANDOM ASSIGNMENT/

22 SINGLE-BLIND STUDIES/

23 DOUBLE-BLIND STUDIES/

24 TRIPLE-BLIND STUDIES/

25 CROSSOVER DESIGN/

26 FACTORIAL DESIGN/

27 ((multicentre OR multicenter OR multi-centre OR multi-center) AND stud*).ti,ab

28 random*.ti,ab

29 (latin AND square).ti,ab

30 (cross-over OR crossover).ti,ab

31 PLACEBOS/

32 placebo*.ti,ab

33 ((singl* OR doubl* OR trebl* OR tripl*) AND (blind* OR mask*)).ti,ab

34 exp CLINICAL TRIALS/

35 (clin* AND trial*).ti,ab

36 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35

37 20 AND 36

Appendix 6. Ovid AMED search strategy

1. exp Pain/

2. Pain measurement/

3. Pain threshold/

4. PAIN CLINICS.mp.

5. Myofascial pain syndromes/

6. Hyperalgesia/

7. exp Headache/

8. (toothache$ or tooth-ache$ or ear-ache$ or earache$ or sciatic$ or neuralgi$ or migraine$ or headache$ or neuralgi$ or cephalalgi$ or metatarsalgia$ or bursitis or hyperalg$).mp. [mp=title, subject heading word, abstract, instrumentation]

9. pain$.ti.

10. pain$.ab.

11. exp angina pectoris/

12. angina.mp. [mp=title, subject heading word, abstract, instrumentation]

13. Metatarsalgia/

14. or/1-13

15. exp Transcutaneous electric nerve stimulation/

16. "TENS".ti.

17. "TENS".ab.

18. "TNS".ti.

19. "TNS".ab.

20. "ENS".ti.

21. "ENS".ab.

22. ("transcutaneous electric$ nerve stimulation" or "transcutaneous nerve stimulation").mp. [mp=title, subject heading word, abstract, instrumentation]

23. ("electric$ nerve stimulation" or "electrostimulation therap$" or "electro-stimulation therap$").mp. [mp=title, subject heading word, abstract, instrumentation]

24. ("electric$ nerve therap$" or electroanalgesi$).mp. [mp=title, subject heading word, abstract, instrumentation]

25. transcutaneous electric$ stimulation.mp. [mp=title, subject heading word, abstract, instrumentation]

26. TES.ti,ab.

27. or/15-26

28. 14 and 27

29. RANDOMIZED CONTROLLED TRIAL.pt.

30. CONTROLLED CLINICAL TRIAL.pt.

31. RANDOMIZED CONTROLLED TRIALS.sh.

32. RANDOM ALLOCATION.sh.

33. DOUBLE BLIND METHOD.sh.

34. "single blind method".mp. [mp=title, subject heading word, abstract, instrumentation]

35. or/29-34

36. (ANIMALS not HUMANS).sh.

37. 35 not 36

38. CLINICAL TRIAL.pt.

39. exp CLINICAL TRIALS/

40. (clin$ adj25 trial$).ti,ab.

41. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.

42. PLACEBOS.sh.

43. placebo$.ti,ab.

44. random$.ti,ab.

45. RESEARCH DESIGN.sh.

46. or/38-45

47. 46 not 36

48. 47 not 37

49. 37 or 48

50. 28 and 49

Appendix 7. PEDro search strategy

Abstract & Title:"electrical stimulation" pain

Therapy: electrotherapies, heat and cold

Problem: pain

Method: Clinical Trial

Note: check “match all search terms”

Appendix 8. OTseeker search strategy

Keywords: electrical stimulation

Methods: clinical trial

Appendix 9. OpenSIGLE search strategy

((pain OR toothache* OR tooth-ache* OR ear-ache* OR earache* OR sciatic* OR neuralgi* OR migraine* OR headache* OR neuralgi* OR cephalalgi* OR metatarsalgia* OR bursitis OR hyperalg* OR myofascial OR angina*) AND (transcutaneous electric nerve stimulation OR tens OR tns OR ens OR transcutaneous electric* OR transcutaneous nerve stimulation OR electric* nerve stimulation OR electrostimulation therap* OR electro-stimulation therap* OR electro-stimulation OR electrostimulation OR electric* nerve therap* OR electroanalgesi*))

Appendix 10. Search strategies for 2014 update

CENTRAL (the Cochrane Library)

#1 MeSH descriptor: [Pain] explode all trees

#2 MeSH descriptor: [Pain Measurement] this term only

#3 MeSH descriptor: [Pain Threshold] this term only

#4 MeSH descriptor: [Pain Clinics] this term only

#5 MeSH descriptor: [Myofascial Pain Syndromes] this term only

#6 MeSH descriptor: [Hyperalgesia] this term only

#7 MeSH descriptor: [Headache Disorders] explode all trees

#8 (toothache* or tooth-ache* or ear-ache* or earache* or sciatic* or neuralgi* or migraine* or headache* or neuralgi* or cephalalgi* or metatarsalgia* or bursitis or hyperalg*):ti,ab,kw (Word variations have been searched)

#9 pain*:ab or pain*:ti (Word variations have been searched)

#10 MeSH descriptor: [Angina Pectoris] explode all trees

#11 angina:ti,ab,kw (Word variations have been searched)

#12 MeSH descriptor: [Metatarsalgia] this term only

#13 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12

#14 MeSH descriptor: [Transcutaneous Electric Nerve Stimulation] explode all trees

#15 ("TENS" or "TNS" or "ENS" or "TES"):ti,ab,kw (Word variations have been searched)

#16 ("transcutaneous electric* nerve stimulation" or "transcutaneous nerve stimulation"):ti,ab,kw (Word variations have been searched)

#17 ("electric* nerve stimulation" or "electrostimulation therap*" or "electro-stimulation therap*"):ti,ab,kw (Word variations have been searched)

#18 ("electric* nerve therap*" or electroanalgesi*):ti,ab,kw (Word variations have been searched)

#19 "transcutaneous electric* stimulation":ti,ab,kw (Word variations have been searched)

#20 #14 or #15 or #16 or #17 or #18 or #19

#21 #13 and #20 from 2011 to 2014

MEDLINE (OVID) & Medline In-Process (OVID)

1. exp Pain/

2. Pain Measurement/

3. Pain Threshold/

4. Pain Clinics/

5. Myofascial Pain Syndromes/

6. Hyperalgesia/

7. exp Headache Disorders/

8. (toothache$ or tooth-ache$ or ear-ache$ or earache$ or sciatic$ or neuralgi$ or migraine$ or headache$ or neuralgi$ or cephalalgi$ or metatarsalgia$ or bursitis or hyperalg$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]

9. pain$.ti.

10. pain$.ab.

11. exp Angina Pectoris/

12. angina.mp.

13. Metatarsalgia/

14. or/1-13

15. exp Transcutaneous Electric Nerve Stimulation/

16. ("TENS" or "TNS" or "ENS").ti.

17. ("TENS" or "TNS" or "ENS").ab.

18. ("transcutaneous electric$ nerve stimulation" or "transcutaneous nerve stimulation").mp.

19. ("electric$ nerve stimulation" or "electrostimulation therap$" or "electro-stimulation therap$").mp.

20. ("electric$ nerve therap$" or electroanalgesi$).mp.

21. transcutaneous electric$ stimulation.mp.

22. TES.ti,ab.

23. or/15-22

24. 14 and 23

25. randomized controlled trial.pt.

26. controlled clinical trial.pt.

27. randomized.ab.

28. placebo.ab.

29. drug therapy.fs.

30. randomly.ab.

31. trial.ab.

32. or/25-31

33. exp animals/ not humans.sh.

34. 32 not 33

35. 24 and 34

36. (2011* or 2012* or 2013* or 2014*).ed.

37. 35 and 36

EMBASE (OVID)

1. exp Pain/

2. Pain Measurement/

3. Pain Threshold/

4. Pain Clinics/

5. Myofascial Pain Syndromes/

6. Hyperalgesia/

7. exp Headache Disorders/

8. (toothache$ or tooth-ache$ or ear-ache$ or earache$ or sciatic$ or neuralgi$ or migraine$ or headache$ or neuralgi$ or cephalalgi$ or metatarsalgia$ or bursitis or hyperalg$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]

9. pain$.ti.

10. pain$.ab.

11. exp Angina Pectoris/

12. angina.mp.

13. Metatarsalgia/

14. or/1-13

15. exp Transcutaneous Electric Nerve Stimulation/

16. ("TENS" or "TNS" or "ENS").ti.
17. ("TENS" or "TNS" or "ENS").ab.
18. ("transcutaneous electric$ nerve stimulation" or "transcutaneous nerve stimulation").mp.
19. ("electric$ nerve stimulation" or "electrostimulation therap$" or "electro-stimulation therap$").mp.
20. ("electric$ nerve therap$" or electroanalgesi$).mp.
21. transcutaneous electric$ stimulation.mp.
22. TES.ti,ab.
23. or/15-22
24. 14 and 23
25. random$.tw.
26. factorial$.tw.
27. crossover$.tw.
28. cross over$.tw.
29. cross-over$.tw.
30. placebo$.tw.
31. (doubl$ adj blind$).tw.
32. (singl$ adj blind$).tw.
33. assign$.tw.
34. allocat$.tw.
35. volunteer$.tw.
36. Crossover Procedure/
37. double-blind procedure.tw.
38. Randomized Controlled Trial/
39. Single Blind Procedure/
40. or/25-39
41. (animal/ or nonhuman/) not human/
42. 40 not 41

43. 24 and 42

AMED (OVID)

1. exp Pain/

2. Pain Measurement/

3. Pain Threshold/

4. Pain Clinics/

5. Myofascial Pain Syndromes/

6. Hyperalgesia/

7. (toothache$ or tooth-ache$ or ear-ache$ or earache$ or sciatic$ or neuralgi$ or migraine$ or headache$ or neuralgi$ or cephalalgi$ or metatarsalgia$ or bursitis or hyperalg$).mp. [mp=abstract, heading words, title]

8. pain$.ti.

9. pain$.ab.

10. exp Angina Pectoris/

11. angina.mp.

12. Metatarsalgia/

13. (or/1-6) or 7 or 8 or 9 or 10 or 11 or 12

14. exp Transcutaneous Electric Nerve Stimulation/

15. ("TENS" or "TNS" or "ENS").ti.

16. ("TENS" or "TNS" or "ENS").ab.

17. ("transcutaneous electric$ nerve stimulation" or "transcutaneous nerve stimulation").mp.

18. ("electric$ nerve stimulation" or "electrostimulation therap$" or "electro-stimulation therap$").mp.

19. ("electric$ nerve therap$" or electroanalgesi$).mp.

20. transcutaneous electric$ stimulation.mp.

21. TES.ti,ab.

22. or/14-21

23. 13 and 22

CINAHL (EBSCO)

S32 S30 AND S31

S31 EM 20110101-20141231

S30 S20 AND S29

S29 S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28

S28 (allocat* random*)

S27 (MH "Quantitative Studies")

S26 (MH "Placebos")

S25 placebo*

S24 (random* allocat*)

S23 (MH "Random Assignment")

S22 (Randomi?ed control* trial*) Limiters - Published Date: 20090101-20130231

S21 (singl* blind*) or (doubl* blind*) or (tripl* blind*) or (trebl* blind*) or (trebl* mask*) or (tripl* mask*) or (doubl* mask*) or (singl* mask*)

S20 S12 AND S19

S19 S13 OR S14 OR S15 OR S16 OR S17 OR S18

S18 "transcutaneous electric* stimulation"

S17 ("electric* nerve therap*" or electroanalgesi*)

S16 ("electric* nerve stimulation" or "electrostimulation therap*" or "electro-stimulation therap*")

S15 ("transcutaneous electric* nerve stimulation" or "transcutaneous nerve stimulation")

S14 ("TENS" or "TNS" or "ENS" or "TES")

S13 (MH "Transcutaneous Electric Nerve Stimulation")

S12 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11

S11 (MH "Metatarsalgia")

S10 angina

S9 (MH "Angina Pectoris+")

S8 TI pain* OR AB pain*

S7 (toothache* or tooth-ache* or ear-ache* or earache* or sciatic* or neuralgi* or migraine* or headache* or neuralgi* or cephalalgi* or metatarsalgia* or bursitis or hyperalg*)

S6 (MH "Hyperalgesia")

S5 (MH "Myofascial Pain Syndromes")

S4 (MH "Pain Clinics")

S3 (MH "Pain Threshold")

S2 (MH "Pain Measurement")

S1 (MH "Pain+")

Cochrane Library

Cochrane Database of Systematic Reviews

Transcutaneous electrical nerve stimulation for primary dysmenorrhoea

Cochrane Systematic Review - **Intervention** | Version published: 21 January 2002 see what's new

Am score 36 View article information

Michelle Proctor | Cindy Farquhar | Will Stones | Lin He | Xiaoshu Zhu | Julie Brown
View authors' declarations of interest

Abstract *available in* English | Español | 日本語

Background

Medical therapy for dysmenorrhoea (painful menstrual cramps of the uterus) such as non-steroidal anti-inflammatory drugs or the oral contraceptive pill work by reducing myometrial (uterine muscle) activity. Transcutaneous electrical nerve stimulation (TENS) is a non-pharmacological intervention shown to be effective for pain relief in a variety of conditions. TENS may be able to alter the body's ability to receive and perceive pain signals rather than having a direct effect on uterine contractions.

Objectives

To determine the effectiveness of high and low-frequency TENS when compared to placebo, no treatment, or medical treatment for primary dysmenorrhoea.

Search methods

Electronic searches of the Cochrane Menstrual Disorders and Subfertility Group Register of controlled trials, *The Cochrane Library* (Issue 1, 2009), MEDLINE, EMBASE, CINAHL, and AMED were performed (updated April 2009) to identify relevant randomised controlled trials. The Cochrane Complementary Medicine Field Register of controlled trials (CISCOM) was also searched. Attempts were also made to identify trials from the UK National Research Register, the Clinical Trial Register, and the citation lists of review articles and included trials.

Selection criteria

The inclusion criteria were: randomised controlled trials (RCTs) of TENS compared to placebo, no treatment, or medical treatment for primary dysmenorrhoea. Exclusion criteria were: mild, infrequent, or secondary dysmenorrhoea and dysmenorrhoea associated with an intrauterine device (IUD).

Data collection and analysis

Seven RCTs were identified that fulfilled the inclusion criteria for this review. No new studies were identified in the update. Quality assessment and data extraction were performed independently by two review authors. Data unsuitable for meta-analysis were reported as descriptive data and were included for discussion. The outcome measures were pain relief (dichotomous, visual analogue scale, descriptive), adverse effects, use of analgesics additional to treatment, and absence from work or school.

Main results

Overall, high-frequency TENS was shown to be more effective for pain relief than placebo TENS (OR 7.2, 95% CI 3.1 to 16.5). Low-frequency TENS was found to be no more effective in reducing pain than placebo TENS (OR 1.48, 95% CI 0.43 to 5.08). There were conflicting results regarding whether high-frequency TENS was more effective than low-frequency TENS.

Authors' conclusions

High-frequency TENS was found to be effective for the treatment of dysmenorrhoea by a number of small trials. The minor adverse effects reported in one trial require further investigation. There is insufficient evidence to determine the effectiveness of low-frequency TENS in reducing dysmenorrhoea.

Plain language summary *available in* English | Deutsch | Español | 日本語

Transcutaneous electrical nerve stimulation for primary dysmenorrhoea

High-frequency nerve stimulation may help relieve painful menstrual cramps. Dysmenorrhoea is a very common complaint that refers to painful menstrual cramps in the uterus. Transcutaneous electrical nerve stimulation (TENS) involves the sending of an electric current by placing electrodes on the skin to stimulate the nerves and reduce pain. It is thought to alter the body's ability to receive and understand pain signals rather than by having a direct effect on the uterine contractions. The review of trials found that high-frequency TENS may help but there is not enough evidence to assess the effect of low-frequency TENS. More research is needed.

Authors' conclusions *available in* English | Español

Implications for practice

The available data on high-frequency TENS suggest it is effective for the treatment of dysmenorrhoea. The clinical importance of the minor adverse effects that were reported in one study is unclear. TENS represents a suitable alternative for women who prefer not to use medication or wish to minimise their NSAID consumption. There are some data to suggest that women using TENS are less likely to require additional analgesia, an observation that supports clinical advice to consider TENS as an option, although the degree of relief obtainable from TENS alone is less than that from analgesic drugs.

The present review has not demonstrated the efficacy of low-frequency TENS. This may be because the single study was insufficiently powered. Clear recommendations for practice cannot be made.

Implications for research

It is likely that women experiencing dysmenorrhoea will continue to seek advice on and treatment with TENS, therefore further research is needed to establish the optimal manner in which TENS modalities should be used. The condition is very common and the lifestyle impact and economic burden justifies a search for effective and acceptable treatments. Inclusion of cost comparisons and outcomes in clinical trials will enable better assessment of the true value of treatment interventions. There is a need to improve the quality of future randomised controlled trials. The methods of trials need to be fully described so as to aid the reader as to the validity and relevance of reported studies. In particular, allocation blinding needs to be meticulous within the practical constraints discussed above.

Methodologically sound and adequately powered clinical trials are needed evaluating the role of low-frequency TENS for primary dysmenorrhoea. More information is needed on the potential adverse effects of high-frequency TENS and the acceptability of TENS treatments to women needs to be explored using both questionnaires and qualitative methods.

Background *available in* English | Español

Description of the condition

Dysmenorrhoea refers to the occurrence of painful menstrual cramps of uterine origin. It is a common gynaecological complaint that can affect as many as 50% of women; 10% of these women suffer severely enough to render them incapacitated for one to three days each menstrual cycle (Dawood 1990b). This has a significant impact on personal health and it also has a global economic impact. In the USA alone, it is estimated that annual losses are 600 million work hours and two billion dollars (Dawood 1984).

Dysmenorrhoea is commonly defined within two subcategories. When the pelvic pain is associated with an identifiable pathological condition, such as endometriosis, it is considered to be secondary dysmenorrhoea. In contrast, menstrual pain without organic pathology is called primary dysmenorrhoea (Lichten 1987).

The initial onset of primary dysmenorrhoea is usually at or shortly (six to 12 months) after menarche (the commencement of menstrual periods), when ovulatory cycles are established. The pain duration is commonly 48 to 72 hours and is associated with the menstrual flow. In contrast, secondary dysmenorrhoea is more likely to occur years after the onset of menarche and occurs premenstrually as well as during menstruation. This distinction is not necessarily robust however as severe primary dysmenorrhoea in young women may indicate endometriosis (Punnonen 1980).

Description of the intervention

Dysmenorrhoea is commonly treated with non-steroidal anti-inflammatory drugs (NSAIDs) or oral contraceptive pills (OCPs), both of which work by reducing myometrial (uterine muscle) activity. However, these treatments are accompanied by a number of adverse effects making an effective non-pharmacological method of treating dysmenorrhoea of great potential value.

Transcutaneous electrical nerve stimulation (TENS) involves stimulation of the skin using electrical currents at various pulse rates (frequencies) and intensities in order to provide pain relief. Since the late 19th century, TENS has been used to treat many conditions, such as acne, abscesses, corns, cramps, gout and impotence (Sheon 1984). It is also currently used to manage pain from contractions during labour (Carroll 1997).

TENS machines are portable and can be used in a home situation as well as a clinical setting. Modern day TENS can be divided into two subcategories, high and low frequency. Low-frequency TENS (also referred to as acupuncture-like TENS) usually consists of pulses delivered at between 1 Hz to 4 Hz, at high intensity and long pulse width so they evoke visible muscle contractions. High-frequency TENS (conventional TENS) usually consists of pulses delivered at between 50 Hz and 120 Hz, at a low intensity (Kaplan 1997; Mannheimer 1985).

How the intervention might work

In dysmenorrhoea, TENS seems to work by alteration of the body's ability to receive or perceive pain signals rather than by having a direct effect on the uterine contractions (Smith 1991). The electrodes can be placed on traditional acupuncture sites or at the site of the pain. This modality has been stated to be effective for

pain relief in a variety of conditions (Gersh 1985) but more recent systematic reviews have established that TENS is ineffective for postoperative pain (Carroll 1996) and labour pain (Carroll 1997). Evidence for the efficacy of TENS in chronic pain conditions is limited (McQuay 1998) although a systematic review indicates benefit for pain associated with knee osteoarthritis (Osiri 2001).

Why it is important to do this review

Consumers generally perceive complementary medicine to be more natural than conventional medicine and have fewer concerns about side effects. If pain relief can be brought about through non-pharmacological means then this may be of benefit to both the consumer and healthcare providers.

Objectives *available in* **English** | Español

To determine the effectiveness of high and low-frequency TENS compared to placebo, no treatment, or medical treatment for primary dysmenorrhoea.

Methods *available in* **English** | Español

Criteria for considering studies for this review

Types of studies

All prospective randomised controlled trials comparing TENS to placebo, no treatment, or medical treatment for the treatment of primary dysmenorrhoea.

Types of participants

Participants in the trials had to meet all the following inclusion criteria for the trial to be included in the review.

Inclusion criteria:

- women of reproductive age;
- women with moderate to severe primary dysmenorrhoea (severe or incapacitating pain for at least one day of menses);

- women affected by dysmenorrhoea in > 50% of their menstrual cycles.

If participants in the trial meet any of the following exclusion criteria the trial was not included in the review.

Exclusion criteria:

- women with secondary dysmenorrhoea (i.e. associated with identifiable pelvic pathology);
- women with dysmenorrhoea due to the presence of an intrauterine device (IUD);
- women with mild or infrequent dysmenorrhoea.

Types of interventions

The specific interventions to be considered were as follows.

1. High-frequency TENS versus placebo or no treatment for primary dysmenorrhoea.
2. Low-frequency TENS versus placebo or no treatment for primary dysmenorrhoea.
3. High-frequency TENS versus low-frequency TENS for primary dysmenorrhoea.
4. High-frequency TENS versus acupuncture for primary dysmenorrhoea.
5. Low-frequency TENS versus acupuncture for primary dysmenorrhoea.
6. TENS versus other medical treatment for primary dysmenorrhoea.

