National Institute for Health and Care Excellence

Final

Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain

[H] Evidence review for electrical physical modalities for chronic primary pain

NICE guideline NG193

Intervention evidence review underpinning recommendation 1.2.6 and the research recommendations in the NICE guideline

April 2021

This evidence review was developed by the National Guideline Centre based at the Royal College of Physicians

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and, where appropriate, their carer or guardian.

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1.1 Review question: What is the clinical and cost effectiveness of electrical physical modalities for the management of chronic primary pain?

1.2 Introduction

Electrical physical modalities of treatment have been used therapeutically for many centuries. Reports of their use have been found in ancient writings, and include techniques still in use today, such as use of heat, cold and electricity.

Contemporary electrical physical modalities are diverse and include treatments regularly used for pain management and self-management. The list below is not exhaustive:

- Thermal modalities, often in the form of reusable hot or cold packs applied to the skin.
- Therapeutic ultrasound, using a probe that generates ultrasonic waves from electricity and delivers them into the tissues.
- Interferential therapy, using medium frequency electrical currents delivered with multiple electrodes over the affected areas.
- Pulsed Shortwave Diathermy, using high frequency electromagnetic energy delivered using electrical coils, to heat the tissues.
- Low level laser therapy (LLLT), involving the non-invasive application of a single wavelength of light to the skin over the injured area using a probe.
- Neuromuscular Electrical Stimulation (NMES), using superficial electrodes to target motor fibres.

For many of these techniques, a mechanism of action is currently unclear. Mechanisms may include activation of pain gate mechanisms, stimulation of cellular activity related to healing and repair, delivery of mechanical forces to alter the physical properties of tissues, alteration of blood flow and reduction of inflammation.

While many of these interventions are popular choices for the self-management of painful conditions, their role in clinical practice is much less clear. This evidence review therefore intends to explore the effectiveness of these interventions for chronic primary pain.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	People, aged 16 years and over, with chronic primary pain (whose pain management is not addressed by existing NICE guidance) (chronic widespread pain, complex regional pain syndrome, chronic visceral pain, chronic orofacial pain, chronic primary musculoskeletal pain other than orofacial) Chronic pain in one or more anatomical regions that is characterized by significant emotional distress (anxiety, anger/frustration or depressed mood) and functional disability (interference in daily life activities and reduced participation in social roles). The diagnosis is appropriate independently of identified biological or psychological contributors unless another diagnosis would better account for the presenting symptoms.

Interventions	Interventions: • Transcutaneous electrical nerve stimulation (TENS) • Percutaneous electrical nerve stimulation (PENS) • Interferential therapy • Laser therapy • Therapeutic ultrasound • Transcranial magnetic stimulation (TMS) • Transcranial direct current stimulation (TDCS).
Comparisons	Comparators: • Each other • Placebo/sham • Usual care • Physical therapies in this guideline.
Outcomes	Outcomes will be extracted at the longest time point up to 3 months and at the longest time point after 3 months. CRITICAL: • Pain reduction (any validated scale) • Health related quality of life (including meaningful activity) • Physical function (5 minute walk, sit to stand, Roland Morris Disability Questionnaire, Oswestry Disability Index, Canadian Occupational Performance Measure) • Psychological distress (depression/anxiety) (preferably Hospital Anxiety and Depression Scale) • Pain interference (brief pain inventory interference subscale) • Pain self-efficacy (pain self-efficacy questionnaire). IMPORTANT: • Use of healthcare services • Sleep • Discontinuation.
Study design	Randomised controlled trials (RCTs) and systematic reviews of RCTs. Cross-over RCTs will be considered if no non-cross-over RCT evidence is identified.

1.4 Clinical evidence

1.4.1 Included studies

34 studies were included in the review; [19, 28, 31, 37, 53, 61, 77, 78, 92, 94, 96, 101, 117, 120, 129, 137, 147, 167, 176, 185, 205, 241, 250, 274, 289, 314, 325, 329, 339, 345, 346, 354, 375] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary tables below (Table 3, Table 4, Table 5, Table 6, Table 7: Clinical evidence summary: TENS versus usual care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute Risk with Control
Quality of life at ≤3 months (SF36 physical component T scores, high is good outcome, change scores)	202 (1 study) 4 weeks	⨁⨁⨁⊖ MODERATE1 due to risk of bias		The mean change in quality of life score in control groups was 1.4

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute Risk with Control
Quality of life at ≤3 months (SF36 mental component T scores, high is good outcome, change scores)	202 (1 study) 4 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean change in quality of life score in control groups was 0.04
Pain reduction at ≤3 months (BPI intensity, 0-10, high is poor outcome, change scores)	242 (2 studies) 4-10 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean change in p score in the control groups was 0.15
Physical function at ≤3 months (6 minute walk test, feet walked, change scores)	202 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean change physical function in th control groups was -42.1
Psychological distress at ≤3 months (PROMIS depression T scores, high is poor outcome, change scores)	202 (1 study) 4 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean change in psychological distress the control groups wa 0.4
Psychological distress at ≤3 months (PROMIS anxiety T scores, high is poor outcome, change scores)	202 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean change in psychological distress the control groups wa -0.7
Pain interference at ≤3 months (BPI interference 0-10, high is poor outcome, change scores)	202 (1 study) 4 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean change in p interference in the co groups was -0.3
Pain self-efficacy at ≤3 months (PSEQ 0-60, high is good outcome, change scores)	202 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean change in p self-efficacy in the co groups was 0.8

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 inc at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence int

Table 8, Table 8, Table 10). See also the study selection flow chart in appendix C, study evidence tables in appendix D, forest plots in appendix E and GRADE tables in appendix F.

1.4.2 Excluded studies

A Cochrane review of TENS for fibromyalgia was identified (Johnson 2017 [174]), and references were cross-checked with this review. However, the review was not included because it deviated from the protocol of this review as it included crossover studies and studies that compared to other interventions, for example pharmacological.

See the excluded studies list in appendix I.

1.4.3 Summary of clinical studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Intervention and comparison	Population	Outcomes	Comments
Altan 2005[19]	2 week interventions **Intervention 1: Laser therapy (n=26)** **Number of sessions**: 10 (over 2 weeks) **Duration of sessions**: Not reported (2mins per trigger point) **Delivered by**: Not reported **Details**: Laser applied over each trigger point for 2 minutes, frequency 1000Hz frequency, 904nm wavelength, maximum power 50W. Participants instructed to perform daily isometric exercises and stretching at home **Intervention 2: Sham laser therapy (n=27)** Details: identical treatment but laser not turned on.	Myofascial pain (n=53) Mean age: 43.4 (2.26) years Duration of pain: 4.56 (1.26) years	At 2 weeks post-intervention and 3 months (follow up, including 2-week intervention): • Pain reduction	Myofascial pain definition: localised pain and taut bands in the neck for a minimum of the previous 3 months, tenderness in the cervical trigger points.
Arbabi-Kalati 2015[28]	2 week interventions **Intervention 1: Laser therapy (n=10)** **Number of sessions**: 4 (over 2 weeks) **Duration**: Estimated 1.5 minutes (laser applied for 10s to 10 areas) **Delivered by:** Not reported **Details**: 630nm wavelength, 30mW power, low level laser therapy applied to oral mucosa. **Intervention 2: Sham laser therapy (n=10)** **Details**: Identical treatment but laser not turned on.	Burning mouth syndrome (n=20) Mean age: 46.9 (4.95) years Duration of pain: 14.45 (6-36) years	At 2 weeks (post-intervention): • Quality of life • Pain reduction	Burning mouth syndrome defined as burning sensation in the oral cavity for at least 4 months without any identified causes.

Study	Intervention and comparison	Population	Outcomes	Comments
Armagan 2006[31]	10 days interventions **Intervention 1: Laser therapy (n=16)** **Number of sessions:** 10 (over 10 days) **Duration:** 1 minute per tender point **Delivered by:** Physician **Details**: 830nm wavelength, 50mW power, laser diameter 1mm, 1 minute per tender point at 2 joules per tender point. **Intervention 2: Sham laser therapy (n=16)** **Details:** Identical treatment but laser not turned on.	Fibromyalgia (n=32) Mean age: 38.25 (5.36) years Duration of pain: 5.8 (3.2) years All women	At 10 days (post-intervention) and 6 months (follow up, including 10 day intervention): • Quality of life	
Bardellini 2019 [37]	10 weeks interventions **Intervention 1: Laser therapy (n=45)** **Number of sessions:** 10 (over 10 weeks) **Duration:** unclear **Delivered by:** Dentist **Details:** K Laser Cube 3® irradiated the most painful areas in the oral cavity, with discontinuous combined wavelengths between 660-970 nm, medium power 3.2 W (6.4 W pulsed at 50%), treatment time 3'51", frequency 1-20000Hz, spot size 1cm². **Intervention 2:** Sham laser therapy (n=45) **Details:** The device was turned on but the hand piece did not work.	Burning mouth syndrome (n=90) Mean age: laser group: 60.31 (9.78) years Duration of pain: inclusion criteria specified >6 months, mean duration not reported All female	At 10 weeks (post-intervention) and 14 weeks (1 month follow up): • Quality of life	
Boyer 2014[53]	10 week interventions **Intervention 1: TMS (n=19)** **Number of sessions:** 14 (over 10 weeks) **Duration:** Not reported	Fibromyalgia (n=38) Mean age: 48.5 (10.5) years	At 10 weeks (post-intervention): • Quality of life • Psychological distress	Inclusion criteria: score of at least 4 on the BPI average pain intensity scale

Study	Intervention and comparison	Population	Outcomes	Comments
	Delivered by: Not reported **Details:** No further details available **Intervention 2: Sham TMS (n=19)** **Details:** Identical treatment but a sham coil used that emitted a similar sound to the active coil	Duration of pain: 3.7 (4.2) years		
Brietzke 2019 [54]	3 month interventions **Intervention 1: TDCS (n=10)** **Number of sessions:** 60 sessions over 12 weeks **Duration: approx.** 30 minutes **Delivered by:** Self-administered **Details:** 2mA current applied through electrodes over the left dorsolateral prefrontal cortex (DLPFC) attached to cap (caps individually fitted to each participant). **Intervention 2: Sham TDCS (n=10)** **Details:** Identical treatment but no electrical stimulation	Fibromyalgia (n=40) Mean age 49.1 years Duration of pain: 6.2 years	At 3 months (post-intervention) • Psychological distress • Sleep	Intervention self-administered at home. The electrode position was accurate for the subjects. To avoid incorrect placement of the electrodes, the anode was painted red and cathode black (although equipment was already set up – participant could not change any part of it).
Carretero 2009 [61]	4 week interventions **Intervention 1: TMS (n=14)** **Number of sessions:** 20 sessions over 4 weeks **Duration: approx.** 30 minutes **Delivered by:** Not reported **Details:** Butterfly coil used, 20 trains at 110% of motor threshold for 60s at 1Hz and a 45s interval between trains. Stimulation area right dorsolateral prefrontal area (total of 1,200 pulses per session) **Intervention 2: Sham TMS (n=12)**	Fibromyalgia (n=26) Mean age: 51.2 (5.3) years Duration of pain not stated	At 3 months (follow up, including 4 week intervention): • Pain reduction	

Study	Intervention and comparison	Population	Outcomes	Comments
	Details: Identical treatment but coil placed perpendicular to the cranium (the magnetic field did not significantly penetrate the brain)			
Chow 2004[77]	7 week interventions **Intervention 1: Laser therapy (n=10)** **Number of sessions: 7** (over 7 weeks) **Duration:** 30 minutes **Delivered by:** Not reported **Details:** 830nm, 15mm laser length and 3mm width, 300mW power, applied 30s per point or until area became less tender **Intervention 2: Sham laser therapy (n=10)** **Details:** Identical treatment but laser did not emit a beam	Chronic neck pain (n=20) Mean age: 57.7(10.9) years Duration of pain: 13.3 years (SE 2.48)	At 3 months (follow up, including 7 week intervention): • Quality of life • Pain reduction	Participants that had previously received laser therapy were excluded (other than laser acupuncture). People with work related or third party injuries in which litigation or compensation were still current were excluded.
Chow 2006[78]	7 week interventions **Intervention 1: Laser therapy (n=45)** **Number of sessions:** 7 (over 7 weeks) **Duration:** 30 minutes **Delivered by:** Not reported **Details:** 830nm wavelength, 300mW, each tender point treated for 30 seconds, up to 50 points treated **Intervention 2: Sham laser (n=45)** **Details:** Identical treatment but device did not emit laser (although did emit sound)	Chronic neck pain (n=90) Mean age: 56 (12.8) years Duration of pain: 15 (12.6) years	At 3 months (follow up, including 7 week intervention): • Quality of life • Pain reduction • Discontinuation	People with work related or third party injuries in which litigation or compensation were still current were excluded.
da Cunha 2008[92]	4 week interventions **Intervention 1: Laser therapy (n=20)** **Number of sessions:** 4 (over 4 weeks)	Temporomandibular disorder (n=40)	At 4 weeks (post-intervention) • Pain reduction	Temporomandibular disorder diagnosed based on complete clinical examination, including patient's

Study	Intervention and comparison	Population	Outcomes	Comments
	Duration: Not reported (each area irradiated for 20s) **Delivered by:** Not reported **Details:** 830nm wavelength, 500mW output, each area irradiated for 20s **Intervention 2: Sham laser (n=20)** **Details:** Identical treatment but without energy output	Mean age: 43.3 years Duration of pain: Not stated		history, at the Center of Occlusion and Temporomandibular Disorder of the Dental School of Sao Paulo State University (UNESP).
Dailey 2019 [94]	4 week interventions **Intervention 1: TENS (n=103)** **Number of sessions:** Not reported **Duration:** at least 2 hours/day during activity **Delivered by:** self-administered (first application delivered in clinic) **Details:** EMPI-Select TENS (DJO Global, Vista, CA) delivered through butterfly electrodes placed at the cervicothoracic junction and lower back. Active-TENS parameters were asymmetrical, biphasic waveform with a modulating frequency (2-125 Hz), pulse duration 200µ sec, and highest tolerable stimulation intensity. Active-TENS was sent home with participants with an instruction manual developed by study personnel. **Intervention 2: sham TENS (n=99)** **Details:** delivered current for 45s ramping down to 0 in the last 15s and the appearance was identical to the active unit. **Intervention 3: Usual care (n=99)** **Details:** used a mock-TENS during visits to blind Outcome-Assessors with electrodes that were attached to a TENS unit that provided no current intensity.	Fibromyalgia (n=301) Mean age: 46.8 (13.06) years Duration of pain median (range): 7 (2-15) years All female	At 4 weeks (post intervention): • Quality of life • Pain reduction • Physical function • Psychological distress • Pain interference • Pain self-efficacy	All participants continued current treatments prescribed by their health care provider and were asked not to change medications during the study.

Study	Intervention and comparison	Population	Outcomes	Comments
Dall'Agnol 2014[96]	10 day interventions **Intervention 1: TMS (n=12)** **Number of sessions:** 10 (over 10 days) **Duration:** Not reported **Delivered by:** Not reported **Details:** Figure 8 coil placed over left motor cortex, trains consisted of 16 series of 10-s pulses at 10Hz, interval of 26s between trains. Intensity was 80% of resting motor threshold **Intervention 2: sham TMS (n=12)** **Details:** Identical treatment but inactive sham coil used (identical sounds and sensations but no brain stimulation)	Myofascial pain (n=24) Mean age: 45.43 (12.86) years Duration of pain: Not stated All women	At 3 months (follow up, including 10 day intervention): • Pain reduction	Number of sessions stated to be 10, but duration of study not specified. Myofascial pain defined as reduced quality of life due to regional pain, decreased range of motion, stiffness in muscles, presence of trigger points, taut bands, tender points, palpable nodules and pain. Must have score of more than 4 on the neuropathic pain diagnostic questionnaire.
Del Vecchio 2019 [101]	1 week interventions **Laser therapy (n=30)** **Number of sessions:** 14 (over 7 days; delivered at home) **Duration:** 1 week **Delivered by:** Self-administered (first application delivered in clinic) **Details:** Laser with 808nm wavelength, 5J/min, 250mW and 15KHz for 8 minutes, for a total of 40J applied directly to each painful area. **Sham laser therapy (n=30)** **Details:** identical device with beam and sound but devoid of therapeutic diode source.	Temporomandibular joint disorder-related pain (n=60) Mean age: 42.55 (14.842) years Duration of pain not specified (minimum duration 6 months)	At 1 week (post-intervention): • Pain reduction	The inclusion criteria were: presence of pain in the joint area and/or radiating to the face, jaw, or neck for at least six months; reduced mouth opening or jaw locks; painful clicking, popping or grating when opening or closing the mouth; occlusal changes; no muscle

Study	Intervention and comparison	Population	Outcomes	Comments
				tenderness at palpation; and no drug consumption for at least three weeks before treatment. The disorder was diagnosed by clinical and radiological examinations and according to the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) Axis I and Axis II
Esenyel 2000[117]	10 day interventions **Intervention 1: Ultrasound (n=36)** **Number of sessions:** 10 (over 10 days) **Duration:** 6 mins per trigger point **Delivered by:** Not reported **Details:** 1.5Wcm^2 applied to each trigger point for 6 minutes. Neck exercises also advised **Intervention 2: Usual care (n=40)** **Details:** Usual care as well as advice on neck stretching exercises	Myofascial pain (n=76) Mean age: 30 (7.7) years Duration of pain: ranged 6 months to 7 years	At 3 months (follow up, including 10 day intervention): • Pain reduction	Myofascial pain followed Travel and Simons criteria for active myofascial trigger points in the upper trapezius muscles
Fagerlund 2015[120]	5 day interventions **Intervention 1: TDCS (n=25)** **Number of sessions:** 5 (over 5 days) **Duration:** 20 minutes	Fibromyalgia (n=50) Mean age: 48.6 (9.4) years	At 4 weeks (follow up, including 5 day intervention): • Quality of life • Pain reduction	

Study	Intervention and comparison	Population	Outcomes	Comments
	Delivered by: Not reported **Details:** Intensity 2mA, anode placed on C3 and cathode placed on contralateral supraorbital area **Intervention 2: Sham TDCS (n=25)** **Details:** Identical treatment but stimulation faded in for 30s, then terminated by 5s fade out (to mimic skin sensation of active treatment with insufficient duration to induce cortical excitability)	Duration of pain: 18.1 (9) years	• Psychological distress	
Fregni 2006[129]	1 week interventions *Note: interventions 1 and 2 pooled in the analysis.* **Intervention 1: TDCS (DLPFC) (n=11)** **Number of sessions:** 5 (over 5 days) **Duration:** 20mins **Delivered by:** Not reported **Details:** Current transferred by pair of saline soaked sponge electrodes, max output 10mA, anode on left DLPFC brain area, constant current of 2mA applied for 20mins **Intervention 2: TDCS (motor cortex [M1]) (n=11)** **Number of sessions:** 5 (over 5 days) **Duration:** 20mins **Delivered by:** Not reported **Details:** Current transferred by pair of saline soaked sponge electrodes, max output 10mA, anode on primary motor cortex brain area, constant current of 2mA applied for 20mins **Intervention 3: Sham TDCS (n=10)** **Details:** Identical treatment but with sham stimulation of the primary motor cortex (stimulator turned off after	Fibromyalgia (n=32) Mean age: 53.2 (8.97) years Duration of pain: 8.4 (9.3) years All women	At 3 weeks (follow up, including 1 week intervention): • Psychological distress	Inclusion criteria: score of at least 4 on the VAS and at least 30 on the total tender point score.