Low-frequency TENS (acupuncture-like TENS) is defined as 1 Hz to 4 Hz pulses delivered at high intensity. High-frequency TENS (conventional TENS) is defined as 50 Hz to 120 Hz pulses delivered at a low intensity. Placebo TENS is when no electrical current is used, so the settings and amplitude do not produce any electrical stimulation.

Types of outcome measures

Primary outcomes

Pain relief (measured either on a visual analogue scale (VAS), other scales, or a dichotomous scale)

Secondary outcomes

1. Adverse effects from treatment (incidence and types of side effects)
2. Requirements for additional medication (measured as a ratio for women requiring analgesics additional to their assigned treatment)
3. Restriction of daily life activities (measured as a ratio for women who report activity restriction)
4. Absence from work or school (measured as a ratio for women reporting absences from work or school)

Search methods for identification of studies

Electronic searches

All reports which described (or might describe) randomised controlled trials of TENS in the treatment of dysmenorrhoea were obtained using the following search strategies (April 2009). The Menstrual Disorders and Subfertility Group Specialised Register of controlled trials was searched for any trials with dysmenorrhoea or dysmenorrhoea in the title, abstract, or keyword sections; see the Review Group Module (*The Cochrane Library*) for more details on the makeup of the Specialised Register (Appendix 3). Other databases searched were: CENTRAL (*The Cochrane Library*) (Appendix 4), MEDLINE (Appendix 1), EMBASE (Appendix 2), AMED (Appendix 5), and PsycINFO (Appendix 6).

Searching other resources

The National Research Register (NRR), a register of ongoing and recently completed research projects funded by or of interest to the United Kingdom's National Health Service, as well as entries from the Medical Research Council's Clinical Trials Register and details on reviews in progress collected by the NHS Centre for Reviews and Dissemination were searched for any trials with dysmenorrhoea as a keyword. The Clinical Trials register, a registry of both federally and privately funded US clinical trials, was also searched for the same keyword.

The Cochrane Complementary Medicine Field Register of controlled trials (CISCOM) was searched for any trials with dysmenorrhoea in the title, abstract, or keyword fields. No additional trials were found.

A letter was written to the Chinese Cochrane Centre requesting information on any useful Chinese databases, however they were unable to help as they are a newly formed centre and are still under-resourced at present. We plan to re-contact them for future updates of this review.

The citation lists of relevant publications, review articles, included studies, and abstracts of scientific meetings were also searched.

Letters were sent to major investigators of TENS or acupuncture techniques and the authors of included studies to seek information on additional published or unpublished trials.

Data collection and analysis

Selection of studies

One review author scanned the titles and abstracts of articles retrieved by the search and removed those that were clearly not relevant. The full text of potentially relevant articles were retrieved. The selection of trials for inclusion in the review was performed independently by two review authors (MW, CS). Where necessary, primary authors were contacted to provide additional information on patient eligibility criteria and methodologies. Any disagreements were resolved by discussion and consensus, or by a third author.

Data extraction and management

Data were extracted from eligible studies using a data extraction form designed by the review authors. Where studies had multiple publications, the main trial report was used as the reference supplemented by additional details from secondary papers. The review authors corresponded with primary authors, where possible, to resolve any data queries.

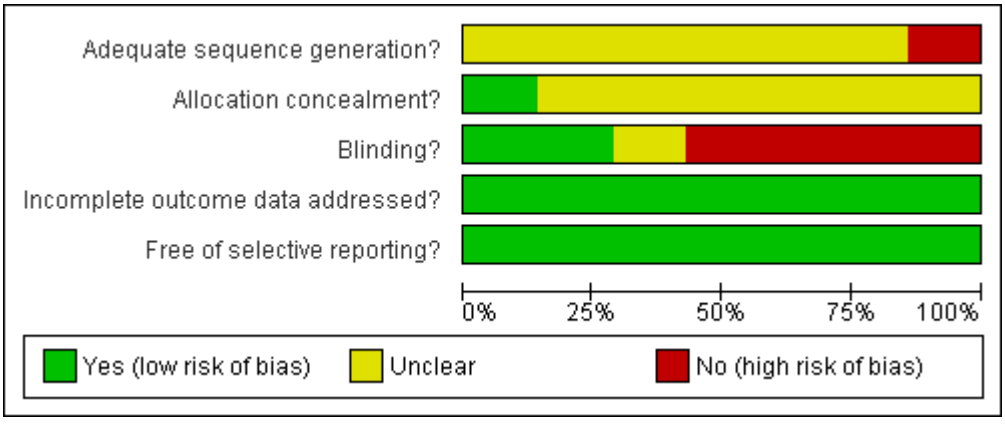
Assessment of risk of bias in included studies

The included studies were assessed for risk of bias. The Cochrane risk of bias assessment tool was used to assess:

- sequence generation;
- allocation concealment;
- blinding;
- completeness of the outcome data;
- selective outcome reporting;
- other potential sources of bias.

The selection of trials for inclusion in the original review was performed independently by the two review authors (MW, CS) after employing the search strategy described previously, and by MS and CF in the update (2009). The conclusions can be referred to in the 'Risk of bias' tables and Figure 1 and Figure 2.

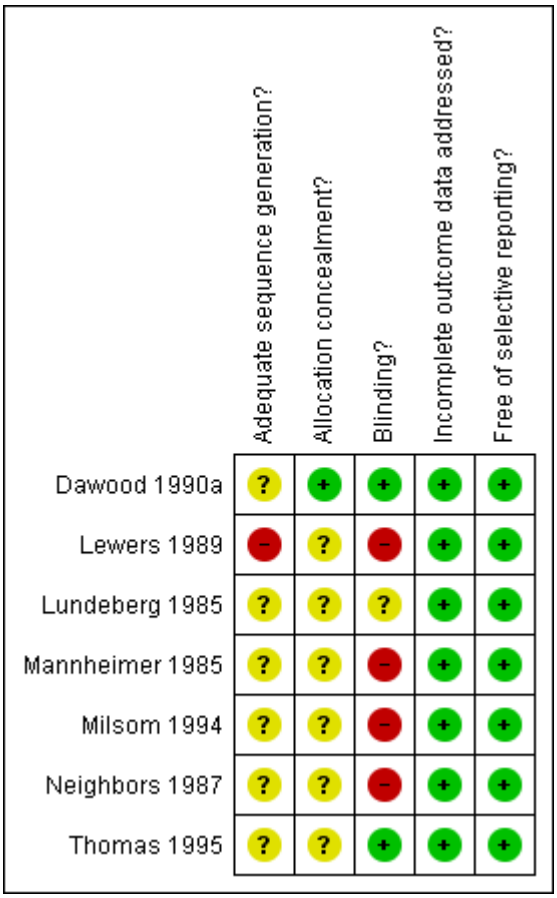
Figure 1 **Open in figure viewer** | **Download as PowerPoint**



Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

Figure 2

Open in figure viewer | Download as PowerPoint



Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

Additional information on trial methodology, original trial data, or both were sought from the authors of the majority of trials. This additional information was sought by sending letters, e-mail, or both to the authors of all the trials except Santiesteban 1985 (no current contact details for the authors could be found). Replies were received from Prof Dawood from the Dawood 1990a study, and D Lewers from the Lewers 1989 study; both supplied extra information regarding trial methodology. As no response was received from the trial by Santiesteban 1985 the study has been moved to the studies awaiting classification until we are able to confirm the methodology.

Measures of treatment effect

Statistical analyses were performed in accordance with the guidelines for statistical analysis developed by the Cochrane Menstrual Disorders and Subfertility Group. Where possible, the outcomes were pooled statistically. For dichotomous data (for example, proportion of participants with a specific adverse side

effect), results for each study were expressed as an odds ratio (OR) with 95% confidence interval (CI) and combined for meta-analysis with RevMan software using the Peto-modified Mantel-Haenszel method. Continuous differences between groups in the meta-analysis were shown as a mean difference (MD) and 95% CI. A fixed-effect model was used and heterogeneity between the results of different studies was examined by inspecting the scatter in the data points and the overlap in their CIs and more formally by checking the results of the Chi^2 tests. No significant heterogeneity was found among studies that were combined in the meta-analysis.

For a number of included studies we were not able to extract data that could be used in the meta-analysis. These data were included as descriptive data in 'other data' tables and can also be viewed in the 'Data and analyses' tables.

Unit of analysis issues

Four of the included studies were of crossover design (Dawood 1990a; Lundeberg 1985; Milsom 1994; Thomas 1995). Phase-one data (data prior to crossover) were not available for any of these trials. Crossover trials have been criticised for leading to invalid estimates of effect when the outcome measure used affects entry to subsequent phase of the trial (for example where pregnancy is the outcome of interest those becoming pregnant in phase one of the trial cannot be crossed over to the alternative treatment). In the case of this review, this problem is less of a concern as the main outcome measure is pain relief.

The only real concern is the potential for carryover effects of TENS from one menstrual cycle to another, which is likely to be minimal as all four crossover trials performed treatment during the menses only. Therefore, due to the small likelihood of bias, the small number of trials, and the minimal pooling of data in the meta-analysis, the results of the crossover trials were included in this review. The only instance where data from a parallel and crossover trial were pooled is for the outcome of overall experience of pain relief for low-frequency TENS versus placebo TENS. Both trials and the meta-analysis reported a non-significant result for this outcome and including or excluding the crossover data did not impact on this conclusion (Lundeberg 1985).

Dealing with missing data

Data were analysed on an intention-to-treat basis, as far as possible, and attempts were made to obtain missing data from the primary investigators, where possible.

Assessment of heterogeneity

The review authors considered whether the clinical and methodological characteristics of the included studies were sufficiently similar for meta-analysis to provide a meaningful summary. Statistical heterogeneity was assessed using the I^2 statistic. An $I^2 > 50\%$ was taken to imply substantial heterogeneity and further exploration was undertaken using sensitivity analyses to explain this, if required.

Assessment of reporting biases

The review authors aimed to minimise the potential impact of reporting bias by ensuring a comprehensive search for eligible studies and by being alert for duplication of data. A funnel plot was not possible due the limited number of studies included in the review.

Data synthesis

The data from the primary studies were combined using a fixed-effect model in the following comparisons.

1. High-frequency TENS versus placebo.
2. Low-frequency TENS versus placebo.
3. High-frequency TENS versus low-frequency TENS.
4. TENS versus medical treatment.

Subgroup analysis and investigation of heterogeneity

There was no planned subgroup analysis in this review.

Sensitivity analysis

In one trial, the mean pain relief figure reported in the trial (26.1) did not correlate with the reported scores for each participant that were also presented (46, 57, 60, 0, 0, 0, 41, 40, 1) (Mannheimer 1985). The authors of the trial did not respond to correspondence, therefore the mean used in the meta-analysis was not that reported in the report but was recalculated from the individual scores that were also given (a mean of 27.2). A sensitivity analysis using both means showed that there was very little difference in the ORs they elicited.

Updating the review

It is the intention of the review authors that a new search for RCTs will be carried out yearly and the review updated accordingly.

Results *available in* English | Español

Description of studies

Results of the search

Nine randomised controlled trials were identified that involved TENS for the treatment of dysmenorrhoea. Seven of these trials were included in this review, one was excluded, and one is awaiting classification.

Included studies

Three of the trials were of parallel design (Lewers 1989; Mannheimer 1985; Neighbors 1987) and four used a crossover design (Dawood 1990a; Lundeberg 1985; Milsom 1994; Thomas 1995).

Five of the trials specified the inclusion of women with primary dysmenorrhoea only. Four of these trials performed some type of physical or gynaecological examination to confirm the diagnosis of 'no pathology'. Other common exclusion criteria were the use of oral contraceptives (OCPs) or an IUD. The range of ages of participants included in all the trials was 15 to 38 years.

Physical treatment regimens are particularly difficult to administer consistently and there are additional problems associated with the use of placebo or sham techniques. Summarised below are details on how the included trials dealt with treatment consistency and the use of placebo or sham therapies. For additional information on trial characteristics see the table 'Characteristics of included studies'. For a summary of the TENS modalities used, such as frequencies and pulse width, see TENS modalities (Table 1; Table 2).

Table 1. TENS modalities - high frequency **Open in table viewer**

Study	Hz; freq; pulse rate	Pulse width	Intensity	Other
Dawood 1990	100	100 microsec	comfortable tingling	Tenzcare portable unit used
Lundeberg 1985	100	200 microsec	low intensity - below pain threshold	square wave pulses
Mannheimer	50-100	40-75 microsec	comfortable	
Milsom	70-100	200 microsec	high - 40-50 mA	
Thomas 1995	100	200 microsec	no info given	monopolar pulses

Table 2. TENS modalities - low frequency **Open in table viewer**

Study	Hz; freq; pulse rate	Pulse width	Intensity	Other
Lewers 1989	1	40 µsec	highest tolerable	Note this trial used msec - also called hyperstimulation
Lundeberg 1985	2	200 µsec	high, muscle contractions produces	pulse trains of 80 msec, 2/sec

Mannheimer 1985	1-4	100-250 µsec	to tolerance level, with visible rhythmic muscle contractions	
Neighbors 1987	1	40 µsec	increased to tolerance	
Santiesteban 1985	5	250 µsec	to tolerance level with minimum of palpable contractions	
Thomas 1995	2	200 µsec	no information	Trains of monopolar square wave pulses with a duration of 0.2 msec

Dawood 1990a (high-frequency TENS, placebo TENS, ibuprofen)
Women were treated with TENS for two cycles, placebo TENS for one cycle, and ibuprofen for one cycle; the treatment sequence was randomised. Portable TENS units were used and for high-frequency TENS the woman was able to adjust the amplitude to produce a comfortable tingling sensation or achieve satisfactory pain relief. The placebo TENS was set up in exactly the same way except the settings and amplitude did not produce any electrical stimulation. The participants and investigators were blinded to whether real or placebo TENS was being used, however for the ibuprofen cycle blinding was not possible. There was no information on how the investigators ensured that the TENS units were correctly used by the women, however daily logs were kept of the amount of TENS use per day.

Lewers 1989 (low-frequency TENS, placebo pill)
Women were randomly assigned to the experimental or control group. Both groups then participated in another study in which the electrical conductance of four auricular acupuncture points was measured, which involved acupressure to these four points. This additional treatment could have affected the main study results. After this study the women in the control group were given a placebo pill and put into the prone position for 30 minutes. The experimental group were hooked up to the TENS unit and also placed in the same position. The intensity of the TENS treatment was adjusted to the highest level tolerable by the participant.

Lundeberg 1985 (high-frequency TENS, low-frequency TENS, placebo TENS)
Women were treated with all three interventions during separate cycles. They were randomised to whichever treatment they received first. The electrodes used, their placement, and the procedure were kept the same for each treatment. For high-frequency TENS the stimulus intensity was below the pain threshold.

Electrodes were placed on the painful area (all participants complained of lower back pain) and TENS was applied for 20 minutes. If this resulted in pain relief then treatment was continued at the same stimulation point for a further 25 minutes. If there was no pain relief then electrodes were moved to either a trigger point or acupuncture point close to the area of pain. If no pain reduction was achieved at any of these points then electrodes were applied for 25 minutes within the painful area. For low-frequency TENS stimulus the

intensity produced muscular contractions. For placebo TENS the apparatus was lacking electrical output but women were told it was ultra-high frequency TENS and that they may not experience any cutaneous sensation.

Mannheimer 1985 (high-frequency TENS, low-frequency TENS, placebo TENS)
All women were instructed separately by the same experimenter in the use of TENS and the expected stimulation sensation for each group. Women were then randomised to: 1) conventional TENS, 2) acupuncture-like TENS, or 3) placebo TENS. The instructions the women received differed on a group basis by the method of adjusting stimulation parameters, electrode placement, and description of electrical sensations.

All participants used the same type of portable TENS unit and the only non-fixed variable was intensity of stimulation. Women in the conventional TENS group were instructed to use an intensity that produced a comfortable, perceptible paraesthesia without muscle contraction. The acupuncture-like TENS group were to use an intensity that produced visible rhythmic muscle contractions. The placebo-TENS group was told to set it at maximum and that they may or may not experience a mild tingling sensation. The placebo group was also told that if a LED light came on their unit was non-functional; this was not possible however as dead batteries were used.

All participants were given instruction cards that illustrated electrode placement. Placement was the same for groups one and three. Those in group two placed the electrodes on acupuncture points and were instructed how to find the area of greatest tenderness. Treatment for all groups was 30 minutes in duration then discontinued until pain returned; a record of use was kept. Pain was rated immediately before and after TENS use.

Milsom 1994 (high-frequency, high-intensity TENS, naproxen)
Women were randomly allocated to either high-intensity TENS or a single dose of naproxen (500 mg). Randomisation occurred after intrauterine pressure had been recorded for 30 minutes via a catheter. Treatment was performed at an outpatient clinic during the first 24 hours of the women's cycles. For the following cycle, participants received the therapy form not received in the first cycle.

For the TENS treatment electrodes were placed on the lower part of the abdomen and the back. It is unclear whether electrode placement was the same for all participants. The intensity of the electrical stimulation was gradually increased and women were informed that they might experience some pain. After 10 seconds, if the participant had not adapted to the intensity it was reduced to a more acceptable level. At 60 seconds of treatment the stimulator was switched off; if pain had not disappeared by this time then participants received a further 60 to 120 seconds of stimulation. Once analgesia had been achieved in the stimulated area some women felt pain in neighbouring regions. In these cases stimulation was repeated until pain relief was

obtained. No information was given about how many women received reduced intensity stimulation or additional stimulation. All measurements lasted at least four hours for both treatment groups; pain relief was measured every 15 minutes with women in the supine position.

Neighbors 1987 (low-frequency TENS, placebo pill)
Treatment was scheduled when the participant called to report pain. Participants were randomly allocated to low-frequency TENS or a placebo pill. All participants were positioned prone on a treatment table for 30 minutes. The placebo group were told they were taking a "drug that has been used in the past for pain relief". The TENS group had eight electrodes attached to four acupuncture points bilaterally and the TENS unit was started. The intensity was slowly increased to a level as intense as was tolerable. After five minutes the intensity was increased, if tolerable. Total treatment time was 30 minutes. Pain assessment occurred prior to treatment and immediately after; participants were sent home with further measures to be completed at 30, 90, and 150 minutes following treatment.

Thomas 1995 (acupuncture: manual stimulation, low-frequency electrical stimulation, high-frequency electrical stimulation, periosteal stimulation; TENS: low-frequency, high-frequency, and placebo TENS)
Acupuncture treatment was performed by one of two trained professionals, TENS treatment was administered by a trained physiotherapist. It is unclear how participants were placed in the TENS or acupuncture group. The acupuncture group were allocated to four different modes of treatment, one per cycle. Entry to the initial treatment was random and followed by the other treatments in a predetermined order, the fifth-cycle treatment was a mode of the participants's choice.

The TENS group were allocated to three different modes of treatment, one per cycle. Entry to the initial treatment was random and followed by the other treatments in a predetermined order, the fourth-cycle treatment was a mode of the participant's choice. For the placebo TENS group there was no electrical output to the electrodes and participants were told it was an ultra-high frequency mode where skin sensations might or might not be perceptible. All treatments (except periosteal stimulation) lasted 20 minutes; all outcome assessments were performed in the same manner. Two treatments were performed each cycle at approximately seven days and three days prior to the onset of menstruation.

Excluded studies

One trial was excluded from the review (Janke 1984). The trial compared low-frequency TENS with a control that was a mixture of high-frequency TENS and placebo TENS. This combination did not clearly fit any of the intended comparisons so the trial was excluded. For more information see the table 'Characteristics of excluded studies'.

Risk of bias in included studies

Allocation

One included study was given an allocation score of A as correspondence with the author revealed that random allocation was performed via a centralised randomisation process (Dawood 1990a). Other included studies were given an allocation score of B due to unclear allocation concealment, except Lewers 1989 which was given an allocation score of C for alternate allocation. One trial reported no information on randomisation or allocation (Thomas 1995). The remaining trials stated that allocation was random but failed to give adequate details regarding the method of allocation or concealment. This represents a source of potential bias.

Blinding

In one trial the participants and the investigators were both blind to assignment status (Dawood 1990a). In two trials only the participants were blinded (Lundeberg 1985; Mannheimer 1985). Two trials were open due to the different types of interventions used (that is TENs versus placebo pill or naproxen) (Lewers 1989; Milsom 1994). The remaining two trials gave no information regarding blinding of assignment status (Neighbors 1987; Thomas 1995); one of these trials was probably open as it compared TENS with a placebo pill, two quite different types of interventions (Neighbors 1987). The other trial involved two arms of treatment, acupuncture and TENS (Thomas 1995). While blinding may have been possible in the TENS arm, the four different types of acupuncture that were compared were too different for the women to have remained unaware of the differences in the interventions so double-blinding would have been impossible. Lack of blinding represents a potential source of bias.

Incomplete outcome data

All but one of the studies (Lewers 1989) analysed all the patients. Lewers 1989 did not analyse the final data from two patients but did use the last-observation-carried-forward method.

Selective reporting

All of the main outcomes were reported.

Other potential sources of bias

No other potential sources of bias were identified.