Study	Intervention and comparison	Population	Outcomes	Comments
	30s to mimic sensation but no current received after this)			
Gokyildiz 2012[137]	12 week interventions **Intervention 1: PENS (n=13)** **Number of sessions:** 12 (over 3 months) **Duration:** 30mins **Delivered by:** Not reported **Details:** Percutaneous tibial nerve stimulation, applied using a needle set and stimulator with 9-volt batteries and current between 0.5-10mA, 20Hz frequency. Needle inserted 3-4cm above inner malleolus and electrode placed on inner side of the heel. Current adjusted based on tolerance **Intervention 2: Usual care (n=13)** **Details:** Routine usual care, no further details	Chronic pelvic pain (n=26) Mean age: Not reported Duration of pain: Not reported (minimum duration 6 months)	At 3 months (post-intervention): • Quality of life • Pain reduction	Score of at least 5 on VAS. Cessation of analgesics at least 2 weeks before treatment, and physiotherapy or electrotherapy at least 3 months before treatment.
Gur 2002[147]	2 week interventions **Intervention 1: Laser therapy (n=25)** **Number of sessions:** 14 (over 2 weeks) **Duration:** Not reported (3 mins per tender point) **Delivered by:** Physical therapists **Details:** 904nm wavelength, 20W max per pulse, 200ns max pulse duration, 2.8Hz pulse frequency, 11.2mW average power, 3 mins at each tender point **Intervention 2: Sham laser therapy (n=25)** **Details:** Identical treatment but no laser beam emitted	Fibromyalgia (n=50) Mean age: 29.44 (6.6) years Duration of pain: 4.74 (3.98) years	At 2 weeks (post-intervention): • Pain reduction	All participants discontinued medications at least 1 month prior to treatment
Jales 2015[167]	10 week interventions **Intervention 1: TDCS (n=10)**	Fibromyalgia (n=20)	At 10 weeks (post-intervention): • Quality of life	

Study	Intervention and comparison	Population	Outcomes	Comments
	Number of sessions: 10 (over 10 weeks) **Duration:** 20 minutes **Delivered by:** Not reported **Details:** 2 electrodes placed on scalp, 1mA impulse applied (anode over m1, cathode over contralateral supraorbital region). Applied for 20 mins **Intervention 2: Sham TDCS (n=10)** **Details:** Identical treatment but device not turned on	Mean age: 46.4 (10.615) years Duration of pain: Not reported All women	• Pain reduction	
Kabay 2009[176]	12 week interventions **Intervention 1: PENS (n=45)** **Number of sessions:** 12 (over 3 months) **Duration:** 30 mins **Delivered by:** Not reported **Details:** Percutaneous posterior tibial nerve stimulation, needle inserted 5cm from medial malleolus and electrode placed on same leg. Electrical stimulation applied with 200us pulses, rate of Hz, intensity level just below motor threshold. Amplitude set at maximum tolerable (using 1.5x threshold for evoking plantar flexion) **Intervention 2: Sham PENS (n=44)** **Details:** Identical treatment but electrical stimulation not applied.	Pelvic pain (n=89) Mean age: 37.7(7.4) years Duration of pain: 4.5 (6.1) years	At 3 months (post-intervention): • Quality of life • Pain reduction	Diagnosis of category IIIB CP/CPPS
Khedr 2017[185]	2 week interventions **Intervention 1: TDCS (n=20)** **Number of sessions:** 10 (over 2 weeks) **Duration:** 20mins **Delivered by:** Not reported	Fibromyalgia (n=40) Mean age: 32.3 (10.9) years Duration of pain: 6.1 (2.5) years	At 8 weeks (follow up, including 2 week intervention): • Pain reduction • Psychological distress	Score of at least 4 on VAS pain scale

Study	Intervention and comparison	Population	Outcomes	Comments
	Details: 2mA, anodal electrode on left M1 over C3, reference electrode over contralateral arm. **Intervention 2: Sham TDCS (n=20)** **Details:** Identical treatment but current applied for 30s only at the beginning and at the end of the session.			
Lee 2012[205]	10 day interventions Note: intervention 1 and 2 pooled in the analysis **Intervention 1: TMS (low frequency) (n=7)** **Number of sessions:** 10 (over 10 days) **Duration:** Not reported **Delivered by:** Physiatrist **Details:** Figure 8 coil, applied to right M1 (at the DLPFC), 1Hz, 110% intensity of resting motor threshold, 800 stimuli of each train and 2 trains with 60s of inter-train interval and a total of 1600 stimuli per session. **Intervention 2: TMS (high frequency) (n=8)** **Details:** Identical treatment to intervention 2 but 80% of resting motor threshold, 2000 stimuli per session. **Intervention 3: Sham TMS (n=7)** **Details:** Identical treatment but coil angle was 90% perpendicular to skull (magnetic field did not penetrate the brain).	Fibromyalgia (n=22) Mean age: 47.2(6.2) years Duration of pain: 44.7(10.3) years All women	At 6 weeks (follow up, including 10 day intervention): • Quality of life • Pain reduction • Psychological distress • Discontinuation	Inclusion criteria: pain for at least 24 months
Mhalla 2011[241]	21 week interventions **Intervention 1: TMS (n=20)** **Number of sessions:** 14 (over 21 weeks) **Duration:** Not reported **Delivered by:** Not reported	Fibromyalgia (n=40) Mean age: 50.2 (10.8) years	At 25 weeks (follow up, including 21 week intervention): • Quality of life • Psychological distress • Pain interference	Score of at least 4 on BPI pain scale.

Study	Intervention and comparison	Population	Outcomes	Comments
	Details: figure 8 coil, positioned to induce current in the anterior posterior direction, 15 series of 10s pulses, frequency 10Hz, interval of 50s between each train, total of 1500 pulses per session (stimulation intensity 80% of resting motor threshold) **Intervention 2: Sham TMS (n=20)** **Details:** Identical treatment but sham coil used	Duration of pain: 13.55 (12.4) years All women		
Murina 2008[250]	10 week interventions **Intervention 1: TENS (n=20)** **Number of sessions:** 20 (over 10 weeks) **Duration:** 15-30 mins **Delivered by:** Not reported **Details:** Electrical stimulation via vaginal probe 20mm in diameter, 110mm in length. Frequencies of 10 and 50Hz at 15min intervals. **Intervention 2: Sham TENS (n=20)** **Details:** Identical treatment but nonactive stimulation (2Hz, pulse duration 2ms followed by 15min pause).	Vestibulodynia (n=40) Mean age: 28 (21-44) years Duration of pain: 15 month (range 7-48 months) All women	At 10 weeks (post-intervention): • Pain reduction • Discontinuation At 22 weeks (including 10 week intervention) • Pain reduction	
Panton 2013[274]	4 week interventions **Intervention 1: Laser therapy (n=23)** **Number of sessions:** 8 (over 4 weeks) **Duration:** 15 mins **Delivered by:** Not reported **Details:** Laser applied to 7 tender points with dual wavelength laser (20% 810nm and 80% 980nm), heat also applied via warm air, each point treated for 60s for total of 600J per point **Intervention 2: Sham laser (n=18)**	Fibromyalgia (n=41) Mean age: 53 (11.5) years Duration of pain: 10.5 (7.5) years All women	At 4 weeks (post-intervention): • Quality of life • Pain reduction • Discontinuation	Participants received $100 for participating in the study.

Study	Intervention and comparison	Population	Outcomes	Comments
	Details: Identical treatment but laser not turned on			
Rohlig 2011[289]	3 week interventions **Intervention 1: Laser therapy (n=20)** **Number of sessions:** 10 (over 3 weeks) **Duration:** Not reported (10s per tender point) **Delivered by:** Not reported **Details:** 820nm wavelength, beam diameter 6mm, 8J/cm2 to each tender point **Intervention 2: Sham laser therapy (n=20)** **Details:** Identical treatment but laser not turned on	Temporomandibular disorder (n=40) Mean age: 42.5 (2.3) years Duration of pain: 10.75 (2.9) years	At 3 weeks (post-intervention): • Pain reduction	Presence of signs and symptoms of TMD of myogenic origin according to the research diagnostic criteria for TMD.
Short 2011[314]	2 week interventions **Intervention 1: TMS (n=10)** **Number of sessions:** 10 (over 2 weeks) **Duration:** 20 mins **Delivered by:** Not reported **Details:** Applied to left prefrontal cortex, 10Hz, 5s train duration, intensity 120% resting motor threshold **Intervention 2: Sham TMS (n=10)** **Details:** Identical treatment but sham TMS coil used	Fibromyalgia (n=20) Mean age: 53 (13.53) years Duration of pain: 11.1 (10.36) years	At 4 weeks (follow up, including 2 week intervention): • Quality of life • Pain reduction • Physical function • Psychological distress	
Spanemberg 2015[325]	3 week interventions *Note: intervention 1 and 2 pooled in analysis* **Intervention 1: Laser therapy (infrared) (n=20)** **Number of sessions:** 9 (over 3 weeks) **Duration:** M50s per point **Delivered by:** Not reported	Burning mouth syndrome (n=58) Mean age: 61.9 (8.76) years	At 8 weeks (follow up, including 3 week intervention): • Quality of life • Pain reduction	Burning or pain in the oral mucosa for at least 6 months with clinically normal mucosa.

Study	Intervention and comparison	Population	Outcomes	Comments
	Details: 830nm wavelength, 100mW output, continuous emissions, 5J energy per point, 50s per point. **Intervention 2: Laser therapy (red laser) (n=19)** **Details:** Identical treatment but red laser at 685nm wavelength, 2J per point, 35mQ output power **Intervention 3: Sham laser therapy (n=19)** **Details:** Identical treatment but sham laser	Duration of pain: Not reported (minimum 6 months)		
Sugaya 2016[329]	2 week interventions **Intervention 1: Laser therapy (n=15)** **Number of sessions:** 4 (over 2 weeks) **Duration:** Not reported **Delivered by:** Not reported **Details:** 6J/cm2, applied to entire area affected by burning sensation. No further details. **Intervention 2: Sham laser therapy (n=15)** **Details:** Identical treatment but no laser energy delivered (machine still appeared active)	Burning mouth syndrome (n=30) Mean age: 59.7(29-83) years Duration of pain: 31.7 months (range 6 to 192)	At 3 months and 16 weeks (follow up, including 2 week intervention): • Pain reduction	Exclusion criteria: Clinical alterations in the oral mucosa potentially associated with the burning symptoms
Tekin 2014[339]	10 day interventions **Intervention 1: TMS (n=27)** **Number of sessions:** 10 (over 10 days) **Duration:** Not reported **Delivered by:** Psychiatry physician **Details:** Figure 8 coil, 30 sequential series each for 5s at 10Hz, at 100% of motor threshold, 12s interval between series	Fibromyalgia (n=52) Mean age: 44.4 (8.1) years Duration of pain: 12.1 (6.47) years	At 10 weeks (post-intervention): • Quality of life • Pain reduction • Psychological distress • Discontinuation	No analgesic use for at least 1 month prior to treatment

Study	Intervention and comparison	Population	Outcomes	Comments
	Intervention 2: Sham TMS (n=25) **Details:** Identical treatment but placebo sham coil used.			
Umezaki 2016[345]	10 day interventions **Intervention 1: TMS (n=14)** **Number of sessions:** 10 (over 10 days) **Duration:** Not reported **Delivered by:** Not reported **Details:** Figure 8 coil, positioned around primary motor cortex, 10Hz frequency, 5s pulse train duration, intensity 110% of resting motor threshold, total 30,000 pulses **Intervention 2: Sham TMS (n=12)** **Details:** Identical treatment but coil was shielded so actual stimulation did not occur.	Burning mouth syndrome (n=26) Mean age: 63.85 (9.56) years Duration of pain: 63.42 (65.51) years	At 8 weeks (follow up, including 10 day intervention): • Pain reduction • Discontinuation (at 1 week)	Diagnosis of BMS confirmed by (1) daily and deep bilateral burning sensation of the oral mucosa, burning sensation for at least 4-56 months, constant intensity or increasing intensity during the day, no worsening but possible improvement on eating or drinking, no interference with sleep and normal appearing oral mucosa.
Valenzuela 2017[346]	4 week interventions *Note: intervention 1 and 2 pooled in the analysis* **Intervention 1: Laser therapy (low intensity) (n=16)** **Number of sessions:** 4 (over 4 weeks) **Duration:** Not reported **Delivered by:** Not reported **Details:** 815nm wavelength, 1W output, 4s per point, 4J, applied intra-orally and spot sizes of 0.03cm^3. **Intervention 2: Laser therapy (high intensity) (n=16)** **Details:** Identical treatment but 6J energy over 6s **Intervention 3: Sham laser therapy (n=12)**	Burning mouth syndrome (n=44) Mean age: 65.5 (10.6) years Duration of pain: Not reported	At 4 weeks (post-intervention): • Quality of life • Pain reduction • Psychological distress	Burning mouth syndrome diagnosis according to international classification of headaches

Study	Intervention and comparison	Population	Outcomes	Comments
	Details: Identical treatment but laser turned off			
Venancio 2005[354]	3 week interventions **Intervention 1: Laser therapy (n=15)** **Number of sessions:** 6 (over 3 weeks) **Duration:** Not reported **Delivered by:** Not reported **Details:** 780nm wavelength, 30mW output, 10s duration at each point **Intervention 2: Sham laser therapy (n=15)** **Details:** Identical treatment but laser device not turned on	Temporomandibular disorder (n=30) Mean age: 36.25 (13-63) years Duration of pain: 44.8 months (range 6-120 months)	At 8 weeks (follow up, including 3 week intervention): • Pain reduction	TMD diagnosis according to criteria of the American Academy of Orofacial pain
Yagci 2014[375]	2 week interventions **Intervention 1: TMS (n=14)** **Number of sessions:** 10 (over 2 weeks) **Duration:** Not reported **Delivered by:** Not reported **Details:** Stimulation of motor cortex area, applied stimulation at 90% of motor threshold for 60s at 1Hz and 45s intervals between trains (1200 pulses in total each session) **Intervention 2: Sham TMS (n=14)** **Details:** Identical treatment but sham coil used	Fibromyalgia (n=28) Mean age: 44.9(8.6) years Duration of pain: 53.5 (29.8) months All women	At 3 months (follow up, including 2 week intervention): • Quality of life • Pain reduction • Psychological distress	

See appendix D for full evidence tables.

1.4.4 Quality assessment of clinical studies included in the evidence review

Table 3: Clinical evidence summary: Laser therapy versus sham laser therapy

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Laser therapy versus sham laser therapy (95% CI)
Quality of life at ≤3 months (Oral health impact profile, FIQ, high is poor outcome, final values)	276 (6 studies) 2 weeks-3 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, inconsistency, imprecision		-	The mean quality of life score in the intervention groups was 0.68 standard deviations lower (1.1 to 0.25 lower)
Quality of life at ≤3 months (SF-36 physical component summary score, 0-100, high is good outcome, change scores)	110 (2 studies) 3 months	⨁⨁⨁⊖ MODERATE1 due to imprecision		The mean quality of life change score in the control groups was 1.26	The mean quality of life score in the intervention groups was 2.09 higher (0.91 lower to 5.09 higher)
Quality of life at ≤3 months (SF-36 mental component summary score, 0-100, high is good outcome, change scores)	110 (2 studies) 3 months	⨁⨁⊖⊖ LOW1,2 due to inconsistency, imprecision		The mean quality of life change score in the control groups was 2.7	The mean quality of life score in the intervention groups was 0.74 lower (5.35 lower to 3.87 higher)
Quality of life at >3 months (FIQ, Oral health impact profile, high is poor outcome, final values)	117 (2 studies) 14-24 weeks	⨁⨁⊖⊖ LOW1,3 due to risk of bias, imprecision		-	The mean quality of life score in the intervention groups was 0.78 standard deviations lower (1.16 to 0.4 lower)
Pain reduction at ≤3 months (VAS, NRS, FIQ pain scale, high is poor outcome, 0-10, final values and change scores)	558 (13 studies) 1 week-3 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, inconsistency, imprecision		The mean pain reduction score in the control groups was 4.97	The mean pain reduction score in the intervention groups was 1.42 lower (2.12 to 0.73 lower)
Pain reduction at >3 months (VAS, high is poor outcome, 0-10, final values)	71 (2 studies) 14-16 weeks	⨁⨁⨁⊖ MODERATE1 due to imprecision		The mean pain reduction score in the control groups was 2.8	The mean pain reduction score in the intervention groups was 0.6 lower (0.91 to 0.3 lower)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Laser therapy versus sham laser therapy (95% CI)
Psychological distress at ≤3 months (Hospital anxiety and depression rating scale, anxiety subscale, 0-21, high is poor outcome, final values)	44 (1 study) 4 weeks	⨁⨁⨀⨀ LOW1,3 due to risk of bias, imprecision		The mean psychological distress score in the control groups was 10.33	The mean psychological score in the intervention groups was 0.83 higher (1.52 lower to 3.18 higher)
Psychological distress at ≤3 months (Hospital anxiety and depression rating scale, depression subscale, 0-21, high is poor outcome, final values)	48 (1 study) 4 weeks	⨁⨁⨀⨀ LOW1,3 due to risk of bias, imprecision		The mean psychological distress score in the control groups was 7.25	The mean psychological distress score in the intervention groups was 1.29 higher (1.39 lower to 3.96 higher)
Discontinuation at ≤3 months	90 (1 study) 3 months	⨁⨁⨁⨀ LOW1 due to imprecision	RR 0.67 (0.12 to 3.8)	67 per 1000	22 fewer per 1000 (from 59 fewer to 188 more)

1 Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.
2 Downgraded for heterogeneity, unexplained by subgroup analysis
3 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Table 4: Clinical evidence summary: TMS versus sham TMS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with TMS versus sham TMS (95% CI)
Quality of life at ≤3 months (SF-36 physical summary score, 0-100, high is good outcome, change scores)	29 (1 study) 10 weeks	⨁⨀⨀⨀ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life change score in the control groups was 0.4	The mean quality of life score in the intervention groups was 1 higher (4.12 lower to 6.12 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with TMS versus sham TMS (95% CI)
Quality of life at ≤3 months (SF-36 mental summary score, 0-100, high is good outcome, change scores)	29 (1 study) 10 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life change score in the control groups was -1.6	The mean quality of score in the intervention groups was 6.6 higher (1.26 to 11.94 higher)
Quality of life at ≤3 months (WHOQOL-BREF physical domain, 4-20, high is good outcome, final values)	51 (1 study) 2 weeks	⊕⊕⊕⊕ HIGH		The mean quality of life score in the control groups was 11.33	The mean quality of score in the intervention groups was 3.27 higher (1.79 to 4.75 higher)
Quality of life at ≤3 months (WHOQOL-BREF psychological domain, 4-20, high is good outcome, final values)	51 (1 study) 2 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean quality of score in the control groups was 12.71	The mean quality of score in the intervention groups was 1.18 higher (0.18 lower to 2.54 higher)
Quality of life at ≤3 months (FIQ, 0-100, high is poor outcome, final values)	60 (3 studies) 4 weeks-3 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life score in the control groups was 49.92	The mean score in the intervention groups was 8.69 lower (18.83 lower to 1.46 higher)
Quality of life at >3 months (FIQ, 0-100, high is poor outcome, final values)	30 (1 study) 25 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life score in the control groups was 63.3	The mean quality of life score in the intervention groups was 7.3 lower (19.04 lower to 4.44 higher)
Pain reduction at ≤3 months (VAS, McGill Pain questionnaire, 0-10, high is poor outcome, final values)	181 (7 studies) 2 weeks-3 months	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, inconsistency, imprecision		The mean pain reduction score in the control groups was 5.68	The mean pain reduction score in the intervention groups was 1.17 lower (2.1 to 0.24 lower)
Physical function at ≤3 months (BPI functional impairment subscale, 0-10, high is poor outcome, final values)	20 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean physical function score in the control groups was 3.79	The mean physical function score in the intervention groups was 0.19 lower (2.34 lower to 1.96 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with TMS versus sham TMS (95% CI)
Psychological distress at ≤3 months (Beck depression inventory, 0-61, high is poor outcome, final values and change scores)	44 (2 studies) 6-10 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		-	The mean psychological score in the intervention groups was 1.59 lower (4.13 lower to 0.94 higher)
Psychological distress at ≤3 months (Hamilton depression rating scale, MADRS, BDI, high is poor outcome, final values)	96 (3 studies) 2 weeks-3 months	⊕⊕⊕⊖ MODERATE1 due to risk of bias		-	The mean psychological distress score in the intervention groups was 0.01 standard deviations higher (0.39 lower to 0.41 higher)
Psychological distress at ≤3 months (HADS anxiety, 0-21, high is poor outcome, change scores)	29 (1 study) 10 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress change score in the control groups was 0.5	The mean psychological distress score in the intervention groups was 0.1 lower (1.6 lower to 1.4 higher)
Psychological distress at >3 months (HADS anxiety, 0-21, high is poor outcome, change scores)	30 (1 study) 25 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress change score in the control groups was 9.4	The mean psychological score in the intervention groups was 0.2 lower (4 lower to 3.6 higher)
Psychological distress at >3 months (HADS depression, 0-21, high is poor outcome, change scores)	30 (1 study) 25 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress change score in the control groups was 7.4	The mean psychological score in the intervention groups was 1.2 higher (1.92 lower to 4.32 higher)
Pain interference at >3 months (BPI pain interference, 0-10, high is poor outcome, final values)	30 (1 study) 25 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean pain interference score in the control groups was 6	The mean pain interference score in the intervention groups was 1.9 lower (3.05 to 0.75 lower)
Discontinuation at ≤3 months	141 (4 studies) 2-6 weeks	⊕⊕⊖⊖ LOW2 due to imprecision	RD 0.03 (-0.06 to 0.12)	20 per 1000	30 more per 1000 (from 60 fewer to 120 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with TMS versus sham TMS (95% CI)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs. 3 Downgraded for heterogeneity, unexplained by subgroup analysis					

Table 5: Clinical evidence summary: TDCS versus sham TDCS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with TDCS versus sham TDCS (95% CI)
Quality of life at ≤3 months (SF-36 mental summary score, 0-100, high is good outcome, final values)	48 (1 study) 4 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life in the control groups was 45.4	The mean quality of life score in the intervention groups was 2.8 higher (4.72 lower to 10.32 higher)
Quality of life at ≤3 months (SF-36 physical summary score, 0-100, high is good outcome, final values)	48 (1 study) 4 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life in the control groups was 35.92	The mean quality of life score in the intervention groups was 1.14 lower (5.92 lower to 3.64 higher)
Quality of life at ≤3 months (SF-36 physical function subscale, 0-100, high is good outcome, final values)	20 (1 study) 10 weeks	⨁⨁⨁⊖ MODERATE1 due to risk of bias		The mean quality of life score in the control groups was 38	The mean quality of score in the intervention groups was 30.5 higher (12.47 to 48.53 higher)
Quality of life at ≤3 months (SF-36 physical role subscale, 0-100, high is good outcome, final values)	20 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of		The mean quality of score in the control groups was 47.5	The mean quality of life score in the intervention groups was 27.5 higher (4.71 lower to 59.71 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with TDCS versus sham TDCS (95% CI)
		bias, imprecision			
Quality of life at ≤3 months (SF-36 bodily pain subscale, 0-100, high is good outcome, final values)	20 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life score in the control groups was 50	The mean quality of life score in the intervention groups was 7 lower (25.49 lower to 11.49 higher)
Quality of life at ≤3 months (SF-36 general health subscale, 0-100, high is good outcome, final values)	20 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life score in the control groups was 63.5	The mean quality of life score in the intervention groups was 5.5 lower (14.54 lower to 3.54 higher)
Quality of life at ≤3 months (SF-36 vitality subscale, 0-100, high is good outcome, final values)	20 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life score in the control groups was 58	The mean quality of life score in the intervention groups was 4.5 lower (12.92 lower to 3.92 higher)
Quality of life at ≤3 months (SF-36 general aspects subscale, 0-100, high is good outcome, final values)	20 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life score in the control groups was 50	The mean quality of life score in the intervention groups was 2.5 lower (16.55 lower to 11.55 higher)
Quality of life at ≤3 months (SF-36 emotional role subscale, 0-100, high is good outcome, final values)	20 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of score in the control groups was 60	The mean quality of life score in the intervention groups was 20 higher (15.04 lower to 55.04 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with TDCS versus sham TDCS (95% CI)
Quality of life at ≤3 months (SF-36 mental health subscale, 0-100, high is good outcome, final values)	20 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of score in the control groups was 54	The mean quality of life score in the intervention groups was 4.4 higher (5.82 lower to 14.62 higher)
Pain reduction at ≤3 months (NRS, VAS, 0-10, high is poor outcome, final values)	104 (3 studies) 4-10 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, inconsistency, imprecision		The mean pain reduction score in the control groups was 6.04	The mean pain reduction score in the intervention groups was 2.12 lower (3.82 to 0.43 lower)
Psychological distress at ≤3 months (Hospital anxiety and depression scale, HAM-A, anxiety subscales, high is poor outcome, final values)	84 (2 studies) 4-8 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, inconsistency, imprecision		-	The mean psychological distress score in the intervention groups was 0.55 standard deviations lower (1.49 lower to 0.39 higher)
Psychological distress at ≤3 months (Hospital anxiety and depression scale, BDI, HAM-D, depression subscales, high is poor outcome, final values)	136 (4 studies) 3-12 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, imprecision, inconsistency		-	The mean psychological distress score in the intervention groups was 0.39 standard deviations lower (1.06 lower to 0.28 higher)
Sleep at ≤3 months (PSQI, scale range not reported, high is poor outcome, final values)	20 (1 study) 12 weeks	⨁⨁⨁⊖ MODERATE2 due to risk of bias		The mean sleep in the control groups was 16.7	The mean psychological distress score in the intervention groups was 8.8 lower (13.96 to 3.64 lower)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with TDCS versus sham TDCS (95% CI)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.
3 Downgraded for heterogeneity, unexplained by subgroup analysis

Table 6: Clinical evidence summary: TENS versus sham TENS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with TENS versus sham TENS (95% CI)
Quality of life at ≤3 months (SF36 physical component T scores, high is good outcome, change scores)	202 (1 study) 4 weeks	⨁⨁⨁⨀ MODERATE1 due to risk of bias		The mean change in quality of life score in the control groups was 1.2	The mean change in quality of life score in the intervention groups was 1.2 higher (0.7 lower to 3.1 higher)
Quality of life at ≤3 months (SF36 mental component T scores, high is good outcome, change scores)	202 (1 study) 4 weeks	⨁⨁⨁⨀ MODERATE1 due to risk of bias		The mean change in quality of life score in the control groups was 1.2	The mean change in quality of life score in the intervention groups was 1.1 higher (1.9 lower to 4.1 higher)
Pain reduction at ≤3 months (VAS, BPI intensity, 0-10, high is poor outcome, final values and change scores)	242 (2 studies) 4-10 weeks	⨁⨀⨀⨀ VERY LOW1,2,3 due to risk of bias, inconsistency, imprecision		The mean pain score in the control groups was 5.7	The mean pain reduction score in the intervention groups was 1.96 lower (5.00 lower to 1.07 higher)
Pain reduction >3 months (VAS, 0-10, high is poor outcome, final values)	40 (1 study) 22 weeks	⨁⨁⨁⨀ **MODERATE**[1] due to risk of bias		The mean pain score in the control group was 5.6	The mean pain reduction at 22 weeks in the intervention group was 2.8 lower (4.23 to 1.37 lower)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with TENS versus sham TENS (95% CI)
Physical function at ≤3 months (6 minute walk test, feet walked, change scores)	202 (1 study) 4 weeks	⨁⨁⨁⨁ HIGH		The mean change physical function in the control groups was -20	The mean change in physical function in the intervention groups was 19 higher (58 lower to 96 higher)
Psychological distress at ≤3 months (PROMIS depression T scores, high is poor outcome, change scores)	202 (1 study) 4 weeks	⨁⨁⨀⨀ LOW1,2 due to risk of bias, imprecision		The mean change in psychological distress in the control groups was -0.1	The mean change in psychological distress in the intervention groups was 2.7 lower (4.7 to 0.7 lower)
Psychological distress at ≤3 months (PROMIS anxiety T scores, high is poor outcome, change scores)	202 (1 study) 4 weeks	⨁⨁⨁⨀ MODERATE1 due to risk of bias		The mean change in psychological distress in the control groups was -0.6	The mean change in psychological distress in the intervention groups was 0.5 lower (2.7 lower to 1.7 higher)
Pain interference at ≤3 months (BPI interference 0-10, high is poor outcome, change scores)	202 (1 study) 4 weeks	⨁⨁⨀⨀ LOW1,2 due to risk of bias, imprecision		The mean change in pain interference in the control groups was -0.3	The mean change in pain interference in the intervention groups was 0.7 lower (1.3 to 0.1 lower)
Pain self-efficacy at ≤3 months (PSEQ 0-60, high is good outcome, change scores)	202 (1 study) 4 weeks	⨁⨁⨁⨁ HIGH		The mean change in pain self-efficacy in the control groups was 1.5	The mean change in pain self-efficacy in the intervention groups was 1.6 higher (1.8 lower to 5 higher)
Discontinuation at ≤3 months	40 (1 study) 10 weeks	⨁⨁⨀⨀ LOW1,2 due to risk of bias, imprecision	RD 0 (-0.09 to 0.09)	0 per 1000	0 fewer per 1000 (from 90 fewer to 90 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with TENS versus sham TENS (95% CI)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs 3 Downgraded for heterogeneity, unexplained by subgroup analysis					

Table 7: Clinical evidence summary: TENS versus usual care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with TENS versus sham TENS (95% CI)
Quality of life at ≤3 months (SF36 physical component T scores, high is good outcome, change scores)	202 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean change in quality of life score in the control groups was 1.4	The mean change in quality of life score in the intervention groups was 1 higher (0.8 lower to 2.8 higher)
Quality of life at ≤3 months (SF36 mental component T scores, high is good outcome, change scores)	202 (1 study) 4 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean change in quality of life score in the control groups was 0.04	The mean change in quality of life score in the intervention groups was 2.5 higher (0.6 lower to 5.4 higher)
Pain reduction at ≤3 months (BPI intensity, 0-10, high is poor outcome, change scores)	242 (2 studies) 4-10 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean change in pain score in the control groups was 0.15	The mean pain reduction score in the intervention groups was 0.9 lower (1.4 to 0.4 lower)
Physical function at ≤3 months (6 minute walk test, feet walked, change scores)	202 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean change physical function in the control groups was -42.1	The mean change in physical function in the intervention groups was 42 higher (34 lower to 118 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with TENS versus sham TENS (95% CI)
Psychological distress at ≤3 months (PROMIS depression T scores, high is poor outcome, change scores)	202 (1 study) 4 weeks	⨁⨁⨀⨀ LOW1,2 due to risk of bias, imprecision		The mean change in psychological distress in the control groups was 0.4	The mean change in psychological distress in the intervention groups was 3.2 lower (5.1 to 1.3 lower)
Psychological distress at ≤3 months (PROMIS anxiety T scores, high is poor outcome, change scores)	202 (1 study) 4 weeks	⨁⨁⨁⨀ MODERATE1 due to risk of bias		The mean change in psychological distress in the control groups was -0.7	The mean change in psychological distress in the intervention groups was 0.4 lower (2.5 lower to 1.7 higher)
Pain interference at ≤3 months (BPI interference 0-10, high is poor outcome, change scores)	202 (1 study) 4 weeks	⨁⨁⨀⨀ LOW1,2 due to risk of bias, imprecision		The mean change in pain interference in the control groups was -0.3	The mean change in pain interference in the intervention groups was 0.6 lower (1.3 lower to 0.1 higher)
Pain self-efficacy at ≤3 months (PSEQ 0-60, high is good outcome, change scores)	202 (1 study) 4 weeks	⨁⨁⨁⨁ HIGH		The mean change in pain self-efficacy in the control groups was 0.8	The mean change in pain self-efficacy in the intervention groups was 2.3 higher (1 lower to 5.6 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 8: Clinical evidence summary: PENS versus sham PENS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with PENS versus sham PENS (95% CI)
Quality of life at ≤3 months (NIH-CPSI, 0-12, high is poor outcome, final values)	89 (1 study) 3 months	⨁⨁⊖⊖ LOW1 due to risk of bias		The mean quality of life score in the control groups was 6.7	The mean quality of life score in the intervention groups was 4.6 lower (5.27 to 3.93 lower)
Pain reduction at ≤3 months (VAS, 0-10, high is poor outcome, final values)	89 (1 study) 3 months	⨁⨁⊖⊖ LOW1 due to risk of bias		The mean pain reduction score in the control groups was 7.2	The mean pain reduction score in the intervention groups was 2.9 lower (3.11 to 2.69 lower)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias					

Table 9: Clinical evidence summary: PENS versus usual care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with PENS versus usual care (95% CI)
Quality of life at ≤3 months (SF-36 physical function, 0-100, high is good outcome, final values)	24 (1 study) 3 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life score in the control groups was 52.91	The mean quality of life score in the intervention groups was 21.25 higher (0.64 lower to 43.14 higher)
Quality of life at ≤3 months (SF-36 physical role, 0-100, high is good outcome, final values)	24 (1 study) 3 months	⨁⨁⊖⊖ LOW1 due to risk of bias		The mean quality of life score in the control groups was 14.58	The mean quality of life score in the intervention groups was 52.08 higher (23.29 to 80.87 higher)
Quality of life at ≤3 months (SF-36 fatigue, 0-100, high is good outcome, final values)	24 (1 study) 3 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of		The mean quality of life score in the control groups	The mean quality of life score in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with PENS versus usual care (95% CI)
		bias, imprecision		was 45	17.91 higher (0.58 to 35.24 higher)
Quality of life at ≤3 months (SF-36 emotional role, 0-100, high is good outcome, final values)	24 (1 study) 3 months	⨁⨁⨀⨀ LOW1 due to risk of bias		The mean quality of life score in the control groups was 13.87	The mean quality of life score in the intervention groups was 47.24 higher (17.93 to 76.55 higher)
Quality of life at ≤3 months (SF-36 mental health, 0-100, high is good outcome, final values)	24 (1 study) 3 months	⨁⨁⨀⨀ LOW1 due to risk of bias		The mean quality of life score in the control groups was 40.33	The mean quality of life score in the intervention groups was 20.33 higher (6.31 to 34.35 higher)
Quality of life at ≤3 months (SF-36 social functioning, 0-100, high is good outcome, final values)	24 (1 study) 3 months	⨁⨀⨀⨀ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life score in the control groups was 50	The mean quality of life score in the intervention groups was 21.87 higher (1.84 to 41.9 higher)
Quality of life at ≤3 months (SF-36 bodily pain, 0-100, high is good outcome, final values)	24 (1 study) 3 months	⨁⨁⨀⨀ LOW1 due to risk of bias		The mean quality of life score in the control groups was 23.33	The mean quality of life score in the intervention groups was 36.67 higher (20.25 to 53.09 higher)
Pain reduction at ≤3 months (VAS, 0-10, high is poor outcome, final values)	24 (1 study) 3 months	⨁⨁⨀⨀ LOW1 due to risk of bias		The mean pain reduction score in the control groups was 7.87	The mean pain reduction score in the intervention groups was 5.25 lower (6.86 to 3.64 lower)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 10: Clinical evidence summary: Therapeutic ultrasound versus usual care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Therapeutic ultrasound versus usual care (95% CI)
Pain reduction at ≤3 months (VAS, 0-10, high is poor outcome, final values)	76 (1 study) 3 months	⨁⨁⨀⨀ LOW1 due to risk of bias		The mean pain score in the control groups was 5.78	The mean pain reduction score in the intervention groups was 2.7 lower (3.54 to 1.86 lower)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias					

See appendix F for full GRADE tables.