Effects of interventions

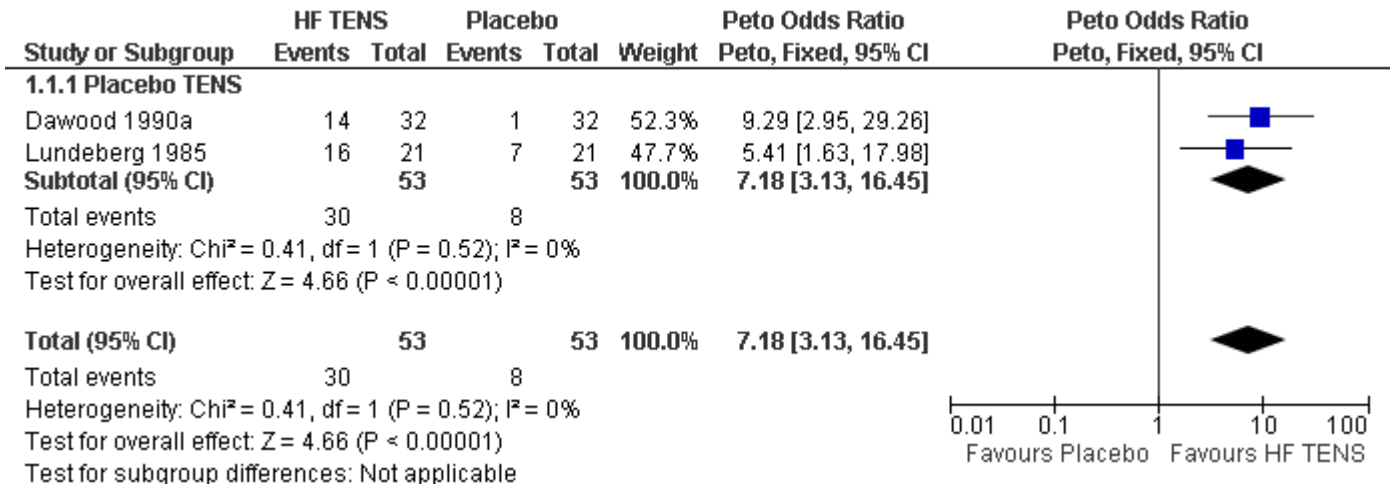
Overall seven studies that involved transcutaneous electrical nerve stimulation for the treatment of primary dysmenorrhoea were identified and included. The studies involved a total of 164 participants.

1) High-frequency TENS versus placebo

Refer to Figure 3

Figure 3

Open in figure viewer | Download as PowerPoint



Forest plot of comparison: 1 High Frequency TENS vs Placebo, outcome: 1.1 Pain relief - overall experience.

There were four studies comparing the use of high-frequency TENS with placebo TENS for the treatment of dysmenorrhoea (Dawood 1990a; Lundeberg 1985; Mannheimer 1985; Thomas 1995). Overall results showed that high-frequency TENS was more effective for pain relief than placebo TENS. For pain relief reported as a dichotomous variable the OR was 7.2 (95% CI 3.1 to 16.5) in favour of high-frequency TENS (two trials). When pain relief was measured with a VAS the weighted mean difference (WMD) was 45.0 (95% CI 22.5 to 67.5) in favour of high-frequency TENS (one trial). One trial could not be included in the meta-analysis due to the form in which results were reported but was included as descriptive data; it found no difference between high-frequency TENS and placebo TENS for pain relief.

Only one of the trials reported any adverse effects associated with treatment (Dawood 1990a): 4/32 women using high-frequency TENS experienced muscle vibrations, tightness, and headaches after use and slight redness or burning of the skin (OR 8.2, 95% CI 1.1 to 60.9). There were no reported adverse effects from placebo TENS.

Two trials reported data on the use of analgesics additional to the TENS treatment (Dawood 1990a;Thomas 1995). There was no significant difference in the number of women needing additional analgesics between high-frequency and placebo TENS (one trial; OR 0.3, 95% CI 0.1 to 1.1). There was also no significant difference in the number of analgesic tablets taken between the two groups (one trial; WMD 0.1, 95% CI -2.1 to 2.4).

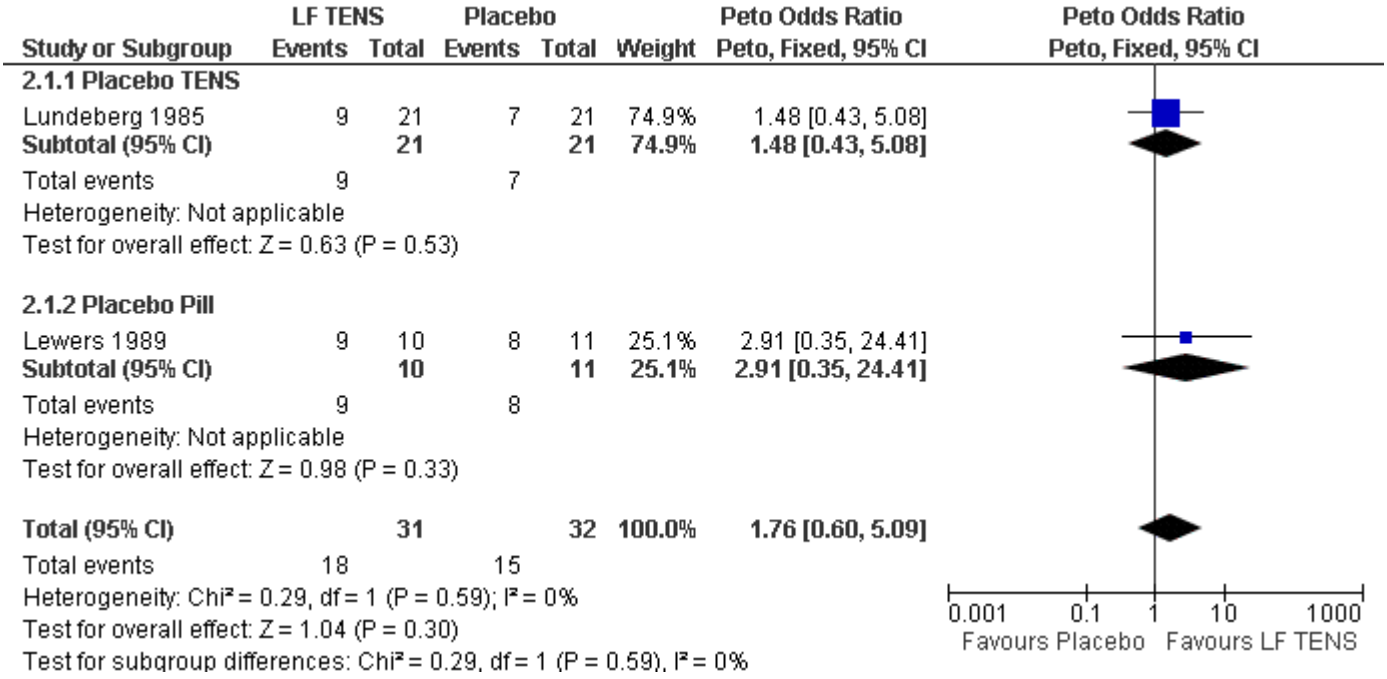
One trial reported absence from work or school as the number of lost hours per menstrual cycle (Thomas 1995). There was no significant difference between high-frequency and placebo TENS for this outcome (WMD 0.04, 95% CI -0.4 to 0.5).

2) Low-frequency TENS versus placebo

Refer to Figure 4 and Figure 5

Figure 4

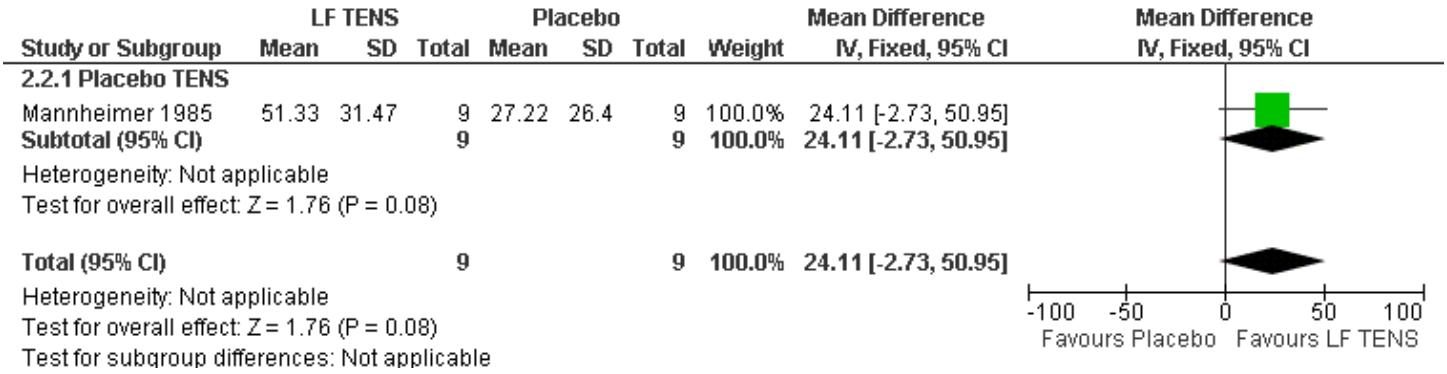
Open in figure viewer | **Download as PowerPoint**



Forest plot of comparison: 2 Low Frequency TENS vs Placebo, outcome: 2.1 Pain relief - overall experience.

Figure 5

Open in figure viewer | **Download as PowerPoint**



Forest plot of comparison: 2 Low Frequency TENS vs Placebo, outcome: 2.2 Pain relief - 100pt VAS.

There were three studies comparing the use of low-frequency TENS with placebo TENS (Lundeberg 1985; Mannheimer 1985; Thomas 1995) and two studies comparing low-frequency TENS with a placebo pill (Lewers 1989; Neighbors 1987) for the treatment of dysmenorrhoea. Overall results suggested no significant difference between low-frequency TENS and placebo TENS or a placebo pill for pain relief. For pain relief reported as a dichotomous variable the OR was 1.48 (95% CI 0.43 to 5.08) when comparing low-frequency TENS and placebo TENS (one trial); and the OR was 2.9 (95% CI 0.35, 24.4) when comparing low-frequency TENS and placebo pill (one trial). When pain relief was measured using a VAS the WMD was 24.1 (95% CI -2.73 to 51.95; 1 trial). Two trials could not be included in the meta-analysis due to the form the results were reported in but they were included as descriptive data. One trial comparing low-frequency TENS and placebo TENS reported a significant difference between low-frequency TENS and placebo TENS in pain relief ($P < 0.05$); the other trial showed that low-frequency TENS was more effective at reducing pain than a placebo pill ($P < 0.05$).

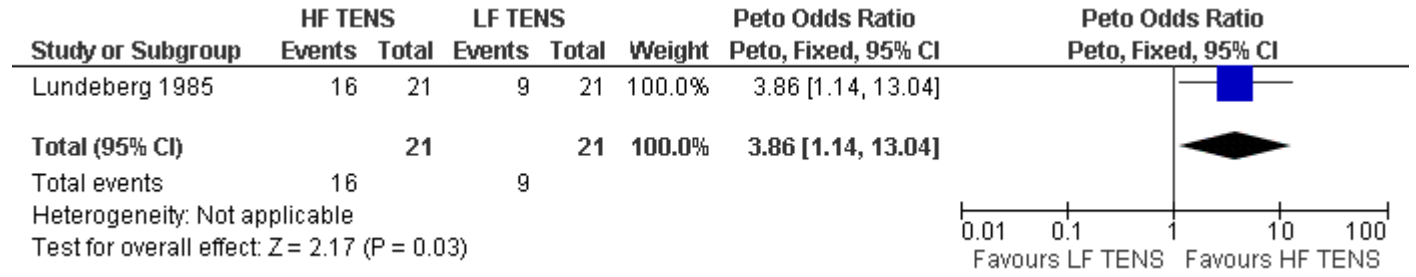
Only one trial reported any information on adverse effects (Lewers 1989) and found there were none in either the TENS group or the placebo pill group.

One trial reported on the number of tablets of additional analgesic used (Thomas 1995): the low-frequency TENS group used significantly less than the placebo TENS group (WMD -3.1, 95% CI -5.5 to -0.7). No significant difference was reported between the two groups for absence from work or school (Thomas 1995) (WMD -0.2, 95% CI -0.6 to 0.2).

3) High-frequency TENS versus low-frequency TENS

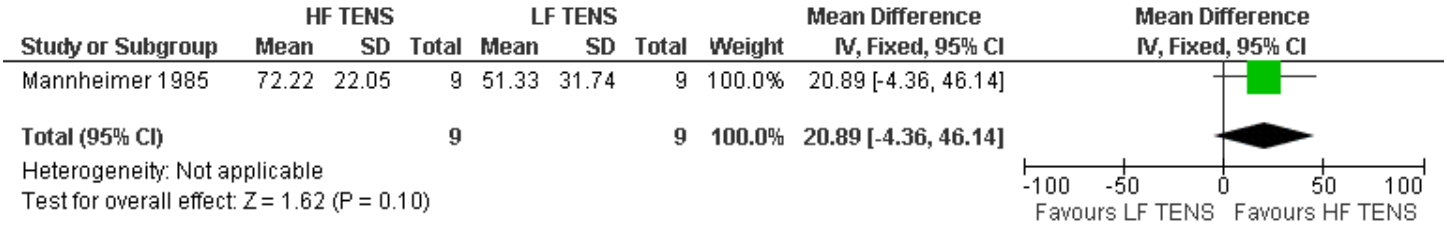
There were three studies that compared high-frequency TENS with low-frequency TENS for the treatment of dysmenorrhoea (Lundeberg 1985; Mannheimer 1985; Thomas 1995). For pain relief reported as a dichotomous variable the OR was 3.9 (95% CI 1.1 to 13.0; 1 trial) in favour of high-frequency TENS (Figure 6). When pain relief was measured with a VAS the WMD was 20.9 (95% CI -4.4 to 46.1) showing no significant difference between the two types of TENS but a trend towards high-frequency TENS as achieving more pain relief (one trial) (Mannheimer 1985); see Figure 7. One trial could not be included in the meta-analysis due to the form the results were reported in and was included as descriptive data, it found low-frequency TENS to be more likely to reduce pain than high-frequency TENS.

Figure 6 **Open in figure viewer** | **Download as PowerPoint**



Forest plot of comparison: 3 High Frequency TENS vs Low Frequency TENS, outcome: 3.1 Pain relief - overall experience.

Figure 7 **Open in figure viewer** | **Download as PowerPoint**



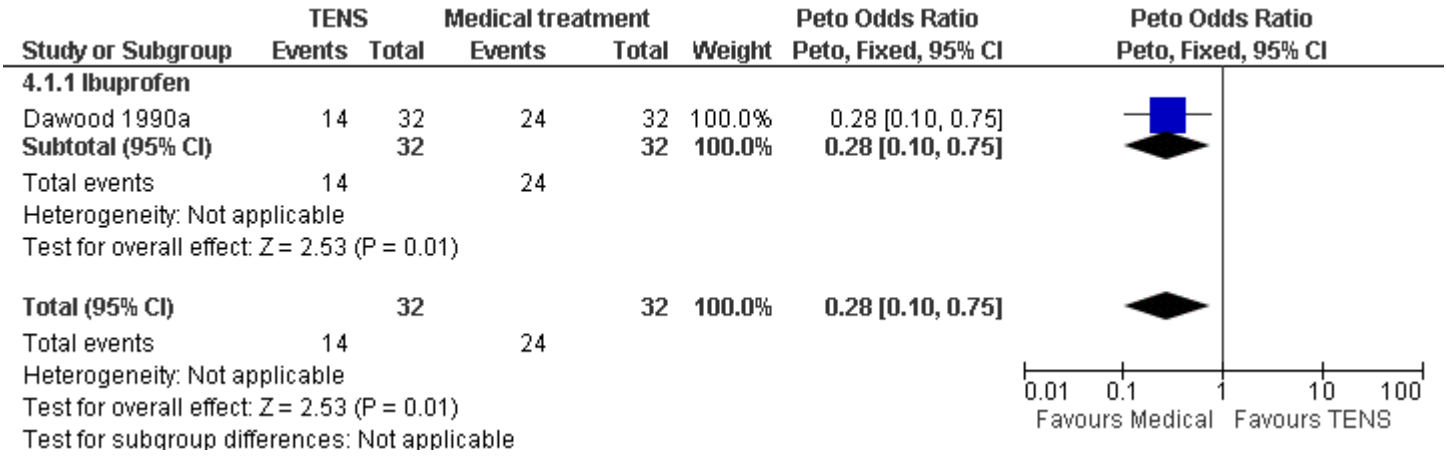
Forest plot of comparison: 3 High Frequency TENS vs Low Frequency TENS, outcome: 3.2 Pain relief - 100pt VAS.

There was a significant difference in favour of low-frequency TENS for the number of analgesic tablets taken in addition to TENS treatment (WMD 3.2, 95% CI 0.5 to 5.9). There was no significant difference between the two groups for the outcome of absence from work or school (WMD 0.2, 95% CI -0.2 to 0.6) (Thomas 1995).

4) TENS versus medical treatment

There were two trials that compared a medical therapy with TENS (Dawood 1990a); Milsom 1994). One trial compared ibuprofen (a non-steroidal anti-inflammatory drug) with high-frequency TENS (Dawood 1990a). For the outcome of pain relief reported as a dichotomous variable ibuprofen proved to be significantly better at reducing pain (OR 0.3, 95% CI 0.1 to 0.8). This trial reported no significant difference between the two treatments for additional use of analgesics (OR 0.4, 95% CI 0.1 to 1.4) (Figure 8).

Figure 8 **Open in figure viewer** | **Download as PowerPoint**



Forest plot of comparison: 4 TENS vs Medical Treatment, outcome: 4.1 Pain relief - overall experience.

Another trial compared high-frequency, high-intensity TENS with naproxen (a non-steroidal anti-inflammatory drug) (Milsom 1994). For the outcome of pain relief there was no significant difference in the pain scores for each group. This trial is reported as descriptive data as it could not be used in the meta-analysis.

There was a significant difference between high-frequency TENS and ibuprofen in the number of adverse effects experienced by participants (OR 26.7, 95% CI 5.5 to 130.9); 10/12 women in the TENS group experienced pain from the treatment while no adverse effects were reported by those taking ibuprofen. The women who reported pain from TENS stated that they were prepared to accept the short-term pain from the treatment in return for relief of dysmenorrhoea.

Discussion *available in* English | Español

Summary of main results

This review aimed to assess the effectiveness of TENS and acupuncture for the treatment of primary dysmenorrhoea. Despite the growing popularity of complementary therapies there is a general lack of well-designed research to evaluate the effectiveness of these therapies to treat specific conditions.

Currently available data suggests that high-frequency TENS is effective in reducing primary dysmenorrhoea. Overall, high-frequency TENS was shown to be more effective for pain relief than placebo TENS. Low-frequency TENS was found to be no different in reducing pain than placebo TENS although there is a trend

towards efficacy. There were conflicting results regarding whether high-frequency TENS is more effective than low-frequency TENS. The small number of participants in the majority of included trials is reflected by the wide confidence intervals and lack of precision in many of the comparisons, meaning that clear recommendations for practice cannot be made.

TENS may be an alternative treatment option for women with dysmenorrhoea who wish to stop using non-steroidal anti-inflammatory drugs (NSAIDs), oral contraceptives, or other analgesics because the existing medication is ineffective, has unacceptable adverse effects, or due to personal choice. An effective non-pharmacological method of treating dysmenorrhoea would be of great potential value in treating dysmenorrhoea; however, there are a number of problems with the trials included in this review and research into physical therapies in general.

Overall completeness and applicability of evidence

The evidence reported here represents small studies which may not be adequately powered to answer the clinical question. The participants and outcomes are representative and valid.

Quality of the evidence

The data presented in this review were from seven RCTs involving 164 women with dysmenorrhoea. The main methodological problems are explored below in the potential biases but are also represented by the small number of women included in the studies and the lack of data which could be entered into a meta-analysis. Blinding of this type of intervention is methodologically difficult and rarely conducted.

Potential biases in the review process

Use of a control or placebo group

A difficult issue in all randomised controlled trials of physical and complementary therapies is the choice of an adequate control or placebo treatment. To control adequately for all the factors that may contribute to the treatment as a comparable placebo treatment, rather than a waiting list control or a no-treatment control, is preferable. Placebo TENS typically consists of TENS units and electrodes set up just like the real TENS but with no electrical output to the electrodes. This means the only potential difference in treatment is the lack of physical stimulation of the skin, making it a good control that can be easily blinded. Placebo TENS can also take the form of working electrodes attached to the wrong meridian points although this is not necessarily an effective control as there is a theoretical opportunity to create adverse effects or possibly a therapeutic effect by stimulating any meridian or acupuncture point. There is no guarantee that using mock TENS on a part of the meridian or other point will have no effect.

Another important aspect to the design of the control arm of these trials is to ensure that participants remain blinded to their group allocation. One way to achieve this is to recruit participants naive to the treatment being evaluated.

Blinding

Double blinding (both the participant and the treatment provider) in physical therapies is generally considered impossible as the treatment provider needs to physically deliver the treatment or placebo. Single blinding (of the participant) is also considered difficult, especially if the control is a different type of treatment for example TENS versus a placebo pill.

Standardisation of treatment

Physical therapies are performed with variations by treatment providers. Treatment is often individually tailored to each participant's set of symptoms. Even if this is not the case the different therapists vary the duration of treatment, the exact placement of electrodes, the frequency of electrical stimulation, frequency of treatments, timing of treatments in the cycle, the number of treatments performed, and the individuality of treatment; for example stimulation intensity and pulse duration are often adjusted to participants' tolerance levels.

Traditional versus western medical approach

TENS uses meridian points for the placement of electrodes. The western approach often advocates placement in the areas that are painful (for example the abdomen and the lower back). These different approaches to dysmenorrhoea can affect how treatments are performed, who receives treatment, and the end results for the outcomes measured. The impact of these factors on treatment outcome is not clear as these types of variations between practitioners of TENS can also be found in conventional medicine.

Other methodological issues

With TENS some of the included trials used self-administered treatment whereas others were physician administered. For self-administered treatments the tendency is to place electrodes on the painful areas, while physician-administered treatments are more likely to be administered on meridian points.

Another aspect that could affect the evaluation of the treatments is the differences in the physiological effects of the two different types of TENS. With high-frequency TENS a small portable unit can be used, therefore users are able to carry on daily activities. However with low-frequency TENS the low rate triggers rhythmic muscle contractions which make it difficult for women to carry out daily activities.