1.5 Economic evidence

1.5.1 Included studies

No relevant health economic studies were included.

1.5.2 Excluded studies

No health economic studies that were relevant to this question were excluded due to assessment of limited applicability or methodological limitations.

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

1.5.3 Unit costs

Unit costs of the devices that could be sourced are illustrated below in Table 12.

For some of the interventions it is possible that the equipment can be provided to the patient (or purchased by the patient) and the patient can undertake the intervention themselves (such as TENS). Other types of intervention require that a healthcare professional provides the treatment.

Table 11 demonstrates the costs of staff per hour.

It is common that some interventions such as interferential therapy, laser therapy and ultrasound therapy, are a shared resource that would be available in most physiotherapy departments, and are counted as part of a physiotherapist's appointment.

Table 11: staff costs

Healthcare professional	Cost (per hour)
Community physiotherapist (band 5/6/7)	£52 / £64 / £78

Source: PSSRU 2018[91]

Note: These costs include the ratio of direct to indirect time with patients of 1.37 from the PSSRU. And qualification costs.

Table 12: Electrical physical modalities costs

Intervention	Cost	Source
TENS	£18 - £50	NHS supply chain 2018[261]
Interferential therapy unit (a)	£1128.	NHS supply chain 2014 (based on costs used in the low back pain guideline (NG59))[259]
Laser therapy unit (a)	£955 and £1609	
Ultrasound therapy unit (a)	£853 and £2159	

(a) These interventions were no longer available from the latest version of the NHS supply chain (at the time of writing), however some costs sources are demonstrated in the table taken from the NICE guideline on low back pain. Note these have not been inflated from 2014 as it is not clear if prices of the machines would have increased or decreased since 2014:

1.6 Evidence statements

1.6.1 Clinical evidence statements

1.6.1.1 Laser therapy versus sham laser therapy

Quality of life

Very low quality evidence from 6 studies with 276 participants showed a clinically important benefit of laser therapy compared to sham laser therapy at ≤3 months. Low to moderate quality evidence from 2 studies with 110 participants showed both a clinically important benefit of laser therapy (physical subscale) and no clinically important difference (mental subscale) compared to sham laser therapy at ≤3 months. Low quality evidence from 2 studies with 117 participants showed no clinically important difference compared to sham laser therapy at >3 months.

Pain reduction

Very low quality evidence from 13 studies with 558 participants showed a clinically important benefit of laser therapy compared to sham laser therapy at ≤3 months. Moderate quality evidence from 2 studies with 71 participants showed a clinically important benefit of laser therapy compared to sham laser therapy at >3 months.

Physical function

No evidence identified.

Psychological distress

Low to moderate quality evidence from 1 study with 44 participants showed no clinically important difference between laser therapy and sham laser therapy at ≤3 months.

Pain interference

No evidence identified.

Pain self-efficacy

No evidence identified.

Use of healthcare services

No evidence identified.

Sleep

No evidence identified.

Discontinuation

Low quality evidence from 1 study with 90 participants showed no clinically important difference between laser therapy and sham laser therapy at ≤3 months.

1.6.1.2 TMS versus sham TMS

Quality of life

Very low quality evidence from 1 study with 29 participants showed no clinically important difference between TMS and sham TMS at ≤3 months. Low quality evidence from 1 study with 29 participants showed a clinically important benefit of TMS compared to sham TMS at ≤3 months. High quality evidence from 1 study with 51 participants showed a clinically important benefit of TMS compared to sham TMS at ≤3 months. Moderate quality evidence from 1 study with 51 participants showed no clinically important difference between TMS and sham TMS at ≤3 months. Very low quality evidence from 3 studies with 60 participants showed no clinically important difference between TMS and sham TMS at ≤3 months. Very low quality evidence from 1 study with 30 participants showed no clinically important difference between TMS and sham TMS at >3 months.

Pain reduction

Very low quality evidence from 7 studies with 181 participants showed a clinically important benefit of TMS compared to sham TMS at ≤3 months.

Physical function

Very low to moderate quality evidence from 1 study with 20 participants showed no clinically important difference between TMS and sham TMS at ≤3 months.

Psychological distress

Very low quality evidence from 2 studies with 44 participants showed no clinically important difference between TMS and sham TMS at ≤3 months. Moderate quality evidence from 3 studies with 96 participants showed no clinically important difference between TMS and sham TMS at ≤3 months. Very low quality evidence from 1 study with 29 participants showed no clinically important difference between TMS and sham TMS at ≤3 months. Very low quality evidence from 1 study with 30 participants showed no clinically important difference between TMS and sham TMS at >3 months.

Pain interference

Very low quality evidence from 1 study with 30 participants showed a clinically important benefit of TMS compared to sham TMS at >3 months.

Pain self-efficacy

No evidence identified.

Use of healthcare services

No evidence identified.

Sleep

No evidence identified.

Discontinuation

Low quality evidence from 4 studies with 141 participants showed no clinically important difference between TMS and sham TMS at ≤3 months.

1.6.1.3 TDCS versus sham TDCS

Quality of life

Very quality evidence from 1 study with 48 participants showed no clinically important difference between TDCS and sham TDCS at ≤3 months. Moderate to low quality evidence from 1 study with 20 participants showed a clinically important benefit, clinically important harm and no clinically important difference (various subscales) of TDCS compared to sham TDCS at ≤3 months.

Pain reduction

Very low quality evidence from 3 studies with 104 participants showed a clinically important benefit of TDCS compared to sham TDCS at ≤3 months.

Physical function

No evidence identified.

Psychological distress

Very low quality evidence from 2 studies with 84 participants showed a clinically important benefit of TDCS compared to sham TDCS at ≤3 months. Very low quality evidence from 4 studies with 136 participants showed no clinically important difference between TDCS and sham TDCS at ≤3 months.

Pain interference

No evidence identified.

Pain self-efficacy

No evidence identified.

Use of healthcare services

No evidence identified.

Sleep

Moderate quality evidence from 1 study with 20 participants showed a clinically important benefit of TDCS compared to sham TDCS at ≤3 months.

Discontinuation

No evidence identified.

1.6.1.4 TENS versus sham TENS

Quality of life

Moderate quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and sham TENS at ≤3 months.

Pain reduction

Very low quality evidence from 2 studies with 242 participants showed a clinically important difference for TENS compared to sham TENS at ≤3 months. Moderate quality evidence from 1 study with 40 participants showed a clinically important difference for TENS at >3 months.

Physical function

High quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and sham TENS at ≤3 months.

Psychological distress

Moderate to low quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and sham TENS at ≤3 months.

Pain interference

Low quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and sham TENS at ≤3 months.

Pain self-efficacy

High quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and sham TENS at ≤3 months.

Discontinuation

Low quality evidence from 1 study with 40 participants showed no clinically important difference between TENS and sham TENS at ≤3 months.

No other evidence identified for TENS versus sham TENS.

1.6.1.5 TENS versus usual care

Quality of life

Moderate to low quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and usual care at ≤3 months.

Pain reduction

Low quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and usual care at ≤3 months.

Physical function

High quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and usual care at ≤3 months.

Psychological distress

Moderate to low quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and usual care at ≤3 months.

Pain interference

Low quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and usual care at ≤3 months.

Pain self-efficacy

High quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and usual care at ≤3 months.

No other evidence identified for TENS versus usual care.

1.6.1.6 PENS versus sham PENS

Quality of life

Low quality evidence from 1 study with 89 participants showed a clinically important benefit of PENS compared to sham PENS at ≤3 months.

Pain reduction

Low quality evidence from 1 study with 89 participants showed a clinically important benefit of PENS compared to sham PENS at ≤3 months.

No other evidence identified for PENS versus sham PENS.

1.6.1.7 PENS versus usual care

Quality of life

Very low to low quality evidence from 1 study with 24 participants showed a clinically important benefit of PENS compared to usual care at ≤3 months.

Pain reduction

Low quality evidence from 1 study with 24 participants showed a clinically important benefit of PENS compared to usual care at ≤3 months.

No other evidence identified for PENS versus usual care.

1.6.1.8 Therapeutic ultrasound versus usual care

Pain reduction

Low quality evidence from 1 study with 76 participants showed a clinically important benefit of therapeutic ultrasound compared to usual care at ≤3 months.

No other evidence identified for therapeutic ultrasound versus usual care.

1.6.2 Health economic evidence statements

- No relevant economic evaluations were identified.

1.7 The committee's discussion of the evidence

1.7.1 Interpreting the evidence

1.7.1.1 The outcomes that matter most

The committee considered health-related quality of life, pain reduction, physical function, psychological distress, pain interference and pain self-efficacy to be critical outcomes for decision-making. Use of healthcare services, sleep and discontinuation were also considered to be important outcomes. The critical and important outcomes agreed by the committee were adapted by consensus from relevant core outcome sets registered under the Core Outcome Measures in Effectiveness Trials (COMET) Initiative. This included the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) recommendations.

Evidence was identified for all critical outcomes, other than pain interference and pain self-efficacy. Evidence for important outcomes was limited; no evidence was identified for sleep or use of healthcare services, and evidence for discontinuation was limited.

1.7.1.2 The quality of the evidence

Evidence from 34 randomised controlled trials was identified for 8 different comparisons. The comparison with the most evidence was laser therapy versus sham laser therapy. No head-to-head comparisons of different electrical therapies were identified and no evidence was identified for interferential therapy. There was little evidence comparing interventions to usual care.

The majority of the evidence was of low to very low quality. The main reasons for downgrading were risk of bias, inconsistency and imprecision. A large number of studies had small sample sizes, which increased the uncertainty around the point estimates. The evidence for many outcomes included studies that looked at heterogeneous populations, and used different electrical parameters (such as wavelength and voltage) and intervention durations. Where there was heterogeneity in the evidence for an outcome, pre-specified subgroup analyses did not explain the variation in effect sizes. As a result, many outcomes were downgraded for inconsistency.

The committee took into account the low to very low quality of evidence in their discussions, particularly when considering the small amount of evidence for comparisons of TENS, PENS and ultrasound versus sham or usual care.

1.7.1.3 Benefits and harms

Evidence for laser therapy versus sham was based on 14 studies and showed a benefit of treatment in terms of pain and quality of life at short term follow up, although there was serious uncertainty around the effect estimates. The long-term data showing a benefit of laser therapy for pain was based on much smaller sample sizes. Contrastingly, evidence from 2 studies showed no clinically important difference (with some uncertainty) between laser therapy and sham for quality of life at less than 3 months, as measured by the mental component summary of the SF-36 questionnaire, but there was evidence to suggest a benefit on the physical component summary of the SF-36. At longer-term follow up, evidence from 2 studies also showed no clinically important difference. The committee noted that they would expect to see a consistent benefit across more domains, if an intervention were to be interpreted as being generally effective. This therefore raised questions about the effectiveness of the intervention for all critical outcomes being assessed. Evidence for psychological distress and discontinuation was limited at less than 3 months, with some low to moderate quality evidence suggesting there was no clinically important benefit of laser

therapy, again based on small sample sizes and with serious uncertainty. No evidence was identified for physical function, pain interference or sleep either in the short or long term. The only long-term evidence was for outcomes of pain and quality of life.

The committee agreed that although there was some evidence of benefit for quality of life and pain, they could not make a recommendation for laser therapy. The evidence from clinical trials was heterogeneous. The physical parameters of the laser light used, the duration of treatment and the time the laser was applied to each painful point varied widely. It was also unclear whether these parameters affected the size, quality and duration of clinical benefit seen within the evidence. This made it difficult for the committee to be confident about the benefits of laser therapy in routine practice, or to make specific recommendations. No cost-effectiveness evidence or evidence assessing longer-term benefit was available. Comparisons were against sham laser therapy, rather than usual care, which is the comparison of greatest interest for implementation in the NHS. Taking all of this into account, the committee agreed they could not make a recommendation for the use of laser therapy in clinical practice. However, they agreed that this preliminary evidence looked promising, and as a result made a recommendation for further research.

Evidence for transcranial magnetic stimulation (TMS) showed a benefit for pain at less than 3 months. This was based on 7 studies, although it was very low quality evidence with serious uncertainty. Evidence for other outcomes, including quality of life, physical function and psychological distress showed no clinical benefit of TMS. Furthermore, the long-term benefit of TMS was unclear with limited evidence. As a result, the committee agreed it could not base a recommendation on pain reduction alone, particularly taking into account the relatively small sample size and low quality of the evidence. The committee instead agreed that the short-term benefit for pain was promising, and that further long-term evidence is needed to determine the effectiveness of TMS. As a result the committee made a recommendation for future research.

Evidence for TENS showed no clinically important difference compared with sham TENS, nor with usual care for quality of life, physical function, psychological distress, pain interference, pain self-efficacy or discontinuation at less than 3 months. For pain, benefits were seen for TENS compared to sham at both time points, but not compared to usual care. The committee noted that there was significant heterogeneity between the two studies in the meta-analysis at less than 3 months compared to sham and the effect was only demonstrated in the smaller of the 2 studies (given more influence in the meta-analysis due to random effects being used in the meta-analysis). The evidence for longer term follow up was only from this single small study. They discussed that in the absence of evidence of benefit in any other outcome or compared to usual care, the significant heterogeneity and the small sample size, they could not place too much weight on this finding. The committee noted that the majority of the evidence came from 1 larger study and the quality of the evidence ranged from high to very low. No longer term evidence was identified with the exception of 1 pain outcome. No evidence was identified for ultrasound or interferential therapy. The committee also noted that these technologies have existed for some time and are being used by some in the NHS without evidence of benefit. The committee agreed that resources should be re-allocated to areas with more evidence of clinical and cost effectiveness. Therefore, the committee decided to make a recommendation against the use of TENS, ultrasound and interferential therapy.

The committee also considered the limited evidence identified for TDCS and PENS. Evidence was limited to a small number of studies with small sample sizes. Both interventions showed a benefit for pain, although TDCS showed mixed results for quality of life and psychological distress. PENS on the other hand also showed a benefit for quality of life. However, the evidence was low to very low quality, with uncertainty around the effect sizes. The committee agreed that this evidence was insufficient to determine the effectiveness of each intervention. However, the committee decided not to recommend against these interventions because neither intervention is commonly used in current

practice. The committee also decided not to make a research recommendation due to this, and agreed that other areas reviewed across the guideline showed more promising results for future research to be warranted.

1.7.2 Cost effectiveness and resource use

No economic evidence was identified for this question.

It is common that some interventions such as interferential therapy, laser therapy and ultrasound therapy are a shared resource that would be available in most physiotherapy departments, as they might be used for a variety of conditions, and are counted as part of a physiotherapist's appointment. Costs of physiotherapist time were presented to the committee. Some interventions such as TMS are specialist and are not used clinically in the NHS for chronic pain.

There is also a distinction between interventions that the person could self-administer, and do not necessarily require appointments with NHS clinical staff to undertake the intervention. Examples of this would include TENS and TDCS.

If the use of these interventions in general is not widespread across the NHS for people with chronic primary pain, then a positive recommendation in favour of any interventions will require capital outlay to purchase more units to allow the interventions to be more widely available. TENS is relatively cheap and the cheapest of all the interventions to purchase. Costs of the devices for interferential therapy, laser therapy, and ultrasound therapy are not currently available on the NHS supply chain, but the costs of such units that were quoted in the low back pain guideline were presented to the committee as an illustration, which were sourced from the NHS supply chain in 2014.

The committee view of the clinical evidence was that there was considerable uncertainty in the data, with little long-term evidence. Additionally, data on who delivered the intervention was lacking and treatments were relatively short term with a wide range in the number of treatment sessions provided. The intervention which had the largest signal of benefit was laser therapy. This is not widely used in the NHS, and, because of a lack of cost effectiveness evidence of laser therapy, the committee decided to make a research recommendation for laser therapy.

The committee also made some recommendations to not offer some types of electrical physical modalities. This was because there was no or very little evidence, and the committee opinion was that as these are technologies that have been around for some time, no new research was likely to be undertaken. Additionally, they were also aware that as those treatments are being used by some people in the NHS, resources should be re-allocated to areas with more evidence of clinical and cost effectiveness.