References

References to studies included in this review

Jump to: **excluded studies** | **studies awaiting assessment** | **additional references** | **other published versions**

Dawood 1990a {published data only}

Dawood MY, Ramos J. Transcutaneous electrical nerve stimulation (TENS) for the treatment of primary dysmenorrhea: a randomized crossover comparison with placebo TENS and ibuprofen. *Obstetrics and Gynecology* 1990;75(4):656-60.

PubMed | **CAS** | **Web of Science® Times Cited: 30**

Lewers 1989 {published data only}

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Link to article | **PubMed** | **CAS** | **Web of Science® Times Cited: 7**

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Link to article | **PubMed** | **CAS** | **Web of Science® Times Cited: 20**

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Mannheimer JS, Whalen EC. The efficacy of transcutaneous electrical nerve stimulation in dysmenorrhea. *Clinical Journal of Pain* 1985;1(2):75-83.

Link to article

Milsom 1994 {published data only}

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PubMed | **CAS**

Milsom I, Hedner N, Mannheimer C. A comparative study of the effect of high intensity transcutaneous nerve stimulation and oral naproxen on intrauterine pressure and menstrual pain in patients with primary dysmenorrhea. *American Journal of Obstetrics and Gynecology* 1994;170(1):123-9.

Link to article | **PubMed** | **CAS** | **Web of Science® Times Cited: 28**

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Link to article

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References to studies excluded from this review

Jump to: **included studies** | **studies awaiting assessment** | **additional references** | **other published versions**

Janke 1984 {published data only}

Janke CL. *Transcutaneous electrical nerve stimulation for pain relief in dysmenorrhoea [Master's thesis]* . Birmingham, Alabama: University of Alabama in Birmingham, 1984.

References to studies awaiting assessment

Jump to: **included studies** | **excluded studies** | **additional references** | **other published versions**

Santiesteban 1985 {published data only}

Santiesteban AJ, Burnham TL, George KL, Kita PJ, Mehring EA. Primary spasmodic dysmenorrhea: the use of TENS on acupuncture points. *American Journal of Acupuncture* 1985;13(1):35-42.

Web of Science® Times Cited: 2

Additional references

Jump to: **included studies** | **excluded studies** | **studies awaiting assessment** | **other published versions**

Carroll 1996

Carroll D, Tramer M, McQuay H, Nye B, Moore A. Randomization is important in studies with pain outcomes: Systematic review of transcutaneous electrical nerve stimulation in acute postoperative pain. *British Journal of Anaesthesia* 1996;77:798-803.

Link to article | **PubMed** | **CAS** | **Web of Science® Times Cited: 69**

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Dawood MY. Ibuprofen and dysmenorrhea. *The American Journal of Medicine* 1984;77(1A):87-94.

Link to article | **PubMed** | **CAS** | **Web of Science® Times Cited: 43**

Dawood 1990b

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Link to article | **PubMed** | **CAS** | **Web of Science® Times Cited: 2**

Gersh 1985

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Link to article | **PubMed** | **CAS** | **Web of Science® Times Cited: 25**

Kaplan 1997

Kaplan B, Rabinerson D, Pardo J, Krieser RU, Neri A. Transcutaneous electrical nerve stimulation (TENS) as a pain-relief device in obstetrics and gynecology. *Clinical and Experimental Obstetrics & Gynecology* 1997;24(3):123-6.

PubMed | **CAS**

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Osiri M, Welch V, Brosseau L, Shea B, McGowan J, Tugwell P, Wells G. Transcutaneous electrical nerve stimulation for knee osteoarthritis (Cochrane Review). *Cochrane Database of Systematic Reviews* 2001, Issue 1. [DOI: 10.1002/14651858.CD002823.]

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Link to article | **PubMed** | **CAS** | **Web of Science® Times Cited: 1**

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PubMed | **CAS** | **Web of Science® Times Cited: 7**

References to other published versions of this review

Jump to: **included studies** | **excluded studies** | **studies awaiting assessment** | **additional references**

Proctor 2002

Proctor ML, Smith CA, Farquhar CM, Stones RW. Transcutaneous electrical nerve stimulation and acupuncture for primary dysmenorrhoea. *Cochrane Database of Systematic Reviews* 2002, Issue 1. [DOI: 10.1002/14651858]

Characteristics of studies

Characteristics of included studies [ordered by study ID]

Dawood 1990a

Methods	Randomised - method unstated in published trial. Communication from author stated it was a centralised randomisation process Double blind - for type of TENS intervention Crossover design 32 women randomised and analysed Communication from author states that intention-to-treat analysis and a power calculation were used however no details were provided
Participants	Inclusion: severe primary dysmenorrhoea (diagnosed according to "predefined clinical criteria", regular cycles) Exclusion: OCP use Age: mean 28.5 (5.2) years Location: USA

Interventions	1. Ibuprofen 400 mg every 6 hrs for 3 days 2. High-frequency TENS (conventional) - 100 pulses/sec, 100 µsec pulse width, amplitude comfortable tingling 3. Placebo TENS Location: abdomen (portable unit) Duration: first 8hrs of cycle, then when needed for pain relief 5 cycles - TENS 2 cycles, placebo TENS 1 cycle, ibuprofen 1 cycle (sequence random)
Outcomes	Pain relief - scale 1-5 Menstrual symptom questionnaire Use of pain medication
Notes	Author supplied some unpublished methodological information No information or baseline comparison on the groups pain characteristics

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	"..enrolled in a randomized crossover study" - method unstated in published trial.
Allocation concealment?	Low risk	No details provided. Communication from author stated it was a centralised randomisation process.
Blinding? All outcomes	Low risk	Double blind - for type of TENS intervention. "subjects and investigators were blinded as to the type of transcutaneous electrical nerve stimulator..."
Incomplete outcome data addressed? All outcomes	Low risk	All patients followed up, no apparent drop outs.
Free of selective reporting?	Low risk	All relevant outcomes reported.

Lewers 1989

Methods	Random - unstated in published trial. Correspondence with authors showed randomisation was done by flipping a coin for the first person and alternate assignment for other participants No blinding Parallel design 21 participants randomised and analysed (pain data estimated for two participants for last two recordings, 180min and next morning)

Participants	Inclusion: primary dysmenorrhoea, pelvic exam in previous two years that showed no pathology Age: 20-38, mean 25.9 years Location: USA
Interventions	1. Low-frequency TENS - low rate 1 pulse/sec, highest intensity tolerable, pulse duration low, 40 msec 2. Placebo pill Location: 4 points, bladder 21 and 29 (back), spleen 6 and stomach 36 (legs) Duration: 30 min, 1 cycle
Outcomes	Pain scales - VAS and the pain rating index from McGill measured pre, post, 30, 60, 120, 180 min, next morning upon awakening
Notes	No information on the baseline similarities of the randomised groups Immediately after collection of baseline measurements all women received auricular acupressure, as part of another study prior to the intervention.

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	High risk	"Subjects were assigned randomly". No further details in paper. Correspondence with authors showed randomisation was done by flipping a coin for the first person and alternate assignment for other participants.
Allocation concealment?	Unclear risk	No details provided.
Blinding? All outcomes	High risk	No blinding.
Incomplete outcome data addressed? All outcomes	Low risk	Two participants in the experimental group did not complete posttreatment measures as they were asleep and needing to take additional medication, therefore used last value carried forward.
Free of selective reporting?	Low risk	Main outcome measures were reported.

Lundeberg 1985

Methods	Random - method unstated Single blind, participant was blind but other unclear Crossover design 21 women randomised and analysed

Participants	Inclusion: primary dysmenorrhoea, gynaecological exam to rule out pathology Age: average 22, 15-29 years Location: Sweden
Interventions	1. High-frequency TENS - duration 0.2 msec, freq 100 Hz 2. Low-frequency TENS - duration 0.2 msec, freq 2 Hz 3. Placebo TENS Location: source of pain, lower back or abdomen Duration: 45 min treatment once every month On fourth month patient given treatment of choice and asked to compare with 500mg naproxen, fifth month asked to compare with 120mg verapamil (calcium-channel blocker)
Outcomes	Pain intensity VAS 0-10 McGill pain questionnaire
Notes	No difference in baseline scores

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	"Randomly assigned to one of three groups", no further details.
Allocation concealment?	Unclear risk	Unclear.
Blinding? All outcomes	Unclear risk	Single blind, participant was blind but other unclear.
Incomplete outcome data addressed? All outcomes	Low risk	All 21 patients were analysed.
Free of selective reporting?	Low risk	All major and relevant outcomes reported on.

Mannheimer 1985

Methods	Random - unstated Parallel design 27 women randomised
Participants	Inclusion: dysmenorrhoea, abdominal pain, women who were not previous users of TENS Exclusion: OCP use, any precautions or contraindications to treatment, only lower back pain Age: 19-27, mean 22.1 years Location: USA

Interventions	1. Conventional high-freq TENS - 50-100 Hz, narrow pulse 40-75 µsec, intensity produces no muscle contractions 2. Acupuncture-like low-frequency TENS - 1-4 Hz, pulse 100-250 µsec, intensity to tolerance 3. Control - placebo TENS Location: conventional and control used electrodes on abdomen, acupuncture-like TENS used points spleen 6 and 10 (legs) Duration: 30 min - until pain returned
Outcomes	Pain ratings - pre and post treatment Duration of pain relief
Notes	No information on the baseline similarities of the randomised groups

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	"randomly assigned" no further details.
Allocation concealment?	Unclear risk	Unclear.
Blinding? All outcomes	High risk	No details of blinding.
Incomplete outcome data addressed? All outcomes	Low risk	All patients were analysed.
Free of selective reporting?	Low risk	All relevant outcomes were reported.

Milsom 1994

Methods	Random - unstated No blinding Crossover design 12 women randomised and analysed
Participants	Inclusion: severe primary dysmenorrhoea, abdomen and back pain Exclusion: OCP, IUD, pelvic pathology on gynaecological exam Age: mean 23.8 (0.8) years Location: Sweden
Interventions	1. High frequency and intensity TENS - 70-100 Hz, 0.2 msec current/pulse duration, intensity 40-50 mA 2. Naproxen - single dose 500mg Location: electrodes placed on lower abdomen and back Duration: until pain free (2 cycles, one treatment per cycle)

Outcomes	Pain score - 1-5 scale every 15 min for 240 min Uterine activity Side effects
Notes	No difference in baseline scores

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	"randomised", no further details.
Allocation concealment?	Unclear risk	Unclear, no details.
Blinding? All outcomes	High risk	Open-label study, no blinding.
Incomplete outcome data addressed? All outcomes	Low risk	All patients analysed.
Free of selective reporting?	Low risk	All relevant outcomes were reported.

Neighbors 1987

Methods	Random - unstated No blinding Parallel design, 20 women randomised and analysed
Participants	Inclusion: dysmenorrhoea, pelvic exam in last two years that had shown no pelvic pathology Age: 19-38 years Location: USA
Interventions	1. Low-frequency TENS - pulse width 40 msec, rate 1 pulse/sec, intensity 0 mA then increased to tolerance 2. Placebo pill Location: bladder 21 and 29 (back), spleen 6 and stomach 36 (legs) Duration: 30min
Outcomes	Pain scales - VAS and abbreviated McGill Measured pre, post, 30 min, 1 hr, 2 hr
Notes	Check this is low frequency No difference in baseline scores

Risk of bias

Bias	Authors' judgement	Support for judgement

Adequate sequence generation?	Unclear risk	"randomly assigned" no further details.
Allocation concealment?	Unclear risk	Unclear, no details.
Blinding? All outcomes	High risk	No evidence of blinding.
Incomplete outcome data addressed? All outcomes	Low risk	All patients analysed.
Free of selective reporting?	Low risk	All relevant outcomes were reported.

Thomas 1995

Methods	Not stated if random Blinding unclear Crossover design 31 women randomised, 29 analysed
Participants	Inclusion: primary dysmenorrhoea, previous ineffective treatment with NSAIDs, contraindications to NSAIDs, gynaecological exam to rule out pathology, women with no previous use of TENS Age: mean 30.2 (7.3) years Location: Sweden
Interventions	7 treatments - participants split into two groups: TENS or acupuncture Duration: 20 min treatment, 7 days and 3 days prior to onset of menstruation every month Acupuncture treatments: different mode each month for 4 months then preferred treatment for 5th month Location: 5 points, bladder 32 (back, bilateral), abdomen CV4, spleen 9 and 6 (legs) 1. manual stimulation at insertion, every 5 min 2. low-frequency electrical stimulation at 2 Hz to evoke muscle contractions 3. high-frequency 100 Hz, intensity adjusted to comfort level 4. periosteal stimulation (for 30 sec) 3 or 4 times for each point TENS treatments: 3 different modes for 3 months, patients preferred treatment for 4th month, pulse duration 0.2 msec Location: Thoracic 10 to Lumbar 1 1. Low-frequency TENS, 2 Hz 2. High-frequency TENS, 100 Hz 3. Placebo TENS
Outcomes	Pain scale - VAS Blood loss Nausea Hours of work lost Analgesics taken (no mention of type or dose) Subjective assessment

Notes	No information on the baseline similarities of the randomised groups

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	"randomised although serial order was maintained".
Allocation concealment?	Unclear risk	Unclear.
Blinding? All outcomes	Low risk	Participants were blinded.
Incomplete outcome data addressed? All outcomes	Low risk	All patients analysed.
Free of selective reporting?	Low risk	All relevant outcomes were reported.

OCP: oral contraceptive pill

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion

Study	Reason for exclusion
Janke 1984	The trial compared low-frequency TENS with a control that was a mixture of high-frequency TENS and placebo TENS. This combination did not clearly fit any of the intended comparisons of the review so the trial was excluded. Methods: low-frequency TENS, high-frequency TENS, and placebo TENS Participants were divided into two treatment groups. The experimental group received low-frequency TENS to four acupuncture points bilaterally. Intensity of stimulation was adjusted to a level as intense as tolerable for 30 min (varied from 35-70 amps). If the participant reached the maximum intensity and could take a stronger stimulation the pulse width was adjusted to a tolerable level for 30 min (varied from 40-100 msec). The control group received high-frequency TENS to four non-acupuncture points close to the acupuncture points used in the experimental group, the intensity was adjusted to a just noticeable level. Electrodes were also placed on the same back points as those used for the experimental group but current was not delivered. Outcome assessment was the same for both treatment groups. Not stated if random No information on blinding Parallel design 20 participants, 10 in each group No drop outs Participants: Inclusion: self-reported dysmenorrhoea, aged between 18-40 years Exclusion: known pelvic pathology, other medical problems, use of NSAIDs or other pain medication 4 hr prior to treatment Age: mean 25.7, range 19-40 years Location: Alabama, USA Source: volunteers from university area Interventions: 1. Experimental group acupuncture-like (low rate) TENS over four acupuncture points bilaterally, intensity 0 mA initially (adjusted to a level as intense as tolerable between 35-70 mA), pulse width 40 msec initially (adjusted to within 40-100 msec as tolerable, rate 1pulse/sec 2. Control group of conventional TENs to 4 non-acupuncture points, rate 40 pulses/sec width 100msec. Electrodes were also placed on 4 acupuncture points but no current delivered. Location: Acupuncture points Spleen 6, Stomach 36, Bladder 21, Bladder 29 were used for the experimental group. For the control electrodes were placed on B21 and B29 bilaterally but not stimulated. Two non-acupuncture points on the leg near ST36 and SP6 were stimulated Duration: 30 min treatment while subject was experiencing dysmenorrhoea, for one cycle Outcomes: Pain scores - VAS (0-10 cm) and McGill Pain Rating Index (scores 1-78) taken at baseline, 30, 60, 90, 150, 210 min after start of treatment. Raw data reported for each participant

Characteristics of studies awaiting assessment [ordered by study ID]

Santiesteban 1985

Methods	Participants blinded Parallel design 8 women randomised and analysed
Participants	Inclusion: dysmenorrhoea Exclusion: any medication Age: average 22 years Location: USA
Interventions	1. Low-frequency TENS - 5 Hz pulse rate, 250 µsec, pulse duration/intensity to patients tolerance 2. Sham (mock) TENS - no intensity administered Duration: 30 min Location: Spleen 6, Gallbladder 34 (on legs)
Outcomes	Pain scale 1-5 measured pre, post, 4 hrs, 24 hrs, 30 days Abdominal pain Back pain
Notes	No difference between the experimental and control group for pretreatment abdominal pain, however there was some difference for pretreatment back pain with the control group having a higher average pain rating

Data and analyses

Comparison 1. High-frequency TENS versus placebo **Open in table viewer**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain relief - overall experience Show forest plot	2	106	Peto Odds Ratio (Peto, Fixed, 95% CI)	7.18 [3.13, 16.45]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 1.1

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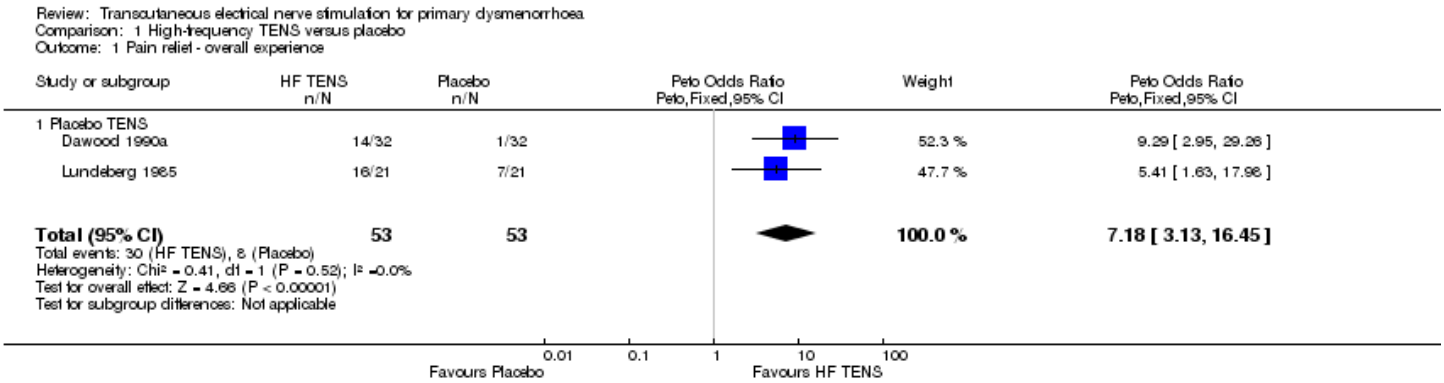

Comparison 1 High-frequency TENS versus placebo, Outcome 1 Pain relief - overall experience.

1.1 Placebo TENS	2	106	Peto Odds Ratio (Peto, Fixed, 95% CI)	7.18 [3.13, 16.45]
2 Pain relief - 100pt VAS Show forest plot	1	18	Mean Difference (IV, Fixed, 95% CI)	45.0 [22.53, 67.47]

Analysis 1.2

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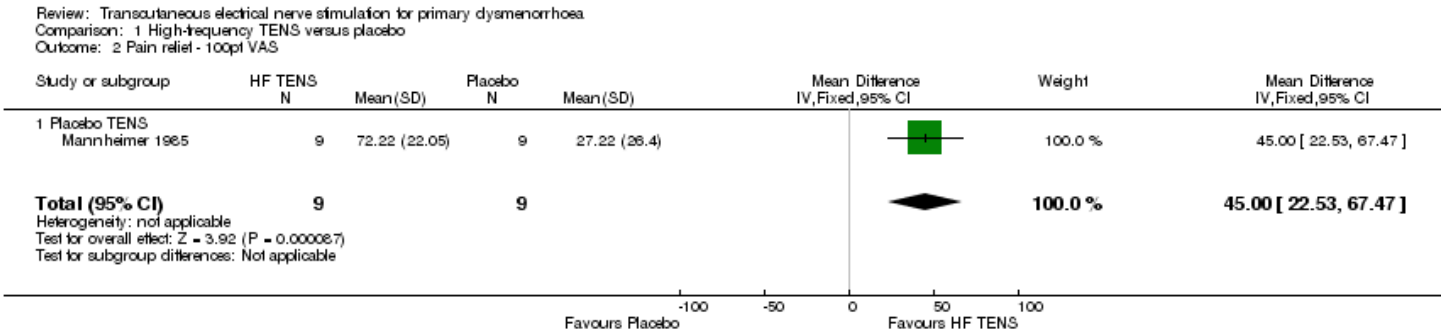

Comparison 1 High-frequency TENS versus placebo, Outcome 2 Pain relief - 100pt VAS.

2.1 Placebo TENS	1	18	Mean Difference (IV, Fixed, 95% CI)	45.0 [22.53, 67.47]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3 Pain relief - descriptive data Show forest plot			Other data	No numeric data

Analysis 1.3

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Comparison 1 High-frequency TENS versus placebo, Outcome 3 Pain relief - descriptive data.

3.1 Placebo TENS			Other data	No numeric data
4 Adverse effects Show forest plot	1	64	Peto Odds Ratio (Peto, Fixed, 95% CI)	8.17 [1.10, 60.85]

Analysis 1.4

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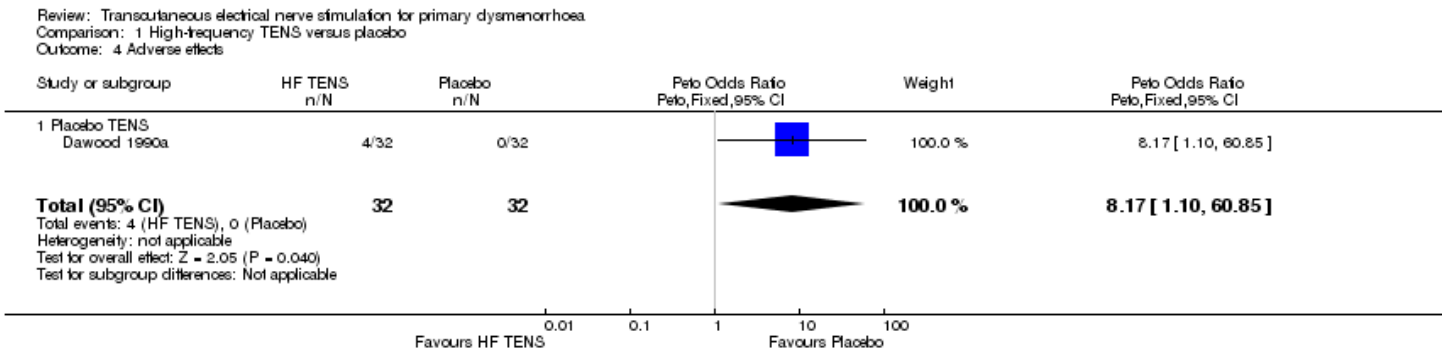


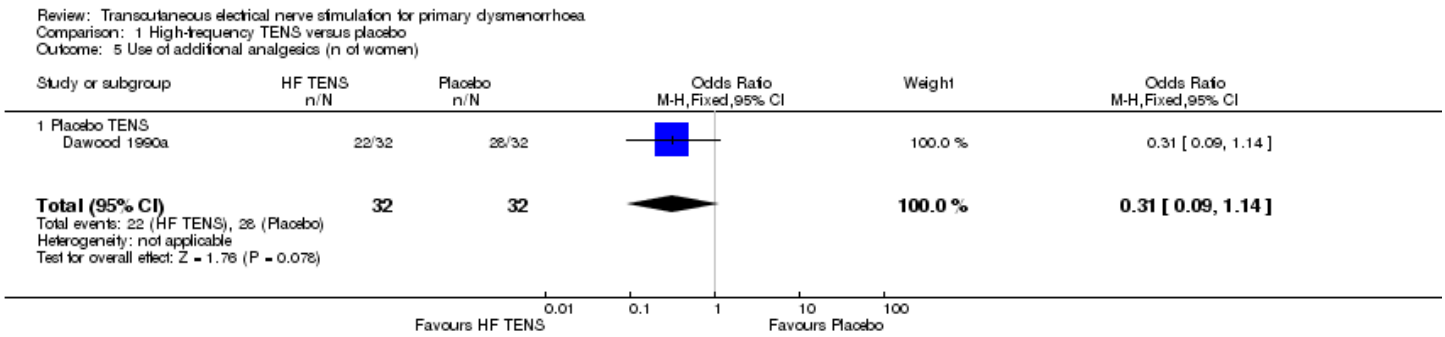
Comparison 1 High-frequency TENS versus placebo, Outcome 4 Adverse effects.

4.1 Placebo TENS	1	64	Peto Odds Ratio (Peto, Fixed, 95% CI)	8.17 [1.10, 60.85]
5 Use of additional analgesics (n of women) Show forest plot	1	64	Odds Ratio (M-H, Fixed, 95% CI)	0.31 [0.09, 1.14]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 1.5

Open in figure viewer | Download as PowerPoint

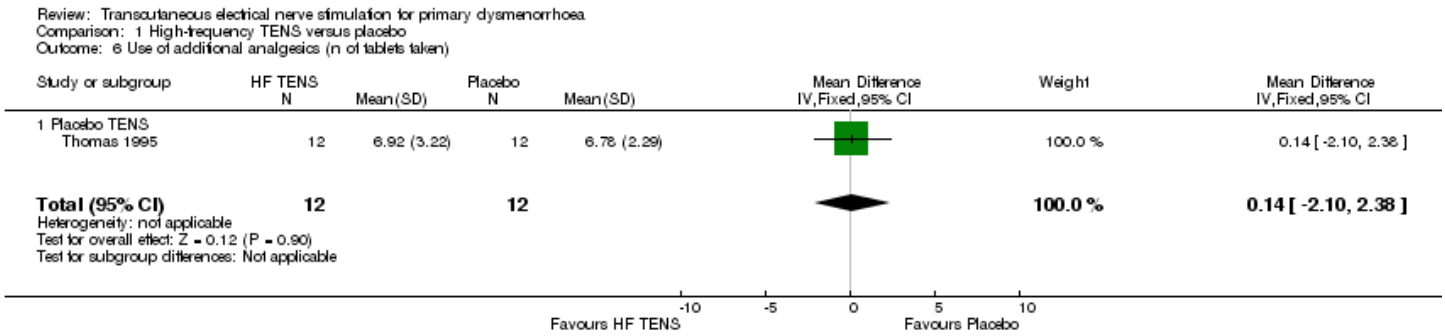


Comparison 1 High-frequency TENS versus placebo, Outcome 5 Use of additional analgesics (n of women).

5.1 Placebo TENS	1	64	Odds Ratio (M-H, Fixed, 95% CI)	0.31 [0.09, 1.14]
6 Use of additional analgesics (n of tablets taken) Show forest plot	1	24	Mean Difference (IV, Fixed, 95% CI)	0.14 [-2.10, 2.38]

Analysis 1.6

Open in figure viewer | Download as PowerPoint



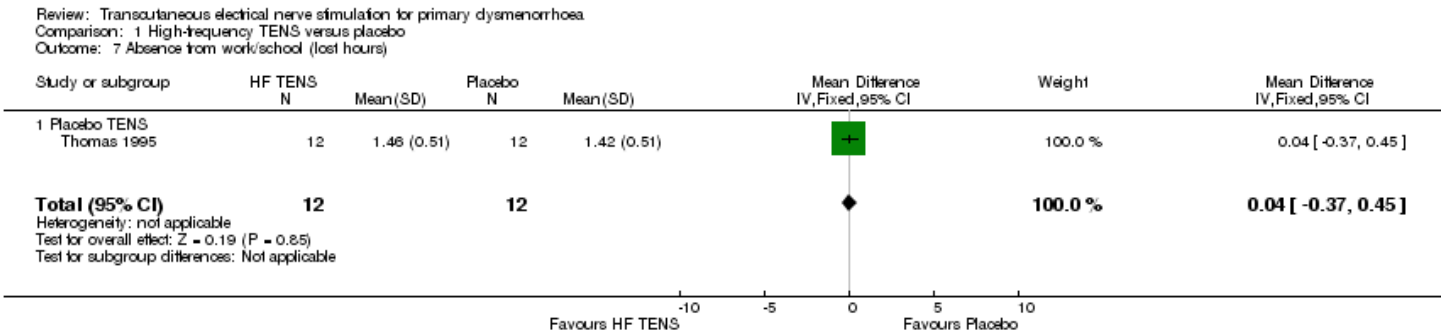
Comparison 1 High-frequency TENS versus placebo, Outcome 6 Use of additional analgesics (n of tablets taken).

6.1 Placebo TENS	1	24	Mean Difference (IV, Fixed, 95% CI)	0.14 [-2.10, 2.38]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7 Absence from work/school (lost hours) Show forest plot	1	24	Mean Difference (IV, Fixed, 95% CI)	0.04 [-0.37, 0.45]

Analysis 1.7

Open in figure viewer | Download as PowerPoint



Comparison 1 High-frequency TENS versus placebo, Outcome 7 Absence from work/school (lost hours).

7.1 Placebo TENS	1	24	Mean Difference (IV, Fixed, 95% CI)	0.04 [-0.37, 0.45]

Comparison 2. Low-frequency TENS versus placebo

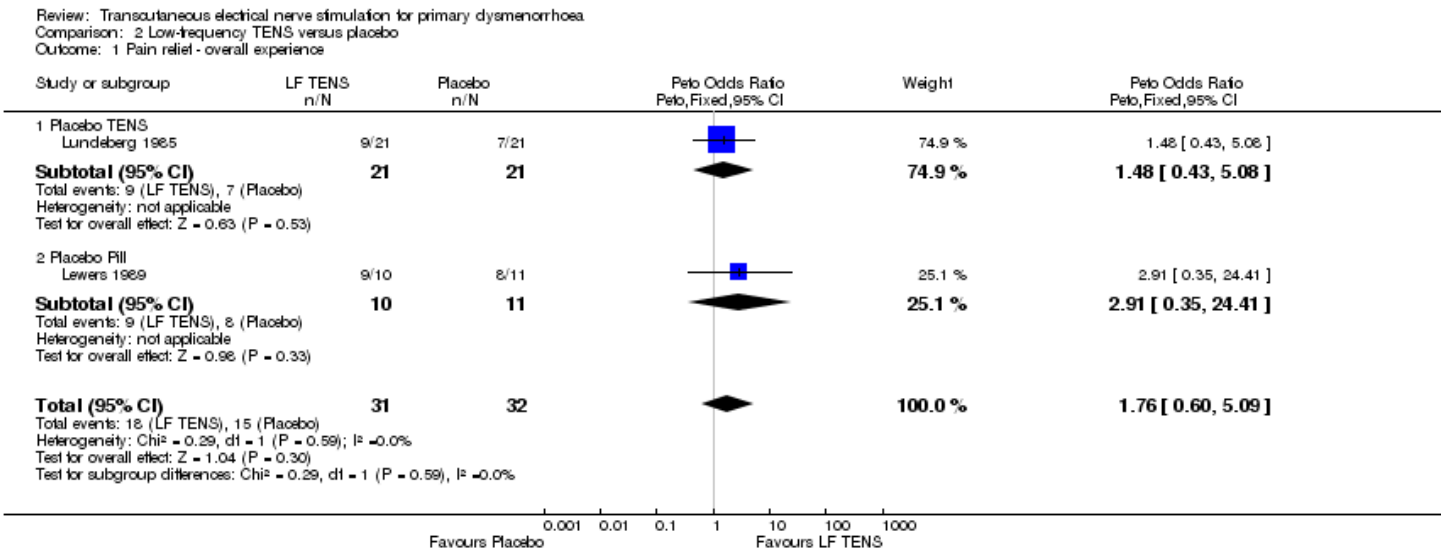
Open in table viewer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain relief - overall experience Show forest plot	2	63	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.76 [0.60, 5.09]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 2.1

Open in figure viewer | Download as PowerPoint



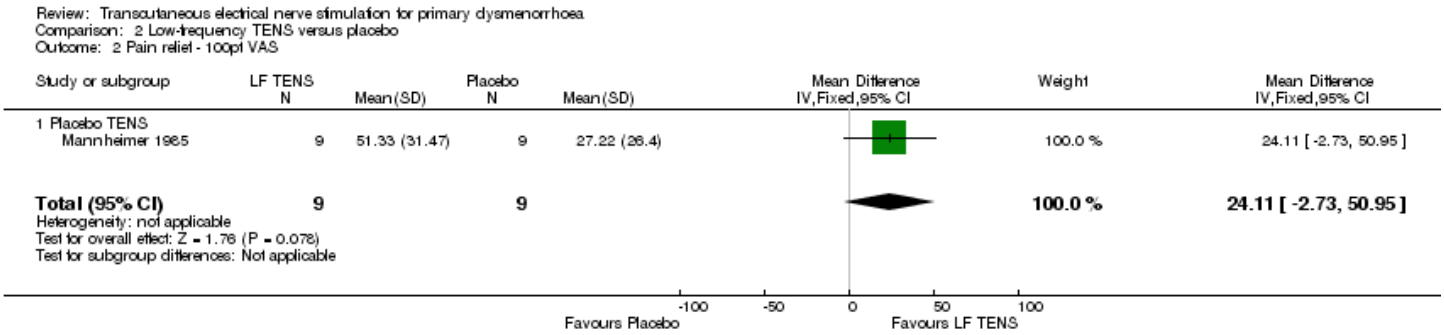
Comparison 2 Low-frequency TENS versus placebo, Outcome 1 Pain relief - overall experience.

1.1 Placebo TENS	1	42	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.48 [0.43, 5.08]
1.2 Placebo Pill	1	21	Peto Odds Ratio (Peto, Fixed, 95% CI)	2.91 [0.35, 24.41]
2 Pain relief - 100pt VAS Show forest plot	1	18	Mean Difference (IV, Fixed, 95% CI)	24.11 [-2.73, 50.95]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 2.2

Open in figure viewer | Download as PowerPoint



Comparison 2 Low-frequency TENS versus placebo, Outcome 2 Pain relief - 100pt VAS.

2.1 Placebo TENS	1	18	Mean Difference (IV, Fixed, 95% CI)	24.11 [-2.73, 50.95]
3 Pain relief - descriptive data Show forest plot			Other data	No numeric data

Analysis 2.3

Open in figure viewer | Download as PowerPoint

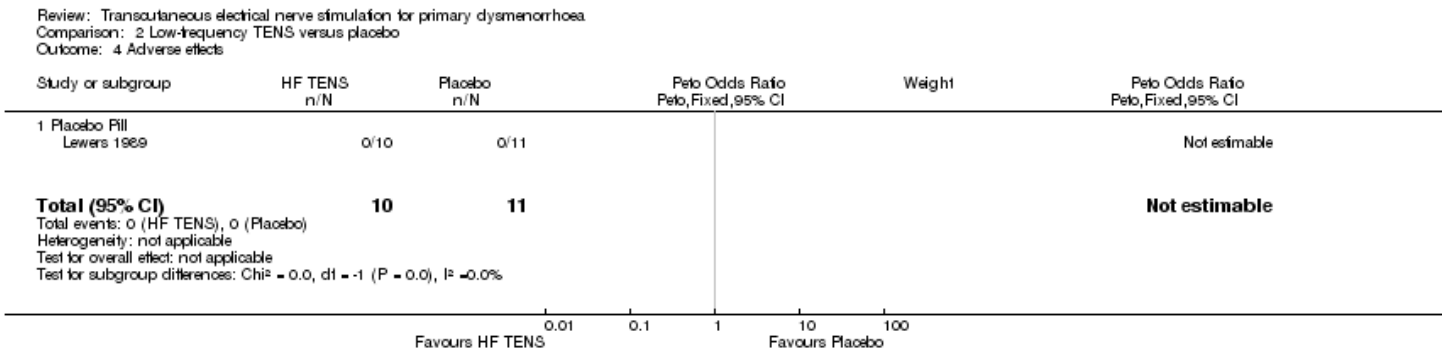
Comparison 2 Low-frequency TENS versus placebo, Outcome 3 Pain relief - descriptive data.

3.1 Placebo TENS			Other data	No numeric data
3.2 Placebo Pill			Other data	No numeric data
4 Adverse effects Show forest plot	1	21	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 2.4

Open in figure viewer | Download as PowerPoint

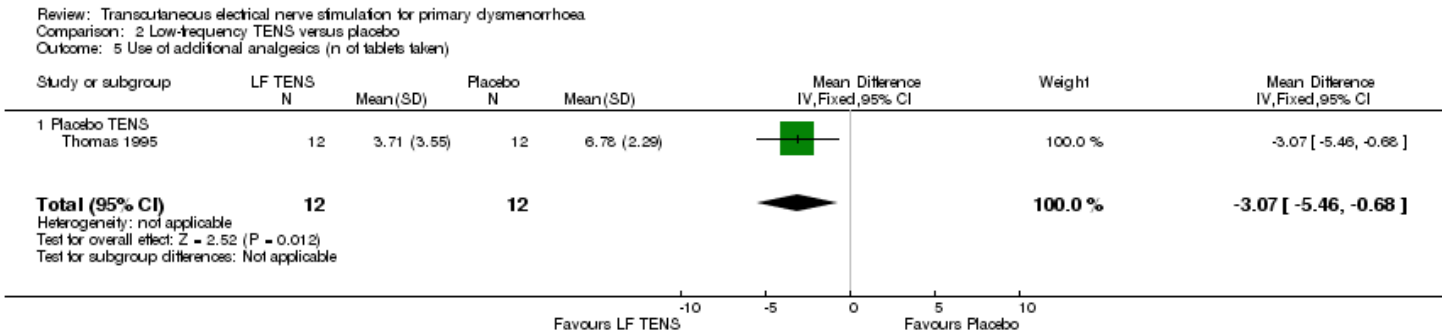


Comparison 2 Low-frequency TENS versus placebo, Outcome 4 Adverse effects.

4.1 Placebo Pill	1	21	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Use of additional analgesics (n of tablets taken) Show forest plot	1	24	Mean Difference (IV, Fixed, 95% CI)	-3.07 [-5.46, -0.68]

Analysis 2.5

Open in figure viewer | Download as PowerPoint



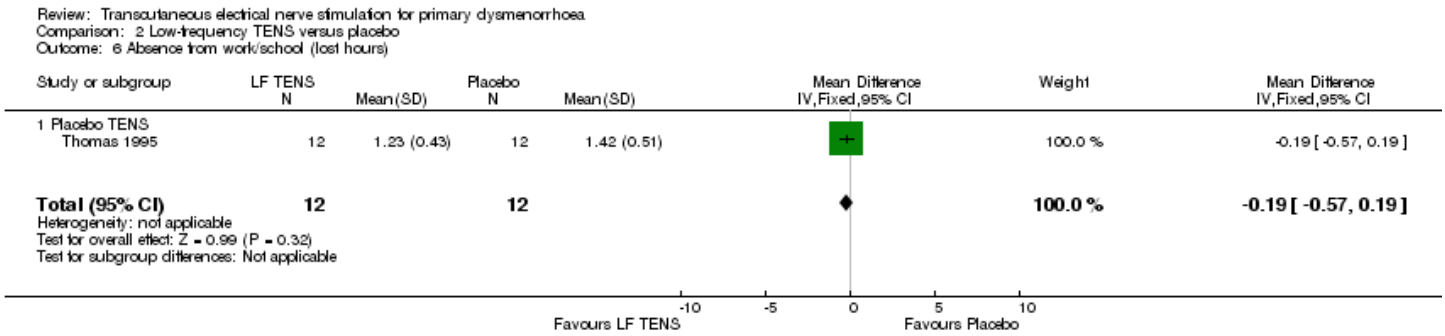
Comparison 2 Low-frequency TENS versus placebo, Outcome 5 Use of additional analgesics (n of tablets taken).

5.1 Placebo TENS	1	24	Mean Difference (IV, Fixed, 95% CI)	-3.07 [-5.46, -0.68]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6 Absence from work/school (lost hours) Show forest plot	1	24	Mean Difference (IV, Fixed, 95% CI)	-0.19 [-0.57, 0.19]

Analysis 2.6

Open in figure viewer | Download as PowerPoint



Comparison 2 Low-frequency TENS versus placebo, Outcome 6 Absence from work/school (lost hours).

6.1 Placebo TENS	1	24	Mean Difference (IV, Fixed, 95% CI)	-0.19 [-0.57, 0.19]

Comparison 3. High-frequency TENS versus low-frequency TENS

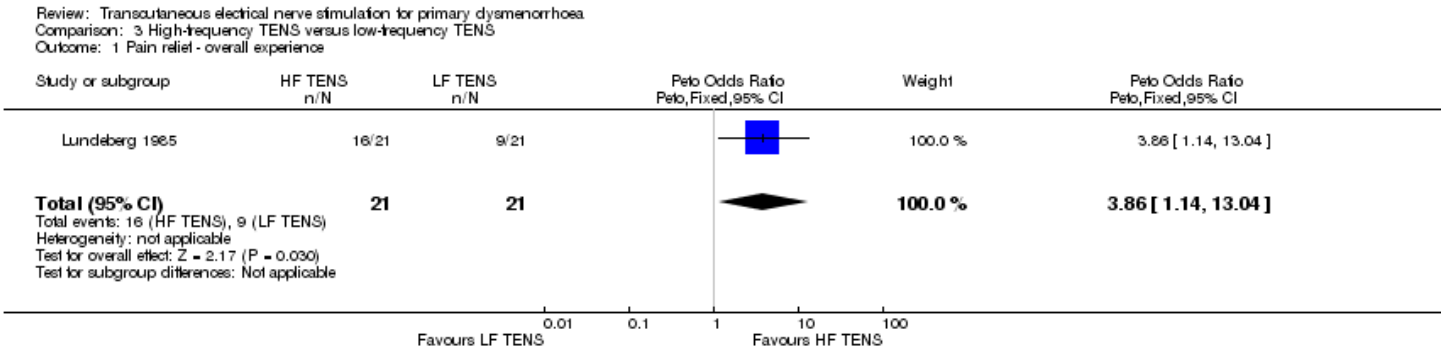
Open in table viewer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain relief - overall experience Show forest plot	1	42	Peto Odds Ratio (Peto, Fixed, 95% CI)	3.86 [1.14, 13.04]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 3.1

Open in figure viewer | Download as PowerPoint

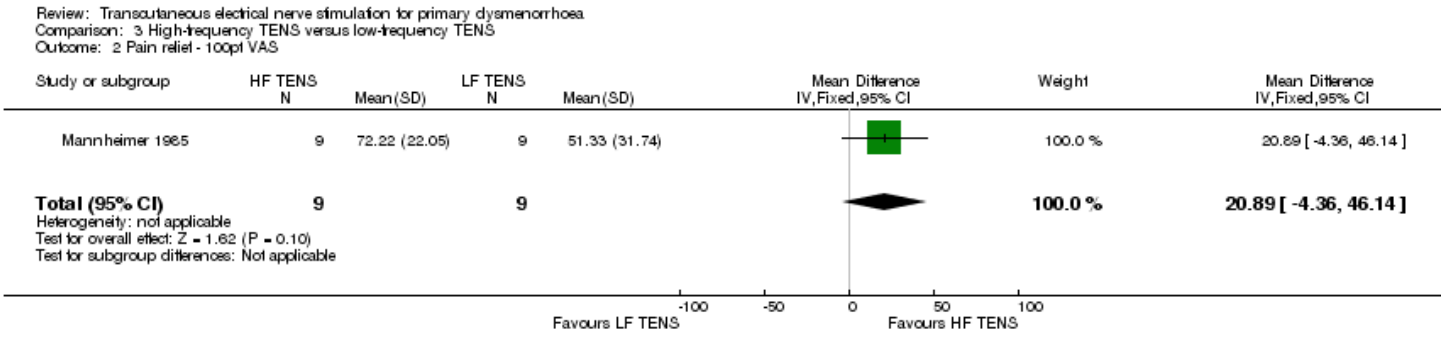


Comparison 3 High-frequency TENS versus low-frequency TENS, Outcome 1 Pain relief - overall experience.