References

1. Aarskog R, Johnson MI, Demmink JH, Lofthus A, Iversen V, Lopes-Martins R et al. Is mechanical pain threshold after transcutaneous electrical nerve stimulation (TENS) increased locally and unilaterally? A randomized placebo-controlled trial in healthy subjects. Physiotherapy Research International. 2007; 12(4):251-63

2. Abdulla A, Adams N, Bone M, Elliott AM, Gaffin J, Jones D et al. Guidance on the management of pain in older people. Age and Ageing. 2013; 42(Suppl 1):i1-57

3. Abram SE. Increased sympathetic tone associated with transcutaneous electrical stimulation. Anesthesiology. 1976; 45(5):575-577

4. Abtahi H, Okhovvat A, Heidari S, Gharagazarloo A, Mirdamadi M, Nilforoush MH et al. Effect of transcranial direct current stimulation on short-term and long-term treatment of chronic tinnitus. American Journal of Otolaryngology - Head and Neck Medicine and Surgery. 2018; 39(2):94-96

5. Acedo AA, Antunes ACL, Dos Santos AB, De Olveira CB, Dos Santos CT, Colonezi GLT et al. Upper trapezius relaxation induced by tens and interferential current in computer users with chronic nonspecific neck discomfort: An electromyographic analysis. Journal of Back and Musculoskeletal Rehabilitation. 2015; 28(1):19-24

6. Adrian G. Comparison of new minimally invasive Er:YAG laser treatment and hormonal replacement therapy in the treatment of vaginal atrophy. Climacteric. 2014; 17(Suppl 1):48-108

7. Ahmed MA, Mohamed SA, Sayed D. Long-term antalgic effects of repetitive transcranial magnetic stimulation of motor cortex and serum beta-endorphin in patients with phantom pain. Neurological Research. 2011; 33(9):953-8

8. Ahsin S, Saleem S, Bhatti AM, Iles RK, Aslam M. Clinical and endocrinological changes after electro-acupuncture treatment in patients with osteoarthritis of the knee. Pain. 2009; 147(1-3):60-6

9. Akturk S, Cetintas D, Gulkesen A, Akgol G, Gucer TK, Tuncer T et al. Comparison of the effectiveness of ESWT and ultrasound treatments in myofascial pain syndrome: A placebo controlled study. Turkish Journal of Physical Medicine and Rehabilitation. 2013; 59(Suppl 1):1-499

10. Akturk S, Kaya A, Cetintas D, Akgol G, Gulkesen A, Kal GA et al. Comparision of the effectiveness of ESWT and ultrasound treatments in myofascial pain syndrome: randomized, sham-controlled study. Journal of Physical Therapy Science. 2018; 30(3):448-453

11. Al-Maweri SA, Javed F, Kalakonda B, AlAizari NA, Al-Soneidar W, Al-Akwa A. Efficacy of low level laser therapy in the treatment of burning mouth syndrome: A systematic review. Photodiagnosis and Photodynamic Therapy. 2017; 17:188-193

12. Alayat MS, Elsoudany AM, Ali ME. Efficacy of multiwave locked system laser on pain and function in patients with chronic neck pain: A randomized placebo-controlled trial. Photomedicine and Laser Surgery. 2017; 35(8):450-455

13. Alayat MS, Mohamed AA, Helal OF, Khaled OA. Efficacy of high-intensity laser therapy in the treatment of chronic neck pain: a randomized double-blind placebo-control trial. Lasers in Medical Science. 2016; 31(4):687-94

14. Albornoz-Cabello M, Maya-Martin J, Dominguez-Maldonado G, Espejo-Antunez L, Heredia-Rizo AM. Effect of interferential current therapy on pain perception and

disability level in subjects with chronic low back pain: a randomized controlled trial. Clinical Rehabilitation. 2017; 31(2):242-249

15. Allais G, De Lorenzo C, Quirico PE, Lupi G, Airola G, Mana O et al. Non-pharmacological approaches to chronic headaches: Transcutaneous electrical nerve stimulation, lasertherapy and acupuncture in transformed migraine treatment. Neurological Sciences. 2003; 24(Suppl 2):S138-S142

16. Almay BGL, Johansson F, Von Knorring L. Long-term high frequency transcutaneous electrical nerve stimulation (hi-TNS) in chronic pain. Clinical response and effects on CSF-endorphins, monoamine metabolites, substance P-like immunoreactivity (SPLI) and pain measures. Journal of Psychosomatic Research. 1985; 29(3):247-257

17. Almeida CC, Silva V, Junior GC, Liebano RE, Durigan JLQ. Transcutaneous electrical nerve stimulation and interferential current demonstrate similar effects in relieving acute and chronic pain: a systematic review with meta-analysis. Brazilian Journal of Physical Therapy. 2018; 22(5):347-354

18. Almeida TF, Roizenblatt S, Benedito-Silva AA, Tufik S. The effect of combined therapy (ultrasound and interferential current) on pain and sleep in fibromyalgia. Pain. 2003; 104(3):665-72

19. Altan L, Bingol U, Aykac M, Yurtkuran M. Investigation of the effect of GaAs laser therapy on cervical myofascial pain syndrome. Rheumatology International. 2005; 25(1):23-7

20. Altas EU, Askin A, Besiroglu L, Tosun A. Is high-frequency repetitive transcranial magnetic stimulation of the left primary motor cortex superior to the stimulation of the left dorsolateral prefrontal cortex in fibromyalgia syndrome? Somatosensory and Motor Research. 2019; 36(1):56-62

21. Amanat D, Ebrahimi H, Lavaee F, Alipour A. The adjunct therapeutic effect of lasers with medication in the management of orofacial pain: double blind randomized controlled trial. Photomedicine and Laser Surgery. 2013; 31(10):474-9

22. Anderssonn SA, Hansson G, Holmgren E. et al. Evaluation of the pain suppressive effect of different frequencies of peripheral electrical stimulation in chronic pain conditions. Acta Orthopaedica Scandinavica. 1976; 47:149-157

23. Andrade Ortega JA, Ceron Fernandez E, Garcia Llorent R, Ribeiro Gonzalez M, Delgado Martinez AD. Microwave diathermy for treating nonspecific chronic neck pain: a randomized controlled trial. Spine Journal: Official Journal of the North American Spine Society. 2014; 14(8):1712-21

24. Andre-Obadia N, Peyron R, Mertens P, Mauguiere F, Laurent B, Garcia-Larrea L. Transcranial magnetic stimulation for pain control. Double-blind study of different frequencies against placebo, and correlation with motor cortex stimulation efficacy. Clinical Neurophysiology. 2006; 117(7):1536-44

25. Anonymous. Comparing the effectiveness of laser treatment with extracorporeal shock wave treatment (ESWT) in patients with myofascial pain syndrome (MPS). Osteoporosis International. 2017; Conference: World Congress on Osteoporosis, Osteoarthritis and Musculoskeletal Diseases,(2017. Italy. 28):pp S232

26. Ansari A, Mathur R, Jain S, Bhattacharjee M. Study of effect of slow frequency repeated transcranial magnetic field on modulation of pain in fibromyalgia patients. Journal of Pain. 2013; 1):S67

27. Ansari AH, Mathur R, Jain S, Mukherjee K. Repeated transcranial magnetic stimulation relieves pain in fibromyalgia patients: An electrophysiological approach to evaluate pain. Acta Physiologica. 2014; 210:179

28. Arbabi-Kalati F, Bakhshani N-M, Rasti M. Evaluation of the efficacy of low-level laser in improving the symptoms of burning mouth syndrome. Journal of clinical and experimental dentistry. 2015; 7(4):e524-e527

29. 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

30. Aridici R, Yetisgin A, Boyaci A, Tutoglu A, Bozdogan E, Sen Dokumaci D et al. Comparison of the efficacy of dry needling and high-power pain threshold ultrasound therapy with clinical status and sonoelastography in myofascial pain syndrome. American Journal of Physical Medicine and Rehabilitation. 2016; 95(10):e149-58

31. Armagan O, Tascioglu F, Ekim A, Oner C. Long-term efficacy of low level laser therapy in women with fibromyalgia: A placebo-controlled study. Journal of Back and Musculoskeletal Rehabilitation. 2006; 19(4):135-140

32. Attal N, Mhalla A, Baudic S, Andrade DC, Perrot S, Texeira MJ. Long term analgesic efficacy of transcranial magnetic stimulation of the motor cortex in patients with fibromyalgia. Clinical Neurophysiology. 2010; 121(Suppl 1):S121

33. Avery DH, Zarkowski P, Krashin D, Rho WK, Wajdik C, Joesch JM et al. Transcranial magnetic stimulation in the treatment of chronic widespread pain: a randomized controlled study. Journal of ECT. 2015; 31(1):57-66

34. Ay S, Dogan SK, Evcik D, Baser OC. Comparison the efficacy of phonophoresis and ultrasound therapy in myofascial pain syndrome. Rheumatology International. 2011; 31(9):1203-8

35. Azatcam G, Atalay NS, Akkaya N, Sahin F, Aksoy S, Zincir O et al. Comparison of effectiveness of Transcutaneous Electrical Nerve Stimulation and Kinesio Taping added to exercises in patients with myofascial pain syndrome. Journal of Back and Musculoskeletal Rehabilitation. 2017; 30(2):291-298

36. Barbosa NG, Gonzaga AKG, de Sena Fernandes LL, da Fonseca AG, Queiroz SIML, Lemos TMAM et al. Evaluation of laser therapy and alpha-lipoic acid for the treatment of burning mouth syndrome: a randomized clinical trial. Lasers in Medical Science. 2018; 33(6):1255-1262

37. Bardellini E, Amadori F, Conti G, Majorana A. Efficacy of the photobiomodulation therapy in the treatment of the burning mouth syndrome. Medicina Oral, Patología Oral y Cirugía Bucal. 2019; 24(6):e787-e791

38. Barnhoorn KJ, Van De Meent H, Van Dongen RTM, Klomp FP, Groenewoud H, Samwel H et al. Pain exposure physical therapy (PEPT) compared to conventional treatment in complex regional pain syndrome type 1: A randomised controlled trial. BMJ Open. 2015; 5(12):e008283

39. Barr JO, Weissenbuehler SA, Bandatra EJ. Effectiveness and comfort level of transcutaneous electrical nerve stimulation (TENS) in elderly with chronic pain. Physical Therapy. 1987; 67(5):775

40. Barr JO, Weissenbuehler SA, Cleary CK. Effectiveness and comfort of transcutaneous electrical nerve stimulation for older persons with chronic pain 1250. Journal of Geriatric Physical Therapy. 2004; 27(3):93-99

41. Bates JAV, Nathan PW. Transcutaneous electrical nerve stimulation for chronic pain. Anaesthesia. 1980; 35:817-822

42. Baudic S, Attal N, Mhalla A, Ciampi de Andrade D, Perrot S, Bouhassira D. Unilateral repetitive transcranial magnetic stimulation of the motor cortex does not affect cognition in patients with fibromyalgia. Journal of Psychiatric Research. 2013; 47(1):72-7

43. Bergeron-Vezina K, Filion C, Couture C, Vallee E, Laroche S, Leonard G. Adjusting pulse amplitude during transcutaneous electrical nerve stimulation does not provide greater hypoalgesia. Journal of Alternative and Complementary Medicine. 2018; 24(3):262-267

44. Bezuur NJ, Habets LL, Hansson TL. The effect of therapeutic laser treatment in patients with craniomandibular disorders. Journal of Craniomandibular Disorders. 1988; 2(2):83-6

45. Biemans JM, van Balken MR. Efficacy and effectiveness of percutaneous tibial nerve stimulation in the treatment of pelvic organ disorders: a systematic review. Neuromodulation. 2013; 16(1):25-33

46. Bilgili A, Cakir T, Dogan SK, Ercalik T, Filiz MB, Toraman F. The effectiveness of transcutaneous electrical nerve stimulation in the management of patients with complex regional pain syndrome: A randomized, double-blinded, placebo-controlled prospective study. Journal of Back and Musculoskeletal Rehabilitation. 2016; 29(4):661-671

47. Bingol U, Altan L, Yurtkuran M. Low-power laser treatment for shoulder pain. Photomedicine and Laser Surgery. 2005; 23(5):459-64

48. Bjordal JM, Couppe C, Chow RT, Tuner J, Ljunggren EA. A systematic review of low level laser therapy with location-specific doses for pain from chronic joint disorders. Australian Journal of Physiotherapy. 2003; 49(2):107-16

49. Boggio PS, Amancio EJ, Correa CF, Cecilio S, Valasek C, Bajwa Z et al. Transcranial DC stimulation coupled with TENS for the treatment of chronic pain: a preliminary study. Clinical Journal of Pain. 2009; 25(8):691-5

50. Borckardt JJ, Romagnuolo J, Reeves ST, Madan A, Frohman H, Beam W et al. Feasibility, safety, and effectiveness of transcranial direct current stimulation for decreasing post-ERCP pain: a randomized, sham-controlled, pilot study. Gastrointestinal Endoscopy. 2011; 73(6):1158-64

51. Botelho L, Angoleri L, Zortea M, Deitos A, Brietzke A, Torres ILS et al. Insights about the neuroplasticity state on the effect of intramuscular electrical stimulation in pain and disability associated with chronic myofascial pain syndrome (mps): A double-blind, randomized, sham-controlled trial. Frontiers in Human Neuroscience. 2018; 12:388

52. Boureau F, Kisielnicki E. Effects of transcutaneous nerve stimulation (TNS), electrotherapy (ET), electroacupuncture (EA) on chronic pain. A comparative study. Pain. 1981; 11(Suppl 1):S277

53. Boyer L, Dousset A, Roussel P, Dossetto N, Cammilleri S, Piano V et al. rTMS in fibromyalgia: a randomized trial evaluating QoL and its brain metabolic substrate. Neurology. 2014; 82(14):1231-8

54. Brietzke AP, Zortea M, Carvalho F, Sanches PRS, Silva DPJ, Torres I et al. Large Treatment Effect With Extended Home-Based Transcranial Direct Current Stimulation

Over Dorsolateral Prefrontal Cortex in Fibromyalgia: A Proof of Concept Sham-Randomized Clinical Study. Journal of Pain. 2019; Epublication

55. Busch V, Zeman F, Heckel A, Menne F, Ellrich J, Eichhammer P. The effect of transcutaneous vagus nerve stimulation on pain perception--an experimental study. Brain Stimulation. 2013; 6(2):202-9

56. CADTH. Home Transcutaneous Electrical Nerve Stimulation for Chronic Pain: A Review of the Clinical Effectiveness. Canadian Agency for Drugs and Technologies in Health, 2016.

57. Canadian Chiropractic A, Canadian Federation of Chiropractic Regulatory B, Clinical Practice Guidelines Development I, Guidelines Development C, Anderson-Peacock E, Blouin JS et al. Chiropractic clinical practice guideline: evidence-based treatment of adult neck pain not due to whiplash. Journal of the Canadian Chiropractic Association. 2005; 49(3):158-209

58. Carbonario F, Matsutani LA, Yuan SL, Marques AP. Effectiveness of high-frequency transcutaneous electrical nerve stimulation at tender points as adjuvant therapy for patients with fibromyalgia. European journal of physical & rehabilitation medicine. 2013; 49(2):197-204

59. Carrasco TG, Guerisoli LD, Guerisoli DM, Mazzetto MO. Evaluation of low intensity laser therapy in myofascial pain syndrome. Cranio. 2009; 27(4):243-7

60. Carrasco TG, Mazzetto MO, Mazzetto RG, Mestriner W, Jr. Low intensity laser therapy in temporomandibular disorder: a phase II double-blind study. Cranio. 2008; 26(4):274-81

61. Carretero B, Martin MJ, Juan A, Pradana ML, Martin B, Carral M et al. Low-frequency transcranial magnetic stimulation in patients with fibromyalgia and major depression. Pain Medicine. 2009; 10(4):748-53

62. Castro-Sanchez AM, Garcia-Lopez H, Fernandez-Sanchez M, Perez-Marmol JM, Leonard G, Gaudreault N et al. Benefits of dry needling of myofascial trigger points on autonomic function and photoelectric plethysmography in patients with fibromyalgia syndrome. Acupuncture in Medicine. 2020:acupmed2017011504

63. Castro-Sanchez AM, Mataran-Penarrocha GA, Arroyo-Morales M, Saavedra-Hernandez M, Fernandez-Sola C, Moreno-Lorenzo C. Effects of myofascial release techniques on pain, physical function, and postural stability in patients with fibromyalgia: a randomized controlled trial. Clinical Rehabilitation. 2011; 25(9):800-13

64. Ceccherelli F, Altafini L, Lo Castro G, Avila A, Ambrosio F, Giron GP. Diode laser in cervical myofascial pain: a double-blind study versus placebo. Clinical Journal of Pain. 1989; 5(4):301-4

65. Cervigni M, Onesti E, Ceccanti M, Gori MC, Tartaglia G, Campagna G et al. Repetitive transcranial magnetic stimulation for chronic neuropathic pain in patients with bladder pain syndrome/interstitial cystitis. Neurourology and Urodynamics. 2018; 37(8):2678-2687

66. Cetiner S, Kahraman SA, Yucetas S. Evaluation of low-level laser therapy in the treatment of temporomandibular disorders. Photomedicine and Laser Surgery. 2006; 24(5):637-41

67. Chabal C, Fishbain DA, Weaver M, Heine LW. Long-term transcutaneous electrical nerve stimulation (TENS) use: impact on medication utilization and physical therapy costs. Clinical Journal of Pain. 1998; 14(1):66-73

68. Chan DK, Johnson MI, Sun KO, Doble SJ, Jenkins S. Electrical acustimulation of the wrist for chronic neck pain: a randomized, sham-controlled trial using a wrist-ankle acustimulation device. Clinical Journal of Pain. 2009; 25(4):320-6

69. Chee EK, Walton H. Treatment of trigger points with microamperage transcutaneous electrical nerve stimulation (TENS)--(the Electro-Acuscope 80). Journal of Manipulative and Physiological Therapeutics. 1986; 9(2):131-4

70. Chen J, Zhou D, Liu Y, Peng J, Li C, Chen W et al. A comparison between ultrasound therapy and laser therapy for symptomatic cervical ectopy. Ultrasound in Medicine and Biology. 2008; 34(11):1770-1774