2 Pain relief - 100pt VAS Show forest plot	1	18	Mean Difference (IV, Fixed, 95% CI)	20.89 [-4.36, 46.14]

Analysis 3.2

Open in figure viewer | Download as PowerPoint



Comparison 3 High-frequency TENS versus low-frequency TENS, Outcome 2 Pain relief - 100pt VAS.

3 Pain relief - descriptive data Show forest plot			Other data	No numeric data

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 3.3

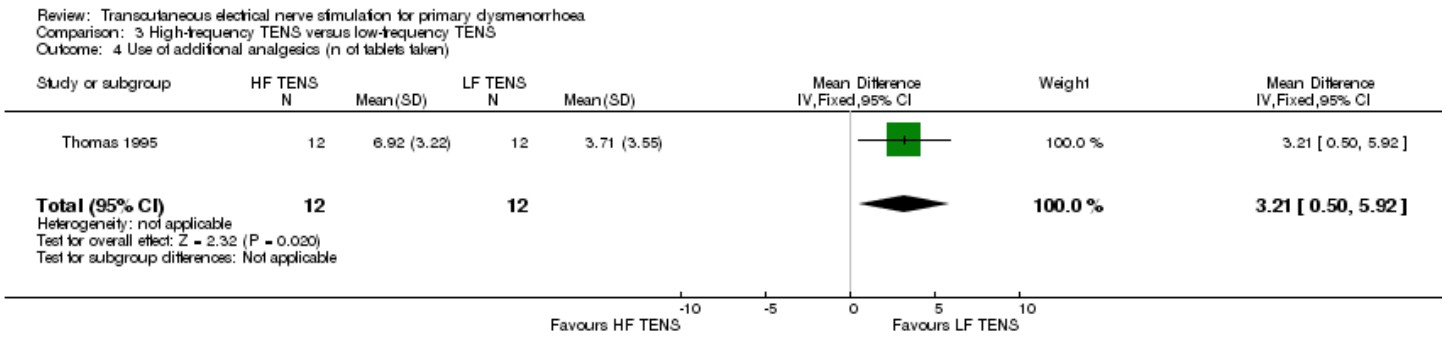
Open in figure viewer | Download as PowerPoint

Comparison 3 High-frequency TENS versus low-frequency TENS, Outcome 3 Pain relief - descriptive data.

4 Use of additional analgesics (n of tablets taken) Show forest plot	1	24	Mean Difference (IV, Fixed, 95% CI)	3.21 [0.50, 5.92]

Analysis 3.4

Open in figure viewer | Download as PowerPoint



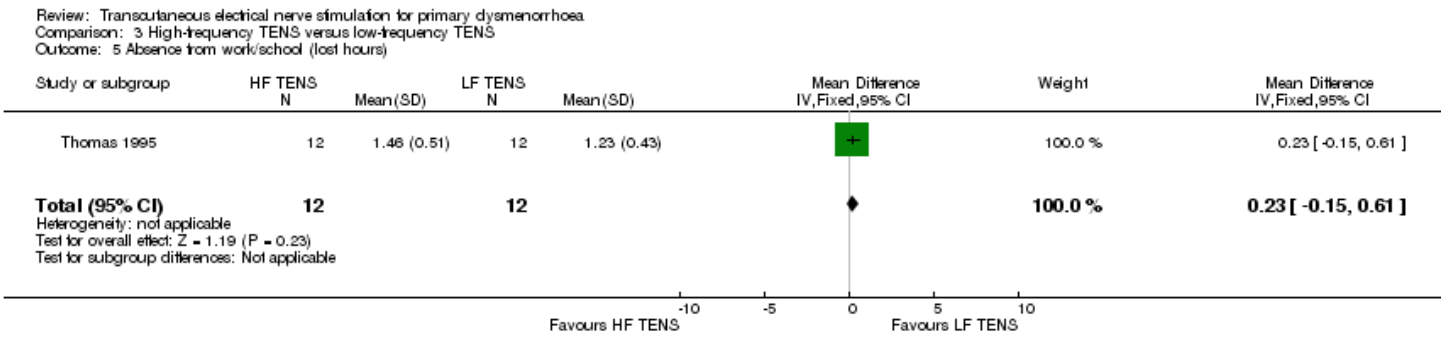
Comparison 3 High-frequency TENS versus low-frequency TENS, Outcome 4 Use of additional analgesics (n of tablets taken).

5 Absence from work/school (lost hours) Show forest plot	1	24	Mean Difference (IV, Fixed, 95% CI)	0.23 [-0.15, 0.61]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 3.5

Open in figure viewer | Download as PowerPoint



Comparison 3 High-frequency TENS versus low-frequency TENS, Outcome 5 Absence from work/school (lost hours).

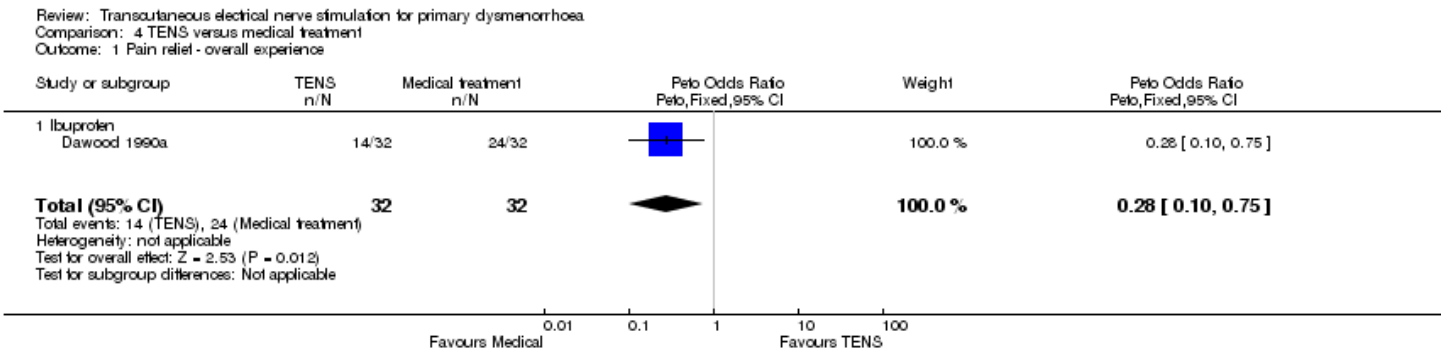
Comparison 4. TENS versus medical treatment

Open in table viewer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain relief - overall experience Show forest plot	1	64	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.28 [0.10, 0.75]

Analysis 4.1

Open in figure viewer | Download as PowerPoint



Comparison 4 TENS versus medical treatment, Outcome 1 Pain relief - overall experience.

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Ibuprofen	1	64	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.28 [0.10, 0.75]
2 Pain relief - descriptive data Show forest plot			Other data	No numeric data

Analysis 4.2

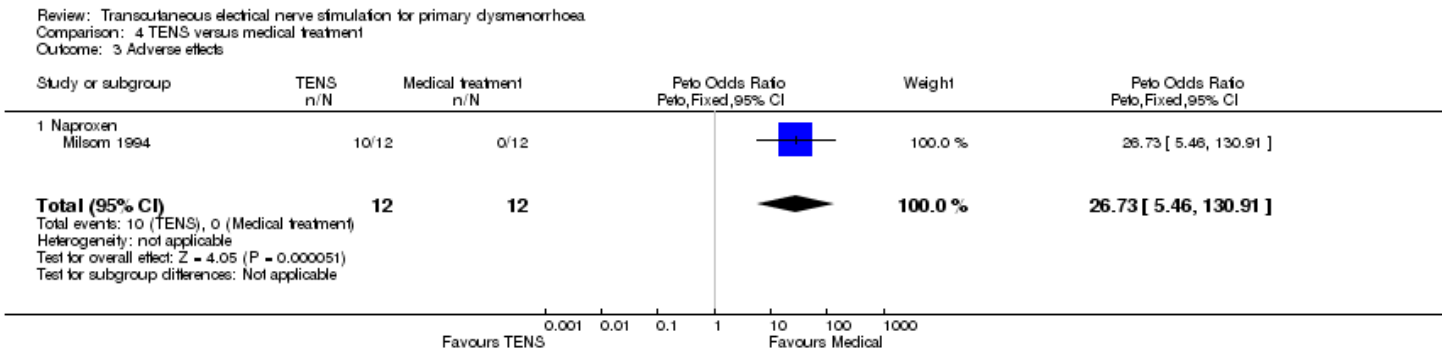
Open in figure viewer | Download as PowerPoint

Comparison 4 TENS versus medical treatment, Outcome 2 Pain relief - descriptive data.

2.1 Naproxen			Other data	No numeric data
3 Adverse effects Show forest plot	1	24	Peto Odds Ratio (Peto, Fixed, 95% CI)	26.73 [5.46, 130.91]

Analysis 4.3

Open in figure viewer | Download as PowerPoint



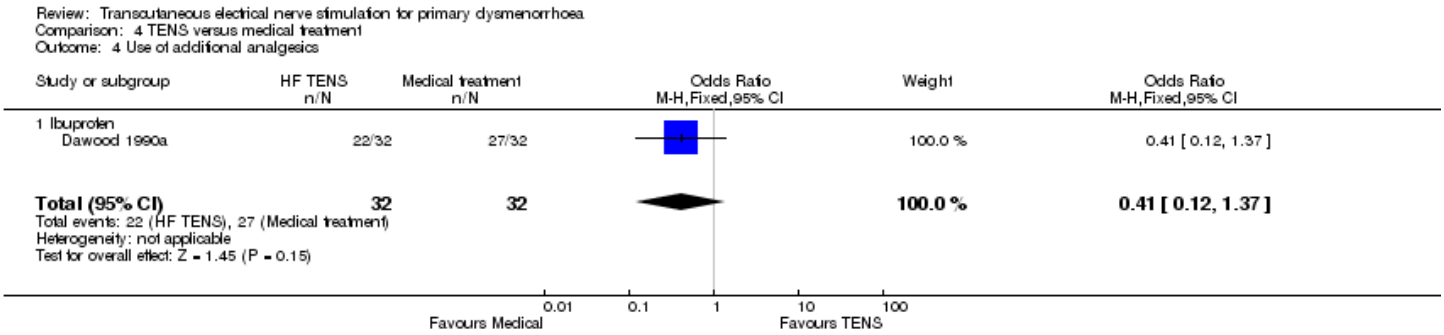
Comparison 4 TENS versus medical treatment, Outcome 3 Adverse effects.

3.1 Naproxen	1	24	Peto Odds Ratio (Peto, Fixed, 95% CI)	26.73 [5.46, 130.91]
4 Use of additional analgesics Show forest plot	1	64	Odds Ratio (M-H, Fixed, 95% CI)	0.41 [0.12, 1.37]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size

Analysis 4.4

Open in figure viewer | Download as PowerPoint



Comparison 4 TENS versus medical treatment, Outcome 4 Use of additional analgesics.

4.1 Ibuprofen	1	64	Odds Ratio (M-H, Fixed, 95% CI)	0.41 [0.12, 1.37]

Information

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10.1002/14651858.CD002123 Check for updates

Database:

Cochrane Database of Systematic Reviews

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21 January 2002 see what's new

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Intervention

Stage:

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Contributions of authors

Michelle Proctor: took the lead in writing the original protocol and review, performed initial searches of databases for trials, involved in selecting trials for inclusion, performed independent data extraction and quality assessment of the included trials, was responsible for statistical analysis and interpretation of the data.
Caroline Smith: involved in selecting trials for inclusion, performed independent data extraction and quality assessment of the included trials, contributed to discussion and interpretation of results.
Cindy Farquhar: initiated and conceptualised the review, commented on drafts of the protocol and review, and participated in the update of the review.
Will Stones: commented on drafts of the protocol and review.

Julie Brown: took the lead in the update of the review and the formatting for Revman 5.

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Internal sources

- University of Auckland, School of Medicine, Auckland, New Zealand.

External sources

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Declarations of interest *available in* English | Español

None known

Acknowledgements *available in* English | Español

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What's new

Last assessed as up-to-date: 2 May 2009.

Date	Event	Description
10 August 2009	Review declared as stable	No new trials were identified
5 May 2009	New search has been performed	This review has now been updated. No new trials were identified. Risk of bias tables have been added and the trial has been formatted as per Cochrane guidelines. An earlier version of the review included acupuncture but at the time of updating the review was split into two reviews, one of TENS and one of acupuncture.

History

Protocol first published: Issue 2, 2000

Review first published: Issue 1, 2002

Date	Event	Description
19 November 2008	Amended	This published review: Proctor ML, Smith CA, Farquhar CM, Stones RW. Transcutaneous electrical nerve stimulation and acupuncture for primary dysmenorrhoea. *Cochrane Database of Systematic Reviews* 2002, Issue 1, has now been divided into two reviews 'Transcutaneous electrical nerve stimulation for primary dysmenorrhoea' and 'Acupuncture for primary dysmenorrhoea'.
16 June 2008	Amended	Converted to new review format.
22 November 2001	New citation required and conclusions have changed	Substantive amendment

Version history

Title	Stage	Authors	Version	Publication Date
Transcutaneous electrical nerve stimulation for primary dysmenorrhoea	Review	Michelle Proctor, Cindy Farquhar, Will Stones, Lin He, Xiaoshu Zhu, Julie Brown	https://doi.org/10.1002/14651858.CD002123	21 January 2002

Differences between protocol and review

The original review contained reference to acupuncture. The trial associated with acupuncture has now been removed from this review and the role of acupuncture in the treatment of dysmenorrhoea will be the subject of a new review.

Notes

Trials relating to acupuncture have now been excluded from this review and will the subject of a new review.

What's new

Last assessed as up-to-date: 2 May 2009.

Date	Event	Description
10 August 2009	Review declared as stable	No new trials were identified
5 May 2009	New search has been performed	This review has now been updated. No new trials were identified. Risk of bias tables have been added and the trial has been formatted as per Cochrane guidelines. An earlier version of the review included acupuncture but at the time of updating the review was split into two reviews, one of TENS and one of acupuncture.

Appendices

Appendix 1. MEDLINE search strategy

1 exp Menstruation disorders/ (21321)
2 Pelvic pain/ (2191)
3 (pelvic adj5 pain).tw. (4323)
4 Dysmenorrhea/ (2469)
5 dysmenorrh$.tw. (2884)
6 (painful adj5 menstrua$).tw. (110)
7 (painful adj5 period$).tw. (212)
8 menstrual disorder.tw. (78)

9 or/1-8 (26974)

10 Transcutaneous electric nerve stimulation/ (2524)

11 TENS.tw. (4211)

12 electric stimulation therapy/ or electroacupuncture/ (14755)

13 electrostimulat$.tw. (2455)

14 electrotherap$.tw. (795)

15 electric stimulat$.tw. (3097)

16 nerve stimulat$.tw. (14604)

17 electroanalges$.tw. (173)

18 or/10-17 (36843)

19 9 and 18 (136)

20 randomized controlled trial.pt. (263105)

21 controlled clinical trial.pt. (78151)

22 (randomized or randomised).ab. (207653)

23 placebo.ab. (108884)

24 drug therapy.fs. (1280145)

25 randomly.ab. (126866)

26 trial.ab. (181582)

27 groups.ab. (879682)

28 or/20-27 (2337353)

29 (animals not (humans and animals)).sh. (3235549)

30 28 not 29 (1980294)

31 30 and 19 (44)

32 limit 31 to yr="2001 - 2009" (26)

33 from 32 keep 1-26 (26)

Appendix 2. EMBASE search strategy

1 exp Menstruation Disorder/ (23479)

2 Pelvis Pain Syndrome/ (4684)

3 Dysmenorrhea/ (3608)

4 menstru$ disorder$.ti,ab,hw,tn,mf. (3213)

5 (pelvi$ adj5 pain).ti,ab,hw,tn,mf. (6495)

6 (painful adj5 menstrua$).ti,ab,hw,tn,mf. (64)

7 (painful adj5 period$).ti,ab,hw,tn,mf. (165)

8 Dysmenorrh$.ti,ab,hw,tn,mf. (4038)

9 or/1-8 (29638)

10 nerve stimulation/ or electroacupuncture/ or transcutaneous nerve stimulation/ (19586)

11 electrostimulation therapy/ (3174)
12 TENS.ti,ab,hw,tn,mf. (3963)
13 electrostimulat$.ti,ab,hw,tn,mf. (32173)
14 electrotherap$.ti,ab,hw,tn,mf. (574)
15 electric stimulat$.ti,ab,hw,tn,mf. (1372)
16 nerve stimulat$.ti,ab,hw,tn,mf. (27444)
17 electroanalges$.ti,ab,hw,tn,mf. (155)
18 or/10-17 (60372)
19 9 and 18 (274)
20 Clinical Trial/ (531633)
21 Randomized Controlled Trial/ (165971)
22 exp randomization/ (26539)
23 Single Blind Procedure/ (7989)
24 Double Blind Procedure/ (71472)
25 Crossover Procedure/ (21005)
26 Placebo/ (123698)
27 Randomi?ed controlled trial$.tw. (32428)
28 Rct.tw. (2659)
29 random allocation.tw. (636)
30 randomly allocated.tw. (10126)
31 allocated randomly.tw. (1347)
32 (allocated adj2 random).tw. (559)
33 Single blind$.tw. (7418)
34 Double blind$.tw. (84352)
35 ((treble or triple) adj blind$).tw. (140)
36 placebo$.tw. (109416)
37 prospective study/ (80141)
38 or/20-37 (698900)
39 case study/ (5939)
40 case report.tw. (118491)
41 abstract report/ or letter/ (491476)
42 or/39-41 (613634)
43 38 not 42 (674549)
44 43 and 19 (105)
45 limit 44 to yr="2007 - 2009" (29)
46 from 45 keep 1-29 (29)

Appendix 3. Menstrual Disorders and Subfertility Group search strategy

Keywords CONTAINS "dysmenorrhea" or "Dysmenorrhea-Symptoms" or "dysmenorrhoea" or "pain-dysmenorrhea" or Title CONTAINS "dysmenorrhea" or "Dysmenorrhea-Symptoms" or "dysmenorrhoea" or "pain-dysmenorrhea"

AND

Keywords CONTAINS "TENS" or "TENS study" or "electro-acupuncture" or "electro-magnetic" or "electroacupuncture" or "electrical activation" or "Transcutaneous Electric Nerve Stimulation" or Title CONTAINS "TENS" or "TENS study" or "electro-acupuncture" or "electro-magnetic" or "electroacupuncture" or "electrical activation" or "Transcutaneous Electric Nerve Stimulation"

Appendix 4. CENTRAL search strategy

1 exp Menstruation disorders/ (1067)
2 Pelvic pain/ (157)
3 (pelvic adj5 pain).tw. (364)
4 Dysmenorrhea/ (259)
5 dysmenorrh$.tw. (517)
6 (painful adj5 menstrua$).tw. (10)
7 (painful adj5 period$).tw. (38)
8 menstrual disorder.tw. (8)
9 or/1-8 (1699)
10 Transcutaneous electric nerve stimulation/ (437)
11 TENS.tw. (450)
12 electric stimulation therapy/ or electroacupuncture/ (1013)
13 electrostimulat$.tw. (166)
14 electrotherap$.tw. (115)
15 electric stimulat$.tw. (141)
16 nerve stimulat$.tw. (1108)
17 electroanalges$.tw. (14)
18 or/10-17 (2429)
19 9 and 18 (23)
20 limit 19 to yr="2001 - 2008" (9)
21 from 20 keep 1-9 (9)

Appendix 5. AMED search strategy

1 exp Menstruation disorders/ (348)

2 Pelvic pain/ (0)

3 (pelvic adj5 pain).tw. (148)

4 Dysmenorrhea/ (71)

5 dysmenorrh$.tw. (125)

6 (painful adj5 menstrua$).tw. (4)

7 (painful adj5 period$).tw. (11)

8 menstrual disorder.tw. (1)

9 or/1-8 (541)

10 Transcutaneous electric nerve stimulation/ (543)

11 TENS.tw. (325)

12 electric stimulation therapy/ or electroacupuncture/ (637)

13 electrostimulat$.tw. (89)

14 electrotherap$.tw. (879)

15 electric stimulat$.tw. (1569)

16 nerve stimulat$.tw. (743)

17 electroanalges$.tw. (8)

18 or/10-17 (3596)

19 9 and 18 (7)

20 limit 19 to yr="2001 - 2008" (2)

21 from 20 keep 1-2 (2)

Appendix 6. PsycINFO search strategy

1 exp Menstruation disorders/ (0)

2 Pelvic pain/ (0)

3 (pelvic adj5 pain).tw. (279)

4 Dysmenorrhea/ (136)

5 dysmenorrh$.tw. (248)

6 (painful adj5 menstrua$).tw. (20)

7 (painful adj5 period$).tw. (40)

8 menstrual disorder.tw. (15)

9 or/1-8 (588)

10 Transcutaneous electric nerve stimulation/ (0)

11 TENS.tw. (492)

12 electric stimulation therapy/ or electroacupuncture/ (0)

13 electrostimulat$.tw. (208)

14 electrotherap$.tw. (110)

15 electric stimulat$.tw. (447)

16 nerve stimulat$.tw. (1215)

17 electroanalges$.tw. (12)

18 or/10-17 (2337)

19 9 and 18 (3)

20 limit 19 to yr="2001 - 2008" (2)

21 from 20 keep 1-2 (2)

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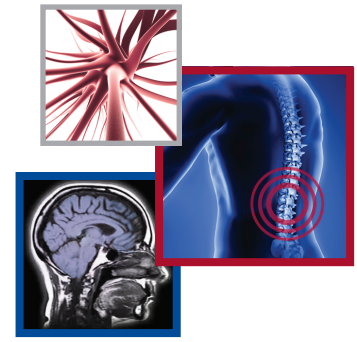

Using TENS for pain control: the state of the evidence

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Practice points

- High frequency (HF) and low frequency (LF) transcutaneous electrical nerve stimulation (TENS) activate different opioid receptors. Both applications have been shown to provide analgesia specifically when applied at a strong, nonpainful intensity. HF TENS may be more effective for people taking opioids.
- Effective analgesia for chronic pain conditions may be limited by the development of tolerance to TENS if repeated application of either LF or HF TENS at the same frequency and intensity is used daily (i.e., same dose). Strategies to prolong analgesia may include varying these parameters.
- Application of TENS electrodes at acupoint sites may increases analgesia.
- Targeting the use of TENS during movement or activity may be most beneficial.
- Systematic reviews suggest that TENS, when applied at adequate intensities, is effective for postoperative pain, osteoarthritis, painful diabetic neuropathy and some acute pain conditions.
- Emerging evidence suggests TENs may be helpful for peoples with fibromyalgia and spinal cord injury.
- TENS may be effective in restoration of central pain modulation, a measure of central inhibition.
- A clearer picture of TENS effectiveness will emerge as trials with attention to optimal dosing and appropriate outcome measures increase in numbers.