71. Cheng CM, Wang SJ, Su TP, Chen MH, Hsieh JC, Ho ST et al. Analgesic effects of repetitive transcranial magnetic stimulation on modified 2010 criteria-diagnosed fibromyalgia: Pilot study. Psychiatry and Clinical Neurosciences. 2019; 73(4):187-193

72. Cheng RSS, Pomeranz B. Electrotheraphy of chronic musculoskeletal pain: Comparison of electroacupuncture and acupuncture-like transcutaneous electrical nerve stimulation. Clinical Journal of Pain. 1986; 2(3):143-149

73. Choi GS, Chang MC. Effects of high-frequency repetitive transcranial magnetic stimulation on reducing hemiplegic shoulder pain in patients with chronic stoke: a randomized controlled trial. International Journal of Neuroscience. 2018; 128(2):110-116

74. Choi YH, Jung SJ, Lee CH, Lee SU. Additional effects of transcranial direct-current stimulation and trigger-point injection for treatment of myofascial pain syndrome: a pilot study with randomized, single-blinded trial. Journal of Alternative and Complementary Medicine. 2014; 20(9):698-704

75. Chong OT, Critchley HOD, Williams LJ, Haraldsdottir E, Horne AW, Fallon M. The impact of meridian balance method electro-acupuncture treatment on chronic pelvic pain in women: a three-armed randomised controlled feasibility study using a mixed-methods approach. British Journal of Pain. 2018; 12(4):238-249

76. Chow RT, Barnsley L. Systematic review of the literature of low-level laser therapy (LLLT) in the management of neck pain. Lasers in Surgery and Medicine. 2005; 37(1):46-52

77. Chow RT, Barnsley L, Heller GZ, Siddall PJ. A pilot study of low-power laser therapy in the management of chronic neck pain. Journal of Musculoskeletal Pain. 2004; 12(2):71-81

78. Chow RT, Heller GZ, Barnsley L. The effect of 300 mW, 830 nm laser on chronic neck pain: a double-blind, randomized, placebo-controlled study. Pain. 2006; 124(1-2):201-10

79. Cohen JM, Fagin AP, Hariton E, Niska JR, Pierce MW, Kuriyama A et al. Therapeutic intervention for chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS): a systematic review and meta-analysis. PloS One. 2012; 7(8):e41941

80. Conti PC. Low level laser therapy in the treatment of temporomandibular disorders (TMD): a double-blind pilot study. Cranio. 1997; 15(2):144-9

81. Conti PC, Stuginski-Barbosa J, Bonjardim LR, Soares S, Svensson P. Contingent electrical stimulation inhibits jaw muscle activity during sleep but not pain intensity or masticatory muscle pressure pain threshold in self-reported bruxers: a pilot study. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology. 2014; 117(1):45-52

82. Cormier S, Piche M, Rainville P. Expectations modulate heterotopic noxious counter-stimulation analgesia. Journal of Pain. 2013; 14(2):114-25

83. Correa JB, Costa LO, Oliveira NT, Lima WP, Sluka KA, Liebano RE. Effects of the carrier frequency of interferential current on pain modulation and central hypersensitivity in people with chronic nonspecific low back pain: A randomized placebo-controlled trial. European Journal of Pain. 2016; 20(10):1653-1666

84. Cossins L, Okell RW, Cameron H, Simpson B, Poole HM, Goebel A. Treatment of complex regional pain syndrome in adults: A systematic review of randomized controlled trials published from June 2000 to February 2012. European Journal of Pain. 2013; 17(2):158-73

85. Costa SAP, Florezi GP, Artes GE, Costa JRD, Gallo RT, Freitas PM et al. The analgesic effect of photobiomodulation therapy (830 nm) on the masticatory muscles: a randomized, double-blind study. Pesquisa Odontologica Brasileira. 2017; 31:e107

86. Cruccu G, Attal N. Neurostimulation in neuropathic pain. European Journal of Neurology. 2016; 23:900-913

87. Cruccu G, Garcia-Larrea L, Hansson P, Keindl M, Lefaucheur JP, Paulus W et al. EAN guidelines on central neurostimulation therapy in chronic pain conditions. European Journal of Neurology. 2016; 23(10):1489-99

88. Cruz VL, Steiner ML, Pompei LM, Strufaldi R, Fonseca FLA, Santiago LHS et al. Randomized, double-blind, placebo-controlled clinical trial for evaluating the efficacy of fractional CO2 laser compared with topical estriol in the treatment of vaginal atrophy in postmenopausal women. Menopause. 2018; 25(1):21-28

89. Cummiford CM, Nascimento TD, Foerster BR, Clauw DJ, Zubieta JK, Harris RE et al. Changes in resting state functional connectivity after repetitive transcranial direct current stimulation applied to motor cortex in fibromyalgia patients. Arthritis Research & Therapy. 2016; 18:40

90. Curatolo M, La Bianca G, Cosentino G, Baschi R, Salemi G, Talotta R et al. Motor cortex tRNS improves pain, affective and cognitive impairment in patients with fibromyalgia: preliminary results of a randomised sham-controlled trial. Clinical and Experimental Rheumatology. 2017; 35(3 Suppl 105):100-105

91. Curtis L, Burns A. Unit costs of health and social care 2018. Canterbury. Personal Social Services Research Unit University of Kent, 2018. Available from: https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2018/

92. da Cunha LA, Firoozmand LM, da Silva AP, Camargo SE, Oliveira W. Efficacy of low-level laser therapy in the treatment of temporomandibular disorder. International Dental Journal. 2008; 58(4):213-7

93. Dailey DL, Rakel BA, Vance CG, Liebano RE, Amrit AS, Bush HM et al. Transcutaneous electrical nerve stimulation reduces pain, fatigue and hyperalgesia while restoring central inhibition in primary fibromyalgia. Pain. 2013; 154(11):2554-62

94. Dailey DL, Vance CG, Rakel BA, Zimmerman MB, Embree J, Merriwether EN et al. A Randomized Controlled Trial of TENS for Movement-Evoked Pain in Women with Fibromyalgia. Arthritis & rheumatology (hoboken, NJ). 2019;

95. Dailey DL, Vance CGT, Rakel BA, Zimmerman MB, Embree J, Merriwether EN et al. Transcutaneous Electrical Nerve Stimulation Reduces Movement-Evoked Pain and Fatigue: A Randomized, Controlled Trial. Arthritis & Rheumatology. 2020; 72(5):824-836

96. Dall'Agnol L, Medeiros LF, Torres IL, Deitos A, Brietzke A, Laste G et al. Repetitive transcranial magnetic stimulation increases the corticospinal inhibition and the brain-derived neurotrophic factor in chronic myofascial pain syndrome: an explanatory double-blinded, randomized, sham-controlled trial. Journal of Pain. 2014; 15(8):845-55

97. de Carli ML, Guerra MB, Nunes TB, di Matteo RC, de Luca CE, Aranha AC et al. Piroxicam and laser phototherapy in the treatment of TMJ arthralgia: a double-blind randomised controlled trial. Journal of Oral Rehabilitation. 2013; 40(3):171-8

98. De Giorgi I, Castroflorio T, Sartoris B, Deregibus A. The use of conventional transcutaneous electrical nerve stimulation in chronic facial myalgia patients. Clinical Oral Investigations. 2017; 21(1):275-280

99. de Souza RC, de Sousa ET, Scudine KG, Meira UM, de Oliveira ESEM, Gomes AC et al. Low-level laser therapy and anesthetic infiltration for orofacial pain in patients with fibromyalgia: a randomized clinical trial. Medicina Oral, Patología Oral y Cirugía Bucal. 2018; 23(1):e65-e71

100. Defrin R, Ariel E, Peretz C. Segmental noxious versus innocuous electrical stimulation for chronic pain relief and the effect of fading sensation during treatment. Pain. 2005; 115(1-2):152-60

101. Del Vecchio A, Floravanti M, Boccassini A, Gaimari G, Vestri A, Di Paolo C et al. Evaluation of the efficacy of a new low-level laser therapy home protocol in the treatment of temporomandibular joint disorder-related pain: A randomized, double-blind, placebo-controlled clinical trial. Cranio. 2019:1-10

102. Deluze C, Bosia L, Zirbs A, Chantraine A, Vischer TL. Electroacupuncture in fibromyalgia: results of a controlled trial. BMJ. 1992; 305(6864):1249-52

103. Demirkol N, Sari F, Bulbul M, Demirkol M, Simsek I, Usumez A. Effectiveness of occlusal splints and low-level laser therapy on myofascial pain. Lasers in Medical Science. 2015; 30(3):1007-12

104. Desantana J, Araujo M, Araujo F. Interferential current reduces pain sensitivity and central sensitization in patients with fibromyalgia: A randomized clinical trial. Journal of Pain. 2017; 18(4 Suppl 1):S52

105. Di Benedetto P, Iona LG, Zidarich V. Clinical evaluation of S-adenosyl-L-methionine versus transcutaneous electrical nerve stimulation in primary fibromyalgia. Current Therapeutic Research. 1993; 53(2):222-229

106. Dibai-Filho AV, de Oliveira AK, Girasol CE, Dias FR, Guirro RR. Additional effect of static ultrasound and diadynamic currents on myofascial trigger points in a manual therapy program for patients with chronic neck pain: A randomized clinical trial. American Journal of Physical Medicine and Rehabilitation. 2017; 96(4):243-252

107. Dimitrijevic IM, Lazovic MP, Kocic MN, Dimitrijevic LR, Mancic DD, Stankovic AM. Effects of low-level laser therapy and interferential current therapy in the treatment of complex regional pain syndrome. Turkiye Fiziksel Tip ve Rehabilitasyon Dergisi. 2014; 60(2):98-105

108. Dorsher PT. Clinical equivalence of laser needle to metal acupuncture needle in treating musculoskeletal pain: A pilot study. Medical Acupuncture. 2010; 22(1):11-17

109. Dundar U, Evcik D, Samli F, Pusak H, Kavuncu V. The effect of gallium arsenide aluminum laser therapy in the management of cervical myofascial pain syndrome: a double blind, placebo-controlled study. Clinical Rheumatology. 2007; 26(6):930-4

110. Dundar U, Turkmen U, Toktas H, Solak O, Ulasli A. The effect of high intensity laser therapy in the management of myofascial pain syndrome of the trapezius: A double blind, placebo-controlled study. Arthritis and Rheumatology. 2014; 66 (Suppl 10):S489

111. Dundar U, Turkmen U, Toktas H, Solak O, Ulasli AM. Effect of high-intensity laser therapy in the management of myofascial pain syndrome of the trapezius: a double-blind, placebo-controlled study. Lasers in Medical Science. 2015; 30(1):325-32

112. Durmus D, Alayli G, Goktepe AS, Taskaynatan MA, Bilgici A, Kuru O. Is phonophoresis effective in the treatment of chronic low back pain? A single-blind randomized controlled trial. Rheumatology International. 2013; 33(7):1737-44

113. Eken A, Kara M, Baskak B, Baltaci A, Gokcay D. Differential efficiency of transcutaneous electrical nerve stimulation in dominant versus nondominant hands in fibromyalgia: placebo-controlled functional near-infrared spectroscopy study. Neurophotonics. 2018; 5(1):011005

114. El-Gendy MH, Lasheen YR, Rezkalla WKS. Multimodal approach of electrotherapy versus myofascial release in patients with chronic mechanical neck pain: A randomized controlled trial. Physiotherapy Quarterly. 2019; 27(4):6-12

115. Emshoff R, Bosch R, Pumpel E, Schoning H, Strobl H. Low-level laser therapy for treatment of temporomandibular joint pain: a double-blind and placebo-controlled trial. Oral Surgery Oral Medicine Oral Pathology Oral Radiology & Endodontics. 2008; 105(4):452-6

116. Escortell-Mayor E, Riesgo-Fuertes R, Garrido-Elustondo S, Asunsolo-del Barco A, Diaz-Pulido B, Blanco-Diaz M et al. Primary care randomized clinical trial: Manual therapy effectiveness in comparison with TENS in patients with neck pain. Manual Therapy. 2011; 16(1):66-73

117. Esenyel M, Caglar N, Aldemir T. Treatment of myofascial pain. American Journal of Physical Medicine and Rehabilitation. 2000; 79(1):48-52

118. Euasobhon P, Payomyam C, Suthananun M, Potranan S. The effects of transcranial direct current stimulation in patients with chronic refractory peripheral neuropathic pain. Pain Practice. 2018; 18(Suppl 1):130

119. Evaluating integrative approaches for fibromyalgia in physical and rehabilitation medicine (PM&R). Archives of Physical Medicine and Rehabilitation. 2017; 98(10):e65-e66

120. Fagerlund AJ, Hansen OA, Aslaksen PM. Transcranial direct current stimulation as a treatment for patients with fibromyalgia: a randomized controlled trial. Pain. 2015; 156(1):62-71

121. Falaki F, Nejat AH, Dalirsani Z. The effect of low-level laser therapy on trigeminal neuralgia: A review of literature. Journal of Dental Research Dental Clinics Dental Prospects. 2014; 8(1):1-5

122. Fernandez-Rodriguez T, Fernandez-Rolle A, Truyols-Dominguez S, Benitez-Martinez JC, Casana-Granell J. Prospective randomized trial of electrolysis for chronic plantar heel pain. Foot and Ankle International. 2018:1-8

123. Ferreira LA, de Oliveira RG, Guimaraes JP, Carvalho AC, De Paula MV. Laser acupuncture in patients with temporomandibular dysfunction: a randomized controlled trial. Lasers in Medical Science. 2013; 28(6):1549-58

124. Field GM, Spanswick CC, Hunter ME. A comparison of two modes of transcutaneous electrical nerve stimulation in chronic back pain. Pain. 1992; Suppl 5:S231

125. Fikackova H, Dostalova T, Navratil L, Klaschka J. Effectiveness of low-level laser therapy in temporomandibular joint disorders: a placebo-controlled study. Photomedicine and Laser Surgery. 2007; 25(4):297-303

126. Foletti A, Egan CG, Baron P. Effect of biophysical therapy on articular pain in a primary care setting compared to ibuprofen and placebo: a randomized controlled trial. Journal of Biological Regulators and Homeostatic Agents. 2018; 32(2):407-413

127. Franco JV, Turk T, Jung JH, Xiao YT, Iakhno S, Garrote V et al. Non-pharmacological interventions for treating chronic prostatitis/chronic pelvic pain syndrome. Cochrane Database of Systematic Reviews 2018, Issue Art. No.: 29372565. DOI: https://dx.doi.org/10.1002/14651858.CD012551.pub2.

128. Frank S, Waschke A, Reichart R, Kalff R. Transcranial magnetic stimulation in neuropathic facial pain-A prospective study of 17 patients. Clinical Neurophysiology. 2013; 124(10):e122

129. Fregni F, Gimenes R, Valle AC, Ferreira MJ, Rocha RR, Natalle L et al. A randomized, sham-controlled, proof of principle study of transcranial direct current stimulation for the treatment of pain in fibromyalgia. Arthritis and Rheumatism. 2006; 54(12):3988-98

130. Fricova J, Klirova M, Masopust V, Novak T, Verebova K, Rokyta R. Repetitive transcranial magnetic stimulation in the treatment of chronic orofacial pain. Physiological Research. 2013; 62(Suppl 1):S125-34

131. Galhardoni R, Correia GS, Araujo H, Yeng LT, Fernandes DT, Kaziyama HH et al. Repetitive transcranial magnetic stimulation in chronic pain: a review of the literature. Archives of Physical Medicine and Rehabilitation. 2015; 96(4 Suppl):S156-72

132. Gam AN, Thorsen H, Lonnberg F. The effect of low-level laser therapy on musculoskeletal pain: A meta-analysis. Pain. 1993; 52(1):63-66

133. Gemmell H, Hilland A. Immediate effect of electric point stimulation (TENS) in treating latent upper trapezius trigger points: a double blind randomised placebo-controlled trial. Journal of Bodywork and Movement Therapies. 2011; 15(3):348-54

134. Gendreau RM, Deering D, Gendreau J, Hargrove J. Treatment of fibromyalgia with neurostimulation: A randomized, double-blinded, sham-controlled trial. Arthritis and Rheumatology. 2014; 66(Suppl 10):S483

135. Germano Maciel D, Trajano da Silva M, Rodrigues JA, Viana Neto JB, de Franca IM, Melo ABM et al. Low-level laser therapy combined to functional exercise on treatment of fibromyalgia: a double-blind randomized clinical trial. Lasers in Medical Science. 2018; 33(9):1949-1959

136. Gibson W, Wand BM, O'Connell NE. Transcutaneous electrical nerve stimulation (TENS) for neuropathic pain in adults. Cochrane Database of Systematic Reviews 2017, Issue 9. Art. No.: CD011976. DOI: 10.1002/14651858.CD011976.pub2.

137. Gokyildiz S, Kizilkaya Beji N, Yalcin O, Istek A. Effects of percutaneous tibial nerve stimulation therapy on chronic pelvic pain. Gynecologic and Obstetric Investigation. 2012; 73(2):99-105

138. Goudra B, Shah D, Balu G, Gouda G, Balu A, Borle A et al. Repetitive transcranial magnetic stimulation in chronic pain: A meta-analysis. Anesthesia Essays and Researches. 2017; 11(3):751-757

139. Graff-Radford SB, Reeves JL, Baker RL, Chiu D. Effects of transcutaneous electrical nerve stimulation on myofascial pain and trigger point sensitivity. Pain. 1989; 37(1):1-5

140. Graham N, Gross AR, Carlesso LC, Santaguida PL, Macdermid JC, Walton D et al. An icon overview on physical modalities for neck pain and associated disorders. The Open Orthopaedics Journal. 2013; 7:440-60

141. Gray RJ, Quayle AA, Hall CA, Schofield MA. Physiotherapy in the treatment of temporomandibular joint disorders: a comparative study of four treatment methods. British Dental Journal. 1994; 176(7):257-61

142. Gross AR, Aker PD, Goldsmith CH, Peloso P. Physical medicine modalities for mechanical neck disorders. Cochrane Database of Systematic Reviews 2000, Issue 2. Art. No.: 10796402. DOI: 10.1002/14651858.CD000961.