SUMMARY: Transcutaneous electrical nerve stimulation (TENS) is a nonpharmacological intervention that activates a complex neuronal network to reduce pain by activating descending inhibitory systems in the central nervous system to reduce hyperalgesia. The evidence for TENS efficacy is conflicting and requires not only description but also critique. Population-specific systemic reviews and meta-analyses are emerging, indicating both HF and LF TENS being shown to provide analgesia, specifically when applied at a strong, nonpainful intensity. The purpose of this article is to provide a critical review of the latest basic science and clinical evidence for TENS. Additional research is necessary to determine if TENS has effects specific to mechanical stimuli and/or beyond reduction of pain and will improve activity levels, function and quality of life.

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Background

Transcutaneous electrical nerve stimulation (TENS) is an inexpensive nonpharmacological intervention used in the treatment of acute and chronic pain conditions. These small battery-powered devices deliver alternating current via cutaneous electrodes positioned near the painful area. The parameters of pulse frequency, and pulse intensity are adjustable and linked to TENS efficacy. This article will provide a critical review of the latest basic science and clinical evidence for TENS. We will summarize mechanisms of action, factors that influence TENS efficacy, and describe and critique the use of TENS for pain control in a variety of patient populations. Findings of systematic reviews of TENS for pain management in the last 7 years will be presented. We will also highlight advances from Randomized Controlled Trials (RCT) published in the last 5–7 years, which are not included in the systematic reviews. This article offers a concise review of the basic science mechanisms for TENS as well as an up to date critique of current clinical research for TENS.

Mechanisms of TENS reduction on analgesia

TENS activates a complex neuronal network to result in a reduction in pain. At frequencies and intensities used clinically, TENS activates large diameter afferent fibers [1,2]. This afferent input is sent to the central nervous system to activate descending inhibitory systems to reduce hyperalgesia. Specifically, blockade of neuronal activity in the periaqueductal gray (PAG), rostral ventromedial medulla (RVM) and spinal cord inhibit the analgesic effects of TENS showing that TENS analgesia is maintained through these pathways [3–5]. In parallel, studies in people with fibromyalgia show that TENS can restore central pain modulation, a measure of central inhibition [6]. Therefore, TENS reduces hyperalgesia through both peripheral and central mechanisms.

• Neurotransmitters & receptors that mediate TENS analgesia

HF TENS increases the concentration of β-endorphins in the bloodstream and cerebrospinal fluid, and methionine-enkephalin in the cerebrospinal fluid, in human subjects [7,8]. The analgesia produced reduction in hyperalgesia by HF TENS is prevented by blockade of opioid receptors in the RVM or spinal cord, or synaptic transmission in the ventrolateral PAG [4–5,9]. This opioid-mediated analgesia produced by HF TENS has been confirmed in human subjects [10]. Furthermore, the reduction in hyperalgesia produced by HF TENS is prevented by blockade of muscarinic receptors (M1 and M3) and $GABA_A$ receptors in the spinal cord [11,12]. However, blockade of serotonin or noradrenergic receptors in the spinal cord has no effect on the reversal of hyperalgesia produced by HF TENS [13]. Thus, HF TENS produces analgesia by activating endogenous inhibitory mechanisms in the central nervous system involving opioid GABA, and muscarinic receptors.

The reduction in hyperalgesia by LF TENS is prevented by blockade of μ opioid receptors in the spinal cord or the RVM or spinal cord, and by synaptic transmission in the ventrolateral PAG [4,5,9]. Further, the reduction in hyperalgesia by LF TENS is prevented by blockade of $GABA_A$, serotonin 5-HT2A and 5-HT3, and muscarinic M1 and M3 receptors in the spinal cord [11–13], and is associated with increased release of serotonin [14]. This opioid mediated effect of LF TENS has been confirmed in human subjects [15]. In addition, LF TENS does not produce analgesia in opioid tolerant people and animals but HF TENS does [16,17]. Thus, LF TENS uses classical descending inhibitory pathways involving the PAG-RVM pathway activating opioid, GABA, serotonin and muscarinic receptors to reduce dorsal horn neuron activity and the consequent pain.

• Reduction in central excitability

In animals without tissue injury, both LF and HF TENS reduce dorsal horn neuron activity [18–22]. In animals with peripheral inflammation or neuropathic pain, enhanced activity of dorsal horn neurons (i.e., central sensitization) to both noxious and innocuous stimuli is reduced by both HF and LF TENS [23–26]. In parallel, there is a reduction in both primary and secondary hyperalgesia by both LF and HF TENS [23,25–31]. Furthermore, in people with fibromyalgia and osteoarthritis, there is a reduction in pressure pain thresholds not only at the site of stimulation, but also at sites outside the area of application [6,32], implicating a reduction in central excitability.

HF TENS also reduces central neuron sensitization [24], and release of the excitatory neurotransmitters glutamate and substance P in the spinal cord dorsal horn in animals with

inflammation [33,34]. The reduction in glutamate is prevented by blockade of δ-opioid receptors. Thus, one consequence of activation of inhibitory pathways by TENS is to reduce excitation and consequent neuron sensitization in the spinal cord.

• Peripheral mechanisms of TENS

Both HF and LF TENS have effects at the site of stimulation. HF TENS reduces substance P, which is increased in dorsal root ganglia neurons in animals after tissue injury [33]. Blockade of peripheral opioid receptors prevents the analgesia produced by LF, but not HF TENS [35,36]. Thus, TENS may also alter excitability of peripheral nociceptors to reduce afferent input to the central nervous system.

In α-2a adrenergic knockout mice, analgesia by LF and HF TENS does not occur [37]. Blockade of peripheral, but not spinal or supraspinal, α-2 receptors prevents the analgesia produced by TENS [37] suggesting a role for peripheral α-2a-adrenergic receptors in analgesia produced by TENS. Further, the reduction in cold allodynia by LF TENS is reduced by administration of systemic phentolamine to block α-adrenergic receptors [25]. This adrenergic effect may alter the autonomic system. There are increases in blood flow with LF TENS at intensities that produce motor contractions; greater than 25% above motor threshold [38–42]. Thus, some of the analgesic effects of TENS are mediated through peripheral adrenergic receptors.

Factors that directly affect TENS efficacy

The factors affecting TENS efficacy include the population and the outcome assessed, timing of the outcome measures, negative interaction of opioid use and the parameters of the TENS dose. Three important factors for TENS efficacy are tolerance to repeated TENS, intensity of the stimulation and electrode placement. A recent article by Sluka *et al.* [43] provides an extensive review of variables that can affect the clinical use of TENS.

• Tolerance to repeated TENS

Repeated application of either LF or HF TENS at the same frequency, intensity and pulse duration daily (i.e., same dose), produces analgesic tolerance in animals [17] and humans [44]. The analgesic tolerance by LF TENS results in cross-tolerance at μ-opioid receptors in the spinal cord, and the analgesic tolerance by HF TENS results in cross-tolerance at δ-opioid receptors in the spinal cord in animals [17]. Prevention of analgesic tolerance occurs with pharmacological modulation of pathways involved in opioid tolerance. Specifically blockade of NMDA-glutamate receptors or CCK receptors in the spinal cord prevents analgesic tolerance to both LF and HF TENS [45,46]. Analgesic tolerance can also be prevented by modulating between LF and HF TENS within a treatment session [47], or by increasing intensity of TENS daily [48]. Thus, animal studies suggest TENS tolerance can be delayed with pharmacological methods as well as with non-pharmacological modulation of TENS parameters.

• Intensity of TENS established as a critical factor in efficacy

The intensity of stimulation utilized is critical with TENS application. Using the strongest intensity that remains comfortable produces hypoalgesia in healthy subjects; lower intensities are ineffective [49–56]. In addition to activation of greater numbers of sensory afferents, higher pulse amplitudes are proposed to activate deeper tissue afferents allowing for greater analgesia [2]. High intensity TENS decreases post-operative opioid requirements and negative opioid-side effects [57,58]. Even as researchers demonstrate the importance of intensity in TENS delivery, TENS systematic reviews continue to include studies with wide ranging intensity settings. In fact, as outlined below, application of TENS at inadequate intensities is one of the primary factors attributed to conflicting reports of TENS efficacy. Therefore, clinicians should strive to apply TENS at the maximally tolerated intensity for each individual person.

• Electrode site placement

The intersection of acupuncture and TENS is receiving increasing attention in research. Numerous studies have examined both electro acupuncture and traditional TENS pad electrodes applied over acupuncture sites [59–67]. Clinically, application of TENS at these acupoints reduces pain and may be more effective than when applied over non-acupoint sites when measuring pain and pain thresholds to heat and pressure in normal subjects [59–63], as well as in patient populations [64–67] when compared with sham TENS. In post-operative hysterectomy subjects, TENS at acupoint sites reduced opioid

intake, nausea and dizziness when compared with TENS at non-acupoint sites [64].

Evidence of TENS for pain management

• Systematic reviews/meta-analyses

In the last 7 years, there have been a number of systematic reviews/meta-analyses that have examined efficacy of TENS for pain reduction in people with neck pain [68], postoperative pain [69], cancer pain [70,71], labor pain [72], acute pain [73], low back pain [74,75] and osteoarthritis pain [58,76]. There have also been systematic reviews on the methodology of TENS [77,78]. As a whole, these reviews are conflicting with some showing efficacy and some showing no efficacy for the use of TENS. The challenge is often a lack of high quality studies or a lack of consistency between high-quality studies included in the systematic reviews with respect to clinical population homogeneity, dose of TENS (i.e., location of TENS electrodes, frequency and intensity of TENS stimulation, and frequency and duration of TENS delivery), description of blinding and the influence of analgesic medication. **Table 1** represents a summary of these systematic reviews. Below we address the evidence on postoperative pain, acute non-postoperative pain, low back pain, osteoarthritis pain and painful diabetic neuropathy as examples.

Postoperative pain

There have been reviews of TENS efficacy in the last 7 years on management of postoperative pain which present differing results. A systematic review shows inconclusive results, [86] and a subsequent review shows positive effects [87]. The review by Bjordal and colleagues grouped trials into those with adequate TENS parameters (adequate frequency: 1-8 Hz for LF -TENS or 25-150 Hz for HF TENS; adequate intensity: strong sub noxious, maximal tolerable, or ≥15 mA) and those that did not meet these criteria. They show that those with adequate TENS parameters (n = 11) showed a 36% reduction in analgesic intake compared with those with inadequate TENS parameters (n = 10) that showed a 4% reduction. In contrast, the Cochrane review [86] did not consider dosing. Additionally, TENS has been found to reduce movement (walking and vital capacity maneuvers), but not resting, pain postoperatively [88] Since the above systematic reviews focused on TENS for resting or overall pain, this factor may have also contributed to the conflicting results.

Acute nonpostoperative pain

A Cochrane review addressing acute pain (i.e., pain less than 12 weeks duration associated with procedures such as cervical laser, venipuncture, sigmoidoscopy screen, postpartum uterine contraction and rib fractures) in adults used a minimum stimulation intensity of 'strong but comfortable' as an inclusion factor. However, with 12 studies included, the authors were unable to make any conclusions due to insufficient evidence [73]. Four studies were included in a separate meta-analysis of RCTs where TENS was utilized in a pre-hospital setting for acute pain, (defined as moderate to severe) with TENS delivered by emergency service personnel. All studies found TENS lead to a clinically significant reduction in pain severity as compared with placebo TENS [89]. This review only included studies where TENS was used short term in ambulance responses. These studies were excluded from the Cochrane review of TENS and acute pain [73] due to low stimulation intensity. Thus, short-term use of TENS in ambulance responses the required intensity may be less than that required for chronic or other types of acute conditions. Recent randomized controlled trials for TENS show significant reductions in postpartum pain [90]) and pain during wound-care procedures [91]. Interestingly, the mechanical triggers of wound-care procedures are similar to movement pain, supporting the effect of TENS for pain caused by mechanical stimulation, such as muscle movement, pressure, or force.

Low back pain

Systematic reviews [74,80] and a meta-analysis [75] have examined the efficacy of TENS for low back pain with conflicting results from not recommended [80], inconclusive [74], and effective [75]. All analyses used different inclusion and exclusion criteria, all examined effects on pain at rest, several used a mixed patient population, and none used dosing or timing of outcome, or examined potential interactions with pharmacological agents.

For example, the systematic review by Dubinsky and Miyasaki [80] was based on only two studies with differing patient populations - one for chronic, non-specific low back pain [92] and the other for low back pain in people with multiple sclerosis. The pain of MS is related to direct injury and permanent damage to the central nervous system [93]; while chronic musculoskeletal pain is generally due to modifiable

Table 1. TENS systematic reviews 2007–2013.

Year	Topic	Author	Review type	Studies (n)	Subjects (n)	Results	Ref.
2013	Neck pain	Kroeling	Systematic review	20	1239	Update on 2009 and 2005 systematic review. Authors were unable to determine effect of TENS in neck pain due to limited quality of evidence, but suggest active TENS may be more effective than placebo TENS. Limited number of studies with standardization and description of treatment characteristics.	[68]
2012	Thoracic surgery	Sbruzzi	Meta-analysis	11	545	Use of random effects models to assess TENS effect s/p thoracic surgery. In thoracotomy and stermotomy, TENS associated with pharmacological analgesia improved pain relief compared with placebo TENS. With stermotomy, TENS was more effective than pharmacological analgesia for pain relief. No change in pulmonary function.	[69]
2012	Cancer pain adults	Hurlow	Systematic review	3	176	Update of 2008 Robb article in cancer pain. Addition of one RCT suggesting TENS may improve bone pain on movement in a cancer population. Results remained inconclusive due to a limited number of RCTs for review.	[71]
2011	Methodological Quality TENS and pain	Bennett	Systematic review	38	2268	Review of three Cochrane systematic reviews: acute pain, chronic pain and cancer pain. Authors identified sources of potential bias related to study design including less than optimal dosing of TENS, outcome assessment and timing as well as blinding and application of TENS. Proposal of criteria for future studies to enhance fidelity.	[77]
2011	Pain in labor	Bedwell	Systematic review	14	1256	Update to 2009 Dowswell article. Limited evidence that TENS reduces pain in labor. TENS does not appear to have effect on other outcomes for mothers and infants.	[72]
2010	Phantom limb pain	Mulvey	Cochrane systematic review	0	0	No RCTs have been completed to examine decreased pain in amputees. Further investigation is needed.	[79]

cLBP: Chronic low back pain; DPN: Diabetic peripheral neuropathy; IFC: Interferential current; LBP: Low back pain; OA: Osteoarthritis; QOL: Quality of life; RA: Rheumatory arthritis; RCT: Randomized controlled trials; TENS: Transcutaneous electrical nerve stimulation.

Table 1. TENS systematic reviews 2007–2013 (cont.).

Year	Topic	Author	Review type	Studies (n)	Subjects (n)	Results	Ref.
2008	TENS dose response for chronic pain	Claydon	Review of systematic reviews	6	Hand RA: 78 cLBP: 175 Knee OA: 294 Chronic musculoskeletal pain: 984 Chronic pain: 1227 Total: 2758	Two of six reviews of TENS and chronic pain reported high intensity TENS applications were more effective compared with placebo than low intensity. Reviewed confounding variables of inadequate design, low statistical power and different TENS protocols – single treatment versus repeated treatments of TENS.	[78]
2010	Neurological disorders (LBP and DPN)	Dubinsky	Systematic review	11		Inconsistent evidence for pain reduction in cLBP; probable evidence for pain reduction with diabetic peripheral neuropathy.	[80]
2010	Diabetic Peripheral Neuropathy	Jin	Meta-analysis	3	78	Pain reduction significantly greater than placebo following 4–6 weeks of treatment. Reduced hyperalgesia and numbness and increased QOL also significantly improved with active TENS.	[81]
2010	Hand RA	Brouseau	Cochrane systematic review	3	78	Update of 2003 review; Acupuncture like TENS has benefit for reducing pain intensity and increasing grip over placebo while conventional TENS no benefit compared with placebo.	[82]
2009	Pain in labor	Dowswell	Cochrane systematic review	17	1466	Limited evidence that TENS reduces pain in labor. Little difference between TENS groups and control groups. Those women receiving TENS to acupuncture points were less likely to report severe pain.	[83]
2009	Non-specific low back pain	Machado	Meta-analysis	4	178	Random effects statistical model demonstrated moderate effect for TENS in acute and chronic LBP	[75]
2009/2011	Acute pain	Walsh	Cochrane systematic review	12	919	Insufficient evidence to draw any conclusions about the effectiveness of TENS for the treatment of acute pain in adults.	[73]
2008	Chronic low back pain	Khadilkar	Cochrane systematic review	4	585	Conflicting evidence about TENS benefit in reducing back pain intensity. Acupuncture like TENS responded similar to conventional TENS, two of four studies lacked adequate stimulation intensity.	[74]

cLBP: Chronic low back pain; DPN: Diabetic peripheral neuropathy; IFC: Interferential current; LBP: Low back pain; OA: Osteoarthritis; QOL: Quality of life; RA: Rheumatory arthritis; RCT: Randomized controlled trials; TENS: Transcutaneous electrical nerve stimulation.

Table 1. TENS systematic reviews 2007–2013 (cont.).

Year	Topic	Author	Review type	Studies (n)	Subjects (n)	Results	Ref.
2008	Cancer pain adults	Robb	Cochrane systematic review	2	64	Due to small number of subjects and studies, there is insufficient evidence to determine the effectiveness of TENS and cancer pain. One RCT no significant difference in active TENS and placebo TENS; one RCT no significant difference in acupuncture-like TENS and sham TENS.	[70]
2008	OA of knee	Rutjes	Cochrane systematic review	18	813	Mixed review of trials for TENS, IFC and pulsed electrical stimulation. Inconclusive for the results of TENS for pain and function of the knee due to small trials and inadequate design and power.	[76]
2008	Chronic pain	Nnoahm	Cochrane systematic review	25	1281	13/22 inactive control studies demonstrate a positive analgesic outcome for active TENS treatments. For multiple treatment comparison studies 8/15 were in favor of active TENS. 7/9 active controlled studies found no difference in analgesic efficacy between high frequency TENS and low frequency TENS.	[84]
2007	Knee OA	Bjordal	Systematic review and meta-analysis	11	425	Seven of 11 studies had optimal TENS dosing and demonstrated clinically relevant pain relief compared with placebo control. These studies included IFC, electro acupuncture and low level laser therapy.	[58]
2007	Chroni cmusculo-skeletal pain	Johnson	Meta-analysis	38	1227	With resting pain as main outcome measure, the overall random effects meta-analysis model showed a decrease in pain with electrical nerve stimulation.	[85]

cLBP: Chronic low back pain; DPN: Diabetic peripheral neuropathy; IFC: Interferential current; LBP: Low back pain; OA: Osteoarthritis; QOL: Quality of life; RA: Rheumatory arthritis; RCT: Randomized controlled trials; TENS: Transcutaneous electrical nerve stimulation.

'plastic' changes in both the peripheral and central pain pathways (sensitization) [94–96]. Machado [75] used people with non-specific low back pain with positive results – however, they combined acute and chronic low back pain, which likely have different underlying mechanisms.

None of the reviews considered adequate dosing of TENS and there were studies included in each review that did not describe TENS parameters or used inadequate doses. For example, the study by Deyo and colleagues [92], comparing TENS with and without exercise to placebo TENS with and without exercise in people with chronic low back pain, was included in two systematic reviews [74,80] and is rated as a well-designed clinical trial using appropriate blinding, randomization and good description of withdrawal and dropouts. However there are significant weaknesses in the application of TENS, some of which have been discovered since the trial was conducted 23 years ago. Intensity was applied by having subjects set the amplitude to a pre-designated setting on the machine which corresponded to 15 mA as obtained from the manufacturer. Patient response to stimulation was not stated. In our preliminary data, application of TENS to the spine that results in a strong but comfortable intensity requires at least 30 mA and, thus, the amplitude used was likely below an effective dose. Thus, it is not clear if TENS is effective for low back pain. Future studies should design clinical trials with adequate dosing and appropriate outcome measures. Future systematic reviews need to use patient populations with similar pain physiology and adequate use of TENS parameters as inclusion criteria.

Osteoarthritis pain

Similar to the reviews of acute pain and low back pain, a recent Cochrane systematic review showed that TENS was not effective for knee osteoarthritis(OA) pain [97], and is in direct contrast to a prior systematic review by the same group that concluded TENS was effective for knee OA pain [98] and a meta-analysis that showed a significant reduction in knee OA pain with TENS [58]. Intensities in the included studies varied widely. For example in the recent Cochrane review [97], 12 included trials used adequate intensities, five trials used inadequate intensities (HF-TENS at sensory threshold or below [99–103] and two trials did not report TENS intensity [104,105]. To address dosing, Bjordal and colleagues performed a systematic review on TENS for osteoarthritis pain and show that when given at adequate intensities and frequencies TENS produces a clinically significant reduction in pain when compared with studies of inadequate dosing [58]. Therefore TENS works for OA pain if used at adequate intensities. A recent randomized controlled trial applied TENS in people with knee OA as an adjunct to primary care and showed no added benefit. However, parameters were not standardized and, and participants were allowed to self-select from eight different TENS protocols in the 6 week trial making interpretation of findings challenging [106].

Diabetic peripheral neuropathy (DPN)

In people with painful DPN, TENS may also provide benefit. A meta-analysis including three RCTs (n = 78) reported reduction of pain that was significantly greater than placebo TENS following 4–6 weeks of treatment [81] In addition, secondary outcomes of overall improvement in DPN symptoms (hyperalgesia, numbness, and quality of life) were significantly greater for active TENS groups when compared with placebo [107–109] Therefore, there is support for the use of TENS in reducing pain and improving quality of life in people with painful DPN.

• TENS interventions: emerging evidence from recent clinical trials

Fibromyalgia (FM)

Recent evidence suggests that TENS can be effective for people with fibromyalgia. Although there have been several randomized controlled-trials [6,110–113], no systematic reviews have been published and the quality of these studies and the intervention have varied significantly. Two trials compared TENS to a placebo and used an adequate dose. Dailey *et al.* [6] showed a one-time session of TENS (using a maximum tolerable intensity) significantly decreased movement pain and hyperalgesia. No changes were observed in resting pain [6] Lauretti *et al.* [111] showed TENS using a strong intensity (60 mA) at two sites and at one site produced a significant decrease in pain at rest compared with placebo when applied over a seven day period. Two additional studies show reductions in pain with strong but comfortable intensity HF TENS compared with warmth therapy and to a no TENS group [110,112.] Thus, when used at a strong but comfortable sensation, TENS may be effective for both resting and movement pain in people with fibromyalgia.

Neuropathic pain

TENS may offer relief to people with neuropathic pain and complex regional pain syndrome. A crossover design trial investigating neuropathic pain in people with spinal cord injury, [114] found a favorable effect of both LF and HF TENS (LF TENS 38%; HF TENS 29%) on a global relief scale and 25% of subjects requested a unit for further treatment. However, this study did not compare against a placebo or control group, intensity was not reported, and there were a low number of study participants (n = 24). A more recent study reports LF TENS provided significant reduction in pain when compared with placebo TENS in people with spinal cord injury. Here the parameters of 4 Hz and 200 µs were applied at sites below the level of injury at a set intensity of 50 mA [115] Thus; LF TENS may be most effective for pain in people with spinal cord injury.

Other pain conditions

A recent randomized controlled trial of TENS as an adjunct treatment in the management of lateral epicondylalgia concludes that TENS does not provide additional benefit when used as an adjunct to primary care (education and therapeutic exercise) [116]. In review, while an appropriate intensity was used, the intervention was not monitored for dosing and low adherence was reported. Further, outcome measures were assessed through questionnaires and not necessarily while wearing the TENS device. Additional TENS reports are favorable for relief of chronic pelvic pain syndrome [117] and pain associated with latent upper trapezius trigger points [118]. Overall, the evidence suggests, TENS may be useful for a variety of pain conditions.

Summary & conclusion

Because no single profession holds all the keys to successful management of pain, further investigation is warranted to ensure optimal use of this safe, noninvasive, inexpensive and patient friendly intervention. The advantages of obtaining pain relief without the negative side effects of many pharmaceutical interventions is welcomed and desired by certain patients. Both HF and LF TENS been shown to provide analgesia specifically when applied at a strong, non-painful intensity and HF TENS may be more effective for people taking opioids. Effective analgesia for chronic pain conditions may be limited by the development of tolerance to TENS if repeated application of either HF or LF TENS at the same frequency, intensity and pulse duration is used daily. Application of TENS electrodes at acupoint sites may increases analgesia and targeting the use of TENS during movement or required activity may provide the most benefit.

Experiments investigating the concept of TENS responders will enable clinicians to select this modality for the correct population. Additional investigation in the area of TENS tolerance is necessary to determine methods to decrease tolerance and to establish if a wash out period is required to determine when tolerance would no longer be a factor in the application of TENS in patient care. Although parameter selection is becoming clearer, investigating the parameters of electrode site selection, daily treatment duration, and long-term usage will further clarify appropriate dosing so that TENS may be given in the most effective manner. Further, examining a variety of outcomes, beyond resting pain, will determine if TENS has effects specific to mechanical stimuli and/or beyond reduction of pain and will improve activity levels, function and quality of life.

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Application of Low Frequency and Medium Frequency Currents in the Management of Acute and Chronic Pain–A Narrative Review

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Application of Low Frequency and Medium Frequency Currents in the Management of Acute and Chronic Pain—A Narrative Review

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ABSTRACT

Trancutaneous electrical nerve stimulation (TENS) and interferential therapy (IFT) have been a regular line of treatment for various types of acute and chronic pain. This review aims to compile the latest literature in pain management using these modalities which use low-frequency and medium-frequency currents. The Cochrane Library, Scopus, PubMed, MEDLINE, and CINAHL were searched and studies were examined from their inception till October 2013. After title and abstract screening the relevant studies were included for this review. We found through this review that even though TENS and IFT are used in management of pain, there is limited amount of high quality research available in this area. Most of the studies lack methodological quality and have a low sample size.

Key words: Acute pain, Chronic pain, Electro physical modalities and electrotherapy, Interferential Therapy, Low-frequency currents, Medium frequency currents, Pain, Transcutaneous electrical nerve stimulation

INTRODUCTION

Evidence-based practice is essential in clinical practice to hasten the recovery of a patient. In electrotherapy the applied energy is the trigger that stimulates or activates physiological events, which achieve therapeutic benefits that bring about pain relief.[1] In this review we would mainly focus on Transcutaneous Electrical Nerve Stimulation (TENS) and interferential therapy (IFT) which use low- and medium-frequency currents, respectively for pain relief.

Data collection

The following databases were searched by the reviewers from their inception till October 2013, The Cochrane Library, Scopus, PubMed, MEDLINE, and CINAHL. After title and abstract screening randomized controlled trials and systematic reviews that compared active TENS/IFT in acute/chronic pain relief were included in this narrative review.

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Transcutaneous electrical nerve stimulation

TENS relieves pain by inhibiting pain-related potentials on the spinal and supraspinal level, known as "gate control." It is alternating current (AC) or modulated DC, comprising rectangular impulses. The analgesic effects of TENS is seen in both the ipsilateral and contralateral spinal segmental regions.[2,3]

Interferential therapy

Interferential therapy involves the use of "medium frequency" current to bring about the effect of a low-frequency (LF) current in the tissues. This is achieved by applying two "medium frequency" currents to the tissues, to generate LF interference current. Thus, the benefits of LF stimulation are achieved without the associated unpleasant side effects like pain, discomfort, skin irritation, etc.[4,5]

History

The history of using electric currents to treat pain goes back to 2500 BC where some stone carvings depict a species of catfish with organs that produce an electrical charge used to treat pain. The physician to the Roman Emperor Claudius in AD46 claimed that standing on an electric fish could relieve symptoms of pain.[6]

TENS—MECHANISM OF ACTION

The gate-control theory

Melzack and Wall in 1965 published the gate-control theory with which increased the use of electroanalgesia.[7] This theory hypothesized that activity in small diameter nerve fibers causes pain and that, by stimulating the larger-diameter sensory nerve fibers, the perception of pain is reduced. They proposed that a physiological gating mechanism exists in the dorsal horn of the spinal cord. This "gate" can be opened or closed to allow or inhibit the transmission of painful stimuli through it, and up to the brain where it is processed. By selectively exciting A-beta nerve fibers in the skin with TENS, the amount of painful stimulation being transmitted by smaller diameter nerve fibers can be reduced, through segmental inhibition.[6,7]

High frequency or conventional TENS (90-130Hz)

High frequency (HF) or conventional TENS (90–130Hz), causes the pain gate to close by stimulating the small A-beta sensory nerve fibers. Conventional TENS also acts by reducing the release of excitatory neurotransmitters such as aspartate and glutamate, increasing the release of inhibitory neurotransmitters such as gamma-aminobutyric acid (GABA) and serotonin.[6]

"Low frequency" or "acupuncture" TENS (2-5Hz)

LF TENS is also known as acupuncture TENS has a low pulse rate. It acts by stimulating the A-delta nerve fibers to produce endorphins which in turn relieve pain.[6]

Burst TENS

Burst TENS stimulates both the A-beta and A-delta nerve types at the same time. In "burst" mode, conventional (HF) TENS is regularly interrupted by 2-3 "bursts" of lower frequency TENS. Different programs can be used interchangeably according to the preference of the patient.[6]

Low frequency TENS vs. high frequency TENS

Kocygit *et al.* in 2012 published a randomized controlled trial which compared 20 patients with subacromial impingement with patients being randomized into low TENS and Sham groups. Both the groups were given painful stimuli before and after TENS treatment. They found on functional magnetic resonance imaging (MRI) that in the LF TENS group, there was a statistically significant decrease in the perceived pain intensity and pain-specific activation of the contralateral primary sensory cortex, bilateral caudal anterior cingulate cortex, and of the ipsilateral supplementary motor area. They also reported in their results a statistically significant correlation between the change of Visual Analog Scale (VAS) value and the change of activity in the contralateral thalamus, prefrontal cortex, and the ipsilateral posterior parietal cortex. It was reported that the sham TENS group had no significant change in VAS value and activity of regions of interest.[2]

The results of this study support the efficacy of LF TENS in acute pain management. Although the sample size is low, MRI is a reliable tool in measuring the pain perceived by the individual.[2] Santos *et al.* in 2013 published a study done on rat paws wherein hyperalgesia and edema was induced by administering serotonin (5-HT). They applied LF and HF TENS on the right paw for 20 mins followed by serotonin induction. They used the Hargreaves method to measure nociception while the hydroplethysmometer was used to measure edema. Hargreaves method measures cutaneous hyperalgesia to thermal stimulation in animals. This study reported that neither HF nor LF TENS inhibited 5-HT-induced edema. However, LF TENS, but not HF TENS, completely reduced 5-HT-induced hyperalgesia. Pre-treatment of the paw with naltrexone, prior to application of TENS, showed a complete blockade of the analgesic effect induced by LF TENS.

This study supports the participation of peripheral endogenous opioid receptors in LF TENS analgesia in addition to its central action.[3]

Length of pain relief

LF TENS takes a longer time to achieve analgesia. Since the analgesia produced by the application of LF TENS is due to the release of endogenous opioids it lasts for a longer time. HF TENS or conventional TENS has a quick onset of analgesia but loses its effect quite rapidly when turning off the stimulation. The post-treatment analgesic effects of TENS can thus last anywhere between 5 minutes to 18 hours. It has been reported that in some patients' pain levels do not return to pre-stimulation levels even after 24 hours.

Post-stimulation analgesia has been widely attributed to the accumulation or depletion of endogenous opioids. There is a wide variation in post treatment pain relief experienced by patients and no reason for this has been documented yet. Cheing *et al.* reported a cumulative effect in pain reduction after repeated applications of TENS and suggested that the mechanisms underlying this may be related to changes

in the neuronal pathway. Breaks between sessions and/or changing electrode positions is essential as with long-term use, the nervous system becomes habituated to TENS, causing poorer pain control.[8]

We have given a brief description of important studies that used TENS for pain relief in Table 1, while in Table 2 we have highlighted studies that focused on Low Frequency TENS.

TENS-EVIDENCE FOR USE

Postoperative/acute pain

Very few systematic reviews have examined the use of TENS for postoperative pain management. Out of 17 randomized controlled trials analyzed by Carroll *et al.* in a systematic review which included studies with pain outcomes, 15 concluded that TENS had no analgesic benefit in the acute postoperative period.[9] A systematic review conducted by Reeve et, included 20 studies of postoperative pain, and concluded that 12 of these had positive TENS outcomes.[10]

A Cochrane review published in 2009 excluded studies that allowed additional analgesics. The authors could extract data from only six of the 12 Randomized Controlled Trials RCT s that met their inclusion criteria. This review reported that only one out of five studies comparing TENS with placebo showed a statistically significant superior effect of active TENS. Owing to insufficient data this review could not come to a definitive conclusion about the effectiveness of TENS as a sole treatment for acute pain.[6]

Table 1: Following is a summary of the important studies for TENS

Article	Author	Objectives	Results	Comments
Transcutaneous electrical nerve stimulation for acute pain-Cochrane review[6]	Walsh *et al.* 2011	To assess the analgesic effectiveness of TENS for acute pain	Twelve RCTs involving 919 participants at entry were included. Due to insufficient extractable data in the studies included in this review, the authors were unable to make any definitive conclusions about the effectiveness of TENS as an isolated treatment for acute pain in adults	It was not possible to perform a meta-analysis due to insufficient data
Randomization is important in studies with pain outcomes: Systematic review of transcutaneous electrical nerve stimulation in acute post operative pain[9]-Systematic review	Carrol *et al.* 1996	To examine the evidence for the importance of randomization of TENS in acute post operative pain	The authors concluded that TENS had a positive analgesic effect	Most of the studies in this review were non-randomized
Transcutaneous electrical nerve stimulation (TENS) forchronic pain-Cochrane review[11]	Nnoaham *et al.*2010	To evaluate the effectiveness of TENS in chronic pain	Twenty-fiveRCTs involving1281 participants were evaluated.There was a positiveanalgesic outcome in favor of active TENS treatments	Included studies varied in design, analgesic outcomes, chronic pain conditions, TENS treatments and methodological quality
Effectiveness of high-frequency transcutaneous electrical nerve stimulation at tender points as adjuvant therapy for patients with Fibromyalgia.[13](controlled clinical trial)	Carbonario *et al.* 2013	To assess the efficacy of high-frequency TENS as an adjuvant therapy to aerobic and stretching exercises for the treatment of fibromyalgia	TENS group had a greater pain reduction as compared to the without TENS group	Patients receiving TENS also showed greater improvement in fatigue levels, stiffness, anxiety, and depression levels
Transcutaneous electrical nerve stimulation (TENS) for phantom pain and stump pain following amputation in adults.[14](Cochrane review)	Mulvey *et al.*2010	To assess the analgesic effectiveness of TENS for the treatment of phantom pain and stump pain following amputation in adults	No RCTs examining the effectiveness of TENS for the treatment of phantom pain and stump pain in adults were identified by the review	No judgment of effectiveness can be madedue to the lack of methodological rigor in the available studies
Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults.[15](Cochrane review)	Hurlow *et al.* 2012	To determine the effectiveness of TENS for cancer-related pain in adults	This review included a total of three RCTs which were heterogeneous with respect to study population, sample size, study design, methodological quality, mode of TENS, Treatmentduration, method of administration and outcome measures used. Results of this systematic review were inconclusive due to a lack of suitable RCTs	LargeMulti-centre RCTs are required to assess the value of TENS in the management of cancer-related pain in adults
Transcutaneous electro stimulation for osteoarthritis of the knee. (Cochrane review)[16]	Rutjes *et al.*2010	To compare transcutaneous electro stimulation with sham or no specific intervention in terms of pain	Themethodological quality and the quality of reporting were poor and ahighdegreeof heterogeneity among the trials was seen	This systematic reviewis inconclusive, duetothe inclusion of only small trials of questionable quality.Well designedtrials ofadequate powerare warranted

TENS: Transcutaneous electrical nerve stimulation, RCT: Randomized controlled trial

Table 2: Following is a summary of some important studies that only focused on LF TENS. Low frequency currents

Article	Author	Objectives	Results	Comments
Electrical low-frequency stimulation induces central neuroplastic changes of pain processing in man[19]	Jung *et al.*, 2012	This systematic review aimed to review studies that evaluated effects of electrical low-frequency stimulation on pain perception and nociceptive processing as shown by psychophysical and electrophysiological means	This review reported that electrical low-frequency stimulation has beneficial effects on pain perception and nociceptive processing as shown by psychophysical and electrophysiological means (long-term depression)	Most of the studies in this review lacked methodological quality
Effects of transcutaneous electrical nerve stimulation on pain, pain sensitivity, and function in people with knee osteoarthritis: A randomized controlled trial[20]	Vance *et al.* 2012	The purpose of this study was to determine the effects of high-frequency TENS (HF-TENS) and low-frequency TENS (LF-TENS) on several outcome measures (pain atrest, movement-evokedpain, andpain sensitivity)	This Randomized Controlled Trial reported thatLowfrequency TENS decreases the pain pressurethresholdin knee osteoarthritis	This study had a good sample size and used reliable outcome measures
Functional magnetic resonance imaging of the effects of low-frequency transcutaneous electrical nerve stimulation on central pain modulation[2]	Kocygit *et al.* 2012	A randomized controlled trial which compared 20 patients with subacromial impingement with patients being randomized into low TENS and Sham groups	This study proved the efficacyoflow-frequencyTENS in Acute pain management	This study had a low sample size but used Functional Magnetic Resonance Imaging FMRI which is a reliable tool in measuring the pain perceived bythe individual

TENS: Transcutaneous electrical nerve stimulation, HF: High frequency, LF: Low frequency, FMRI: Functional magnetic resonance imaging

Chronic pain

Nnoaham and Kumbang in a cochrane systematic review evaluated the effectiveness of TENS interventions in chronic pain. Out of the 22 inactive control (placebo) studies they reviewed, 13 had a positive analgesic outcome and favored active TENS treatments. Whereas out of the 15 multiple-dose treatment comparison studies reviewed by them, only eight favored active TENS treatments.[11]

Neuropathic pain

Cruccu *et al.* in a systematic review recommended the use of standard high-frequency TENS when compared with placebo treatment for neuropathic pain. This review also suggested that TENS should be considered specifically to treat painful diabetic neuropathy. This review was endorsed by the European Federation of Neurological Societies guidelines for the treatment of neuropathic pain.[12]

Fibromyalgia

Carbonario *et al.* in 2013 in a clinical trial on 28 patients concluded that TENS as an adjuvant therapy is effective in relieving pain in fibromyalgia.[1]

IFT—Mechanism of action

It is suggested that by adjusting the frequency produced in the interference zone, it is possible to influence a range of different nerves. By changing the type of nerve which is primarily stimulated, the physiological outcome of the stimulation is modified, and hence, so is the therapeutic outcome. Frequencies can be utilized which primarily activate motor nerves, resulting in a muscle stimulation ranging from LF twitching (<15 Hz) to a tetanic, sustained contraction (>40 Hz) each of which have their therapeutic uses.[4]

There is at present, no evidence to suggest that muscle stimulation with electrical stimulation is anymore (or less) effective than by active exercise, but it can be utilized as a means of ensuring the muscle activity level is raised. This in turn will influence the local blood flow as a normal physiological response to an adjusted metabolic rate. Frequency ranges from 1–150 Hz or more can be employed in this respect, though it is suggested that clinically, the most appropriate ranges are between 10 and 20 or 25 Hz. At the lower end of this scale, a rapid muscular twitching will be produced, whilst at the upper end, a partial tetany will result. Using appropriate frequencies, sensory nerve stimulation can be achieved, thereby producing a mechanism to activate the pain gate (e.g. between 80-130 Hz) and opioid (<10 Hz) mechanisms which are associated with physiological pain relief.[5]

IFT EVIDENCE FOR USE

Musculoskeletal pain

Fuentes *et al.* in 2010 in a systematic review and metanalysis reported that IFT was found to be effective in treating various musculoskeletal conditions.[17]

Pain threshold

Ward *et al.* in 2009 in a single-blinded, within-group crossover study reported that medium frequency current is as effective as TENS in decreasing pain threshold.[18]

In Table 3 we have highlighted some important studies that used IFT(Medium Frequency Current) for pain relief.

Table 3: Following is a summary of some important studies for IFT that uses medium frequency currents. Medium frequency currents/IFT

Article	Author	Objectives	Results	Comments
Effectiveness of interferential current therapy in the management of musculoskeletal pain: A systematic review and metaanalysis[17]	Fuentes *et al.* 2010	To analyze the available information regarding the efficacy of Interferential Therapy (IFT) in the management of musculoskeletal pain	Fourteen studies were included in the meta-analysis. Interferential current as a supplement to another intervention seems to be more effective for reducing pain than a control treatment at discharge and more effective than a placebo treatment at the 3-month follow-up	The heterogeneity across studies and methodological limitations prevent conclusive statements regarding analgesic efficacy
A comparison of the analgesic efficacy of medium-frequency alternating current and TENS[18]	Ward *et al.* 2009	To compare the analgesic efficacy of medium frequency alternating current and transcutaneous electrical nerve stimulation on pain threshold. They concluded that medium frequency current is as effective as TENS in decreasing pain threshold	This was a single-blinded, within-group crossover study. They found out that medium frequency current is as effective as TENS in decreasing pain	Though the sample size was low this is one of the very few studies comparing the effectsof mediumfrequency currentwith other types

TENS: Transcutaneous electrical nerve stimulation, IFT: Interferential therapy

Recommendations

The published literature in this area is lacking in quality and there is a need for studies with good methodological quality in this area. In our clinical practise we have seen the benefits of TENS and IFT as an adjunct in pain relief in different conditions and in some cases like musculoskeletal pain a primary modality in pain relief. But this clinical experience should be supplemented by high quality research in this area.

Implacations in palliative care

Since the palliative care primarily revolves around giving pain relief, TENS and IFT could be of great benefit. They could be used as adjuncts or alternatives to pharmacological pain management. There is a need for research to complement the use and efficacy of these modalities in palliative care.

CONCLUSION

There is a plethora of evidence available to support the use of TENS and IFT of various frequencies in pain relief. Further research with more randomized controlled trials and studies with better methodological quality are warranted.

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