143. Gross AR, Dziengo S, Boers O, Goldsmith CH, Graham N, Lilge L et al. Low Level Laser Therapy (LLLT) for Neck Pain: A Systematic Review and Meta-Regression. The open orthopaedics journal. 2013; 7:396-419

144. Guedj E, Dousset A, Boyer L, Roussel P, Cammilleri S, Mundler O et al. Transcranial magnetic stimulation in fibromyalgia: A randomized trial evaluating quality of life and its brain metabolic substrat. European Journal of Nuclear Medicine and Molecular Imaging. 2013; 40 Suppl 2:S217

145. Guirro RRJ, Dibai-Filho AV, Dias FRC, Oliveira AK. Efficacy static ultrasound and manual therapy in the treatment myofascial trigger points individuals with neck pain: A pilot clinical study. Physiotherapy. 2015; 101(Suppl 1):e494-e495

146. Guo XJ, Jia J. Comparison of therapeutic effects on fibromyalgia syndrome between dermal-neurological electric stimulation and electric acupuncture. Chinese Journal of Clinical Rehabilitation. 2005; 9(46):171-173

147. Gur A, Karakoc M, Nas K, Cevik R, Sarac J, Ataoglu S. Effects of low power laser and low dose amitriptyline therapy on clinical symptoms and quality of life in fibromyalgia: a single-blind, placebo-controlled trial. Rheumatology International. 2002; 22(5):188-93

148. Gur A, Karakoc M, Nas K, Cevik R, Sarac J, Demir E. Efficacy of low power laser therapy in fibromyalgia: a single-blind, placebo-controlled trial. Lasers in Medical Science. 2002; 17(1):57-61

149. Gur A, Koca I, Karagullu H, Altindag O, Madenci E. Comparison of the efficacy of ultrasound and extracorporeal shock wave therapies in patients with myofascial pain syndrome: A randomized controlled study. Journal of Musculoskeletal Pain. 2013; 21(3):210-216

150. Hakguder A, Birtane M, Gurcan S, Kokino S, Turan FN. Efficacy of low level laser therapy in myofascial pain syndrome: an algometric and thermographic evaluation. Lasers in Surgery and Medicine. 2003; 33(5):339-43

151. Hargrove JB, Bennett RM, Simons DG, Smith SJ, Nagpal S, Deering DE. A randomized placebo-controlled study of noninvasive cortical electrostimulation in the treatment of fibromyalgia patients. Pain Medicine. 2012; 13(1):115-24

152. Harvey MP, Lorrain D, Martel M, Bergeron-Vezina K, Houde F, Seguin M et al. Can we improve pain and sleep in elderly individuals with transcranial direct current stimulation? - Results from a randomized controlled pilot study. Clinical Interventions in Aging. 2017; 12:937-947

153. He DP, Zhang J, Bai ZF. Percutaneous Electrical Nerve Stimulation for Chronic Knee Pain: A Randomized, Sham-controlled Trial. Alternative Therapies in Health and Medicine. 2017; 25(2):30-34

154. Hong CZ, Chen YC, Pon CH, Yu J. Immediate effects of various physical medicine modalities on pain threshold of an active myofascial trigger point. Journal of Musculoskeletal Pain. 1993; 1(2):37-53

155. Hou CR, Tsai LC, Cheng KF, Chung KC, Hong CZ. Immediate effects of various physical therapeutic modalities on cervical myofascial pain and trigger-point sensitivity. Archives of Physical Medicine and Rehabilitation. 2002; 83(10):1406-14

156. Hou WH, Wang TY, Kang JH. The effects of add-on non-invasive brain stimulation in fibromyalgia: a meta-analysis and meta-regression of randomized controlled trials. Rheumatology. 2016; 55(8):1507-17

157. Hruby G, Ames C, Chen C, Yan Y, Sagar J, Baron P et al. Assessment of efficacy of transcutaneous electrical nerve stimulation for pain management during office-based flexible cystoscopy. Urology. 2006; 67(5):914-917

158. Hsu JH, Daskalakis ZJ, Blumberger DM. An Update on Repetitive Transcranial Magnetic Stimulation for the Treatment of Co-morbid Pain and Depressive Symptoms. Current Pain & Headache Reports. 2018; 22(7):51

159. Hsueh TC, Cheng PT, Kuan TS, Hong CZ. The immediate effectiveness of electrical nerve stimulation and electrical muscle stimulation on myofascial trigger points. American Journal of Physical Medicine and Rehabilitation. 1997; 76(6):471-6

160. Hurt K, Zahalka F, Halaska M, Rakovicova I, Krajcova A. Extracorporeal shock wave therapy for treatment of vulvodynia: a prospective, randomized, double-blind, placebo-controlled study. European Journal of Physical and Rehabilitation Medicine. 2020;

161. Ilbuldu E, Cakmak A, Disci R, Aydin R. Comparison of laser, dry needling, and placebo laser treatments in myofascial pain syndrome. Photomedicine and Laser Surgery. 2004; 22(4):306-11

162. Ilter L, Dilek B, Batmaz I, Ulu MA, Sariyildiz MA, Nas K et al. Efficacy of pulsed and continuous therapeutic ultrasound in myofascial pain syndrome: A randomised controlled study. Annals of the Rheumatic Diseases Conference: Annual European Congress of Rheumatology of the European League Against Rheumatism, EULAR. 2014; 73(Suppl 2)

163. Ilter L, Dilek B, Batmaz I, Ulu MA, Sariyildiz MA, Nas K et al. Efficacy of pulsed and continuous therapeutic ultrasound in myofascial pain syndrome: A randomized controlled study. American Journal of Physical Medicine and Rehabilitation. 2015; 94(7):547-54

164. Istek A, Gungor Ugurlucan F, Yasa C, Gokyildiz S, Yalcin O. Randomized trial of long-term effects of percutaneous tibial nerve stimulation on chronic pelvic pain. Archives of Gynecology and Obstetrics. 2014; 290(2):291-8

165. Ito M, Kurita K, Ito T, Arao M. Pain threshold and pain recovery after experimental stimulation in patients with burning mouth syndrome. Psychiatry and Clinical Neurosciences. 2002; 56(2):161-168

166. Ivanishvili Z, Poologaindran A, Honey CR. Cyclization of motor cortex stimulation for neuropathic pain: A prospective, randomized, blinded trial. Neuromodulation. 2017; 20(5):497-503

167. Jales Junior LH, Costa MD, Jales Neto LH, Ribeiro JPM, Freitas WJ, Teixeira MJ. Transcranial direct current stimulation in fibromyalgia: effects on pain and quality of life evaluated clinically and by brain perfusion scintigraphy. Revista Dor. 2015; 16(1):37-42

168. Janice Jimenez-Torres G, Weinstein BL, Walker CR, Christopher Fowler J, Ashford P, Borckardt JJ et al. A study protocol for a single-blind, randomized controlled trial of adjunctive transcranial direct current stimulation (tDCS) for chronic pain among patients receiving specialized, inpatient multimodal pain management. Contemporary Clinical Trials. 2017; 54:36-47

169. Jeans ME. Relief of chronic pain by brief, intense transcutaneous electrical stimulation. A double-blind study. Advances in Pain Research Therapy. 1979; 3:601-607

170. Jeon JH, Jung YJ, Lee JY, Choi JS, Mun JH, Park WY et al. The effect of extracorporeal shock wave therapy on myofascial pain syndrome. Annals of Rehabilitation Medicine. 2012; 36(5):665-74

171. Jin Y, Xing G, Li G, Wang A, Feng S, Tang Q et al. High frequency repetitive transcranial magnetic stimulation therapy for chronic neuropathic pain: A meta-analysis. Pain Physician. 2015; 18(6):E1029-46

172. Johansson F, Almay BGL, Knorring L. Predictors for the outcome of treatment with high frequency transcutaneous electrical nerve stimulation in patients with chronic pain. Pain. 1980; 6:55-61

173. Johnson M, Martinson M. Efficacy of electrical nerve stimulation for chronic musculoskeletal pain: a meta-analysis of randomized controlled trials. Pain. 2007; 130(1-2):157-65

174. Johnson MI, Claydon LS, Herbison GP, Jones G, Paley CA. Transcutaneous electrical nerve stimulation (TENS) for fibromyalgia in adults. Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD012172. DOI: 10.1002/14651858.CD012172.pub2.

175. Johnson S, Goebel A, Richey R, Holmes E, Hughes D. A randomised, patient-assessor blinded, sham-controlled trial of external non-invasive peripheral nerve stimulation for chronic neuropathic pain following peripheral nerve injury (EN-PENS trial): study protocol for a randomised controlled trial. Trials. 2016; 17(1):574

176. Kabay S, Kabay SC, Yucel M, Ozden H. Efficiency of posterior tibial nerve stimulation in category IIIB chronic prostatitis/chronic pelvic pain: a Sham-Controlled Comparative Study. Urologia Internationalis. 2009; 83(1):33-8

177. Kadhim-Saleh A, Maganti H, Ghert M, Singh S, Farrokhyar F. Is low-level laser therapy in relieving neck pain effective? Systematic review and meta-analysis. Rheumatology International. 2013; 33(10):2493-501

178. Kara M, Ozçakar L, Gökçay D, Ozçelik E, Yörübulut M, Güneri S et al. Quantification of the effects of transcutaneous electrical nerve stimulation with functional magnetic resonance imaging: a double-blind randomized placebo-controlled study. Archives of Physical Medicine and Rehabilitation. 2010; 91(8):1160-1165

179. Kato MT, Kogawa EM, Santos CN, Conti PC. TENS and low-level laser therapy in the management of temporomandibular disorders. J Appl Oral Sci. 2006; 14(2):130-5

180. Katsoulis J, Ausfeld-Hafter B, Windecker-Getaz I, Katsoulis K, Blagojevic N, Mericske-Stern R. Laser acupuncture for myofascial pain of the masticatory muscles.

A controlled pilot study. Schweizer Monatsschrift für Zahnmedizin. 2010; 120(3):213-25

181. Kavadar G, Caglar N, Ozen S, Tutun S, Demircioglu D. Efficacy of conventional ultrasound therapy on myofascial pain syndrome: a placebo controlled study. Agri Dergisi. 2015; 27(4):190-6

182. Kavvadias T, Baessler K, Schuessler B. Pelvic pain in urogynecology. Part II: treatment options in patients with lower urinary tract symptoms. International Urogynecology Journal. 2012; 23(5):553-61

183. Kemler MA, Reulen JP, Barendse GA, van Kleef M, de Vet HC, van den Wildenberg FA. Impact of spinal cord stimulation on sensory characteristics in complex regional pain syndrome type I: a randomized trial. Anesthesiology. 2001; 95(1):72-80

184. Kessler TM, Mordasini L, Weisstanner C, Juni P, da Costa BR, Wiest R et al. Sono-electro-magnetic therapy for treating chronic pelvic pain syndrome in men: a randomized, placebo-controlled, double-blind trial. PloS One. 2014; 9(12):e113368

185. Khedr EM, Omran EAH, Ismail NM, El-Hammady DH, Goma SH, Kotb H et al. Effects of transcranial direct current stimulation on pain, mood and serum endorphin level in the treatment of fibromyalgia: A double blinded, randomized clinical trial. Brain Stimulation. 2017; 10(5):893-901

186. Kim Y, Yang HR, Lee JW, Yoon BC. Effects of the high-power pain threshold ultrasound technique in the elderly with latent myofascial trigger points: a double-blind randomized study. Journal of Back and Musculoskeletal Rehabilitation. 2014; 27(1):17-23

187. Kiraly M, Bender T, Hodosi K. Comparative study of shockwave therapy and low-level laser therapy effects in patients with myofascial pain syndrome of the trapezius. Rheumatology International. 2018; 38(11):2045-2052

188. Knijnik LM, Dussan-Sarria JA, Rozisky JR, Torres IL, Brunoni AR, Fregni F et al. Repetitive transcranial magnetic stimulation for fibromyalgia: Systematic review and meta-analysis. Pain Practice. 2016; 16(3):294-304

189. Koca I, Tutoglu A, Boyaci A, Ucar M, Yagiz E, Isik M et al. A comparison of the effectiveness of low-, moderate- and high-dose ultrasound therapy applied in the treatment of myofascial pain syndrome. Modern Rheumatology. 2014; 24(4):662-6

190. Kohutova B, Fricova J, Klirova M, Novak T, Rokyta R. Theta burst stimulation in the treatment of chronic orofacial pain: a randomized controlled trial. Physiological Research. 2017; 66(6):1041-1047

191. Kriek N, Groeneweg JG, Stronks DL, Huygen FJ. Comparison of tonic spinal cord stimulation, high-frequency and burst stimulation in patients with complex regional pain syndrome: a double-blind, randomised placebo controlled trial. BMC Musculoskeletal Disorders. 2015; 16:222

192. Kroeling P, Gross A, Graham N, Burnie SJ, Szeto G, Goldsmith CH et al. Electrotherapy for neck pain. Cochrane Database of Systematic Reviews 2013, Issue 8. Art. No.: CD004251. DOI: 10.1002/14651858.CD004251.pub5.

193. Kroeling P, Gross AR, Goldsmith CH, Cervical Overview G. A Cochrane review of electrotherapy for mechanical neck disorders. Spine. 2005; 30(21):E641-8

194. Kruger LR, van der Linden WJ, Cleaton-Jones PE. Transcutaneous electrical nerve stimulation in the treatment of myofascial pain dysfunction. South African Journal of Surgery. 1998; 36(1):35-8

195. Kulekcioglu S, Sivrioglu K, Ozcan O, Parlak M. Effectiveness of low-level laser therapy in temporomandibular disorder. Scandinavian Journal of Rheumatology. 2003; 32(2):114-8

196. La Bianca G, Curatolo M, Romano M, Fierro B, Brighina F. Motor cortex tRNS ameliorates pain, anxiety, depression, quality of life and cognitive impairment in patients with fibromyalgia: preliminary results of a randomized sham-controlled trial. Neurology Conference: 69th American Academy of Neurology Annual Meeting, AAN. 2017; 88(16 Supplement 1)

197. Laakso EL, Richardson C, Cramond T. Pain scores and side effects in response to low level laser therapy (lllt) for myofascial trigger points. Laser Therapy. 1997; 9(2):67-72

198. Lagueux E, Bernier M, Bourgault P, Whittingstall K, Mercier C, Leonard G et al. The effectiveness of transcranial direct current stimulation as an add-on modality to graded motor imagery for treatment of complex regional pain syndrome: A randomized proof of concept study. Clinical Journal of Pain. 2018; 34(2):145-154

199. Langley GB, Sheppeard H, Johnson M, Wigley RD. The analgesic effects of transcutaneous electrical nerve stimulation and placebo in chronic pain patients. A double-blind non-crossover comparison. Rheumatology International. 1984; 4(3):119-23

200. Lara-Palomo IC, Aguilar-Ferrandiz ME, Mataran-Penarrocha GA, Saavedra-Hernandez M, Granero-Molina J, Fernandez-Sola C et al. Short-term effects of interferential current electro-massage in adults with chronic non-specific low back pain: a randomized controlled trial. Clinical Rehabilitation. 2013; 27(5):439-49

201. Lassemi E, Jafari SM, Motamedi MHK, Navi F, Lasemi R. Low-level laser therapie in the management of temporomandibular joint disorder. The Journal of Oral Laser Applications. 2008; 8(2):83-86

202. Lauretti GR, Chubaci EF, Mattos AL. Efficacy of the use of two simultaneously TENS devices for fibromyalgia pain. Rheumatology International. 2013; 33(8):2117-22

203. Leandri M, Parodi CI, Corrieri N, Rigardo S. Comparison of TENS treatments in hemiplegic shoulder pain. Scandinavian Journal of Rehabilitation Medicine. 1990; 22(2):69-71

204. Lee JC, Lin DT, Hong CZ. The effectiveness of simultaneous thermotherapy with ultrasound and electrotherapy with combined AC and DC current on the immediate pain relief of myofascial trigger points. Journal of Musculoskeletal Pain. 1997; 5(1):81-90

205. Lee SJ, Kim DY, Chun MH, Kim YG. The effect of repetitive transcranial magnetic stimulation on fibromyalgia: a randomized sham-controlled trial with 1-mo follow-up. American Journal of Physical Medicine and Rehabilitation. 2012; 91(12):1077-85

206. Lee SU, Lee CH, Choi YH. Synergistic effects of transcranial direct current stimulation and trigger point injection for treatment of myofascial pain syndrome: A pilot study with randomized, single-blinded trial. Arthritis and Rheumatism. 2013; 10:S464

207. Lev-Sagie A, Kopitman A, Brzezinski A. Low-Level Laser Therapy for the Treatment of Provoked Vestibulodynia-A Randomized, Placebo-Controlled Pilot Trial. Journal of Sexual Medicine. 2017; 14(11):1403-1411

208. Lewis GK, Jr., Langer MD, Henderson CR, Jr., Ortiz R. Design and evaluation of a wearable self-applied therapeutic ultrasound device for chronic myofascial pain. Ultrasound in Medicine and Biology. 2013; 39(8):1429-39

209. Lewis GN, Rice DA, Kluger M, McNair PJ. Transcranial direct current stimulation for upper limb neuropathic pain: A double-blind randomized controlled trial. European Journal of Pain. 2018; 22(7):1312-1320

210. Lichtbroun AS, Raicer MM, Smith RB. The treatment of fibromyalgia with cranial electrotherapy stimulation. JCR: Journal of Clinical Rheumatology. 2001; 7(2):72-8

211. Lima MC, Fregni F. Motor cortex stimulation for chronic pain: systematic review and meta-analysis of the literature. Neurology. 2008; 70(24):2329-37

212. Lindholm P, Lamusuo S, Taiminen T, Pesonen U, Lahti A, Virtanen A et al. Right secondary somatosensory cortex-a promising novel target for the treatment of drug-resistant neuropathic orofacial pain with repetitive transcranial magnetic stimulation. Pain. 2015; 156(7):1276-83

213. Lopez-Martos R, Gonzalez-Perez LM, Ruiz-Canela-Mendez P, Urresti-Lopez FJ, Gutierrez-Perez JL, Infante-Cossio P. Randomized, double-blind study comparing percutaneous electrolysis and dry needling for the management of temporomandibular myofascial pain. Medicina Oral, Patología Oral y Cirugía Bucal. 2018; 23(4):e454-62

214. Luan S, Zhu ZM, Ruan JL, Lin CN, Ke SJ, Xin WJ et al. Randomized Trial on Comparison of the Efficacy of Extracorporeal Shock Wave Therapy and Dry Needling in Myofascial Trigger Points. American Journal of Physical Medicine and Rehabilitation. 2019; 98(8):677-684

215. Luedtke K, Rushton A, Wright C, Geiss B, Juergens TP, May A. Transcranial direct current stimulation for the reduction of clinical and experimentally induced pain: a systematic review and meta-analysis. Clinical Journal of Pain. 2012; 28(5):452-61

216. Lyskov E, Kalezic N, Markov M, Mild KH, Thunberg J, Johansson H. Low frequency therapeutic EMF differently influences experimental muscle pain in female and male subjects. Bioelectromagnetics. 2005; 26(4):299-304

217. Macdonald AJR, Coates TW. The discovery of transcutaneous spinal electroanalgesia and its relief of chronic pain. Physiotherapy. 1995; 81(11):653-661

218. MacPherson H, Vickers A, Bland M, Torgerson D, Corbett M, Spackman E et al. Acupuncture for chronic pain and depression in primary care: a programme of research. NIHR Journals Library Programme Grants for Applied Research. 2017; 5(3):342

219. Madani A, Ahrari F, Fallahrastegar A, Daghestani N. A randomized clinical trial comparing the efficacy of low-level laser therapy (LLLT) and laser acupuncture therapy (LAT) in patients with temporomandibular disorders. Lasers in Medical Science. 2020; 35(1):181-192

220. Maestu C, Blanco M, Nevado A, Romero J, Rodriguez-Rubio P, Galindo J et al. Reduction of pain thresholds in fibromyalgia after very low-intensity magnetic stimulation: a double-blinded, randomized placebo-controlled clinical trial. Pain Research & Management. 2013; 18(6):e101-6

221. Magri LV, Carvalho VA, Rodrigues FC, Bataglion C, Leite-Panissi CR. Effectiveness of low-level laser therapy on pain intensity, pressure pain threshold, and SF-MPQ indexes of women with myofascial pain. Lasers in Medical Science. 2017; 32(2):419-428

222. Magri LV, Carvalho VA, Rodrigues FCC, Bataglion C, Leite-Panissi CRA. Non-specific effects and clusters of women with painful TMD responders and non-responders to LLLT: double-blind randomized clinical trial. Lasers in Medical Science. 2018; 33(2):385-392

223. Maia ML, Bonjardim LR, Quintans Jde S, Ribeiro MA, Maia LG, Conti PC. Effect of low-level laser therapy on pain levels in patients with temporomandibular disorders: a systematic review. Journal of Applied Oral Science. 2012; 20(6):594-602

224. Majithia N, Smith TJ, Coyne PJ, Abdi S, Pachman DR, Lachance D et al. Scrambler Therapy for the management of chronic pain. Supportive Care in Cancer. 2016; 24(6):2807-14

225. Majlesi J, Unalan H. High-power pain threshold ultrasound technique in the treatment of active myofascial trigger points: a randomized, double-blind, case-control study. Archives of Physical Medicine and Rehabilitation. 2004; 85(5):833-6

226. Maloney R, Shanks S. Evaluation of low-level laser therapy at 635nm for the treatment of acute and chronic neck and shoulder pain: A placebo-controlled, randomized study. Lasers in Surgery and Medicine. 2014; 46(S25):1-81

227. Manafnezhad J, Salahzadeh Z, Salimi M, Ghaderi F, Ghojazadeh M. The effects of shock wave and dry needling on active trigger points of upper trapezius muscle in patients with non-specific neck pain: A randomized clinical trial. Journal of Back and Musculoskeletal Rehabilitation. 2019; 32(5):811-818

228. Manca A, Limonta E, Pilurzi G, Ginatempo F, De Natale ER, Mercante B et al. Ultrasound and laser as stand-alone therapies for myofascial trigger points: a randomized, double-blind, placebo-controlled study. Physiotherapy Research International. 2014; 19(3):166-75

229. Manfredini D, Favero L, Cocilovo F, Monici M, Guarda-Nardini L. A comparison trial between three treatment modalities for the management of myofascial pain of jaw muscles: A preliminary study. Cranio. 2017:1-5

230. Marchand S, Bushnell MC, Molina-Negro P, Martinez SN, Duncan GH. The effects of dorsal column stimulation on measures of clinical and experimental pain in man. Pain. 1991; 45(3):249-57

231. Marineo G, Iorno V, Gandini C, Moschini V, Smith TJ. Scrambler therapy may relieve chronic neuropathic pain more effectively than guideline-based drug management: Results of a pilot, randomized, controlled trial. Journal of Pain and Symptom Management. 2012; 43(1)

232. Marini I, Gatto MR, Bonetti GA. Effects of superpulsed low-level laser therapy on temporomandibular joint pain. Clinical Journal of Pain. 2010; 26(7):611-6

233. Marlow NM, Bonilha HS, Short EB. Efficacy of transcranial direct current stimulation and repetitive transcranial magnetic stimulation for treating fibromyalgia syndrome: a systematic review. Pain Practice. 2013; 13(2):131-45

234. Matsutani LA, Marques AP, Ferreira EA, Assumpcao A, Lage LV, Casarotto RA et al. Effectiveness of muscle stretching exercises with and without laser therapy at tender points for patients with fibromyalgia. Clinical and Experimental Rheumatology. 2007; 25(3):410-5

235. Mazzetto MO, Carrasco TG, Bidinelo EF, de Andrade Pizzo RC, Mazzetto RG. Low intensity laser application in temporomandibular disorders: a phase I double-blind study. Cranio. 2007; 25(3):186-92

236. Medeiros LF, Caumo W, Dussan-Sarria J, Deitos A, Brietzke A, Laste G et al. Effect of deep intramuscular stimulation and transcranial magnetic stimulation on neurophysiological biomarkers in chronic myofascial pain syndrome. Pain Medicine. 2016; 17(1):122-35

237. Mekhail N, Deer TR, Poree L, Staats PS, Burton AW, Connolly AT et al. Cost-effectiveness of dorsal root ganglion or spinal cord stimulation for complex regional pain syndrome and peripheral causalgia. Pain Practice. 2018; 18(Suppl 1):32-33

238. Melchior MO, Venezian GC, Zanandrea Machado BC, Borges RF, Mazzetto MO. Does low intensity laser therapy reduce pain and change orofacial myofunctional conditions? Cranio - Journal of Craniomandibular Practice. 2013; 31(2):133-139

239. Mendonca ME, Santana MB, Baptista AF, Datta A, Bikson M, Fregni F et al. Transcranial DC stimulation in fibromyalgia: optimized cortical target supported by high-resolution computational models. Journal of Pain. 2011; 12(5):610-7

240. Mendonca ME, Simis M, Grecco LC, Battistella LR, Baptista AF, Fregni F. Transcranial direct current stimulation combined with aerobic exercise to optimize analgesic responses in fibromyalgia: A randomized placebo-controlled clinical trial. Frontiers in Human Neuroscience. 2016; 10 (March):68

241. Mhalla A, Baudic S, Ciampi de Andrade D, Gautron M, Perrot S, Teixeira MJ et al. Long-term maintenance of the analgesic effects of transcranial magnetic stimulation in fibromyalgia. Pain. 2011; 152(7):1478-85

242. Moisset X, de Andrade DC, Bouhassira D. From pulses to pain relief: an update on the mechanisms of rTMS-induced analgesic effects. European Journal of Pain. 2016; 20(5):689-700

243. Molina-Torres G, Rodriguez-Archilla A, Mataran-Penarrocha G, Albornoz-Cabello M, Aguilar-Ferrandiz ME, Castro-Sanchez AM. Laser therapy and occlusal stabilization splint for temporomandibular disorders in patients with fibromyalgia syndrome: A randomized, clinical trial. Alternative Therapies in Health and Medicine. 2016; 22(5):23-31

244. Mordasini L, Kessler TM, Weisstanner C, Wiest R, Juni P, Da Costa B et al. Sono-electro-magnetic therapy for treating chronic pelvic pain syndrome in men: A randomized, placebo-controlled, double-blind trial. European Urology, Supplements. 2014; 13(1):e467

245. Moretti FA, Marcondes FB, Provenza JR, Fukuda TY, de Vasconcelos RA, Roizenblatt S. Combined therapy (ultrasound and interferential current) in patients with fibromyalgia: once or twice in a week? Physiotherapy Research International. 2012; 17(3):142-9

246. Morin A, Leonard G, Gougeon V, Cyr MP, Waddell G, Bureau YA et al. Efficacy of transcranial direct-current stimulation in women with provoked vestibulodynia. American Journal of Obstetrics and Gynecology. 2017; 216(6):584.e1-584.e11

247. Müller CE, Aranha MF, Gavião MB. Two-dimensional ultrasound and ultrasound elastography imaging of trigger points in women with myofascial pain syndrome treated by acupuncture and electroacupuncture: a double-blinded randomized controlled pilot study. Ultrasonic Imaging. 2015; 37(2):152-167

248. Munguia FM, Jang J, Salem M, Clark GT, Enciso R. Efficacy of low-level laser therapy in the treatment of temporomandibular myofascial pain: A systematic review and meta-analysis. Journal of Oral & Facial Pain and Headache. 2018; 32(3):287-297

249. Muniswamy VK, Powell E, Sloan P, Sawaki L. Modulating neuropathic pain with transcranial direct current stimulation: Preliminary findings from an ongoing study (10265). Neuromodulation. 2016; 19 (3):e4

250. Murina F, Bianco V, Radici G, Felice R, Di Martino M, Nicolini U. Transcutaneous electrical nerve stimulation to treat vestibulodynia: a randomised controlled trial. BJOG: An International Journal of Obstetrics and Gynaecology. 2008; 115(9):1165-70

251. Murina F, Felice R, Di Francesco S, Oneda S. Vaginal diazepam plus transcutaneous electrical nerve stimulation to treat vestibulodynia: A randomized controlled trial. European Journal of Obstetrics, Gynecology, and Reproductive Biology. 2018; 228:148-153

252. Mutlu B, Paker N, Bugdayci D, Tekdos D, Kesiktas N. Efficacy of supervised exercise combined with transcutaneous electrical nerve stimulation in women with fibromyalgia: a prospective controlled study. Rheumatology International. 2013; 33(3):649-55

253. Mutlu B, Paker N, Yylmaz E, Soy D. Comparison of therapeutic efficacy of transcutaneous electrical nerve stimulation (TENS) and exercise program in fibromyalgia syndrome: a prospective randomized study. Annals of the Rheumatic Diseases. 2006; 65:649-55

254. Mysliwiec A, Saulicz E, Kuszewski M, Wolny T, Saulicz M, Knapik A. The effect of Saunders traction and transcutaneous electrical nerve stimulation on the cervical spine range of motion in patients reporting neck pain - pilot study. Ortopedia Traumatologia Rehabilitacja. 2012; 14(6):515-24

255. Nadershah M, Abdel-Alim HM, Bayoumi AM, Jan AM, Elatrouni A, Jadu FM. Photobiomodulation Therapy for Myofascial Pain in Temporomandibular Joint Dysfunction: A Double-Blinded Randomized Clinical Trial. Journal of Maxillofacial and Oral Surgery. 2020; 19(1):93-97

256. Nardone R, Brigo F, Holler Y, Sebastianelli L, Versace V, Saltuari L et al. Transcranial magnetic stimulation studies in complex regional pain syndrome type I: A review. Acta Neurologica Scandinavica. 2018; 137(2):158-164

257. Naterstad I, Joensen J, Lopes-Martins RAB, Haslerud S, Bjordal JM. Treating tendinopathy with low level laser therapy. Physiotherapy. 2015; 101(Suppl 1):e1077

258. National Institute for Health and Care Excellence. Developing NICE guidelines: the manual [updated October 2018]. London. National Institute for Health and Care Excellence, 2014. Available from: http://www.nice.org.uk/article/PMG20/chapter/1%20Introduction%20and%20overview

259. National Institute for Health and Care Excellence. Low back pain and sciatica in over 16s: assessment and management. NICE guideline 59. London. National Institute for Health and Care Excellence, 2016. Available from: https://www.nice.org.uk/guidance/ng59

260. NCT. Low level laser light therapy and chronic neck and shoulder pain [NCT00929305]. 2009. Available from: https://clinicaltrials.gov/ct2/show/nct00929305 Last accessed: 31/07/2018

261. NHS Supply Chain Catalogue. NHS Supply Chain, 2018. Available from: http://www.supplychain.nhs.uk/

262. Niddam DM, Chan RC, Lee SH, Yeh TC, Hsieh JC. Central modulation of pain evoked from myofascial trigger point. Clinical Journal of Pain. 2007; 23(5):440-8

263. Noehren B, Dailey DL, Rakel BA, Vance CG, Zimmerman MB, Crofford LJ et al. Effect of transcutaneous electrical nerve stimulation on pain, function, and quality of life in fibromyalgia: a double-blind randomized clinical trial. Physical Therapy. 2015; 95(1):129-40

264. Nordin M, Campello M. Physical therapy: Exercises and the modalities: When, what, and why? Neurologic Clinics. 1999; 17(1):75-89

265. O'Connell NE, Cossar J, Marston L, Wand BM, Bunce D, De Souza LH et al. Transcranial direct current stimulation of the motor cortex in the treatment of chronic nonspecific low back pain: a randomized, double-blind exploratory study. Clinical Journal of Pain. 2013; 29(1):26-34

266. O'Connell NE, Marston L, Spencer S, DeSouza LH, Wand BM. Non-invasive brain stimulation techniques for chronic pain. Cochrane Database of Systematic Reviews 2018, Issue 4. Art. No.: CD008208. DOI: 10.1002/14651858.CD008208.pub5.

267. O'Connell NE, Wand BM, Marston L, Spencer S, Desouza LH. Non-invasive brain stimulation techniques for chronic pain. A report of a Cochrane systematic review and meta-analysis. European journal of physical & rehabilitation medicine. 2011; 47(2):309-26

268. Ofluoglu D, Aydin Bulak E, Kablan N, Akyu ZG. Short-term effects of interferential currents on chronic myofascial pain syndrome. Turkiye Fiziksel Tip ve Rehabilitasyon Dergisi. 2013; 59(3):209-213

269. Okmen BM, Okmen K. Comparison of photobiomodulation therapy and suprascapular nerve-pulsed radiofrequency in chronic shoulder pain: a randomized controlled, single-blind, clinical trial. Lasers in Medical Science. 2017; 32(8):1719-1726

270. Oosterhof J, De Boo TM, Oostendorp RA, Wilder-Smith OH, Crul BJ. Outcome of transcutaneous electrical nerve stimulation in chronic pain: short-term results of a double-blind, randomised, placebo-controlled trial. Journal of Headache and Pain. 2006; 7(4):196-205

271. Oosterhof J, Samwel HJ, de Boo TM, Wilder-Smith OH, Oostendorp RA, Crul BJ. Predicting outcome of TENS in chronic pain: a prospective, randomized, placebo controlled trial. Pain. 2008; 136(1-2):11-20

272. Oosterhof J, Wilder-Smith OH, de Boo T, Oostendorp RA, Crul BJ. The long-term outcome of transcutaneous electrical nerve stimulation in the treatment for patients with chronic pain: a randomized, placebo-controlled trial. Pain Practice. 2012; 12(7):513-22

273. Oosterhof J, Wilder-Smith OH, Oostendorp RA, Crul BJ. Different mechanisms for the short-term effects of real versus sham transcutaneous electrical nerve stimulation (TENS) in patients with chronic pain: a pilot study. Journal of Pain & Palliative Care Pharmacotherapy. 2012; 26(1):5-12

274. Panton L, Simonavice E, Williams K, Mojock C, Kim JS, Kingsley JD et al. Effects of Class IV laser therapy on fibromyalgia impact and function in women with fibromyalgia. Journal of Alternative and Complementary Medicine. 2013; 19(5):445-52

275. Park KD, Lee WY, Park MH, Ahn JK, Park Y. High- versus low-energy extracorporeal shock-wave therapy for myofascial pain syndrome of upper trapezius: A prospective randomized single blinded pilot study. Medicine. 2018; 97(28):e11432

276. Passard A, Attal N, Benadhira R, Brasseur L, Saba G, Sichere P et al. Effects of unilateral repetitive transcranial magnetic stimulation of the motor cortex on chronic widespread pain in fibromyalgia. Brain. 2007; 130(Pt 10):2661-70

277. Peng AT, Behar S, Yue SJ. Long-term therapeutic effects of electro-acupuncture for chronic neck and shoulder pain--a double blind study. Acupuncture and Electro-Therapeutics Research. 1987; 12(1):37-44

278. Perrot S, Russell IJ. More ubiquitous effects from non-pharmacologic than from pharmacologic treatments for fibromyalgia syndrome: a meta-analysis examining six core symptoms. European Journal of Pain. 2014; 18(8):1067-80

279. Pezelj-Ribaric S, Kqiku L, Brumini G, Urek MM, Antonic R, Kuis D et al. Proinflammatory cytokine levels in saliva in patients with burning mouth syndrome before and after treatment with low-level laser therapy. Lasers in Medical Science. 2013; 28(1):297-301

280. Picarelli H. The effects of repetitive transcranial magnetic stimulation (rTMS) over the motor cortex on complex regional pain syndrome patients. Arquivos de Neuro-Psiquiatria. 2012; 70(9):751

281. Picarelli H, Teixeira MJ, de Andrade DC, Myczkowski ML, Luvisotto TB, Yeng LT et al. Repetitive transcranial magnetic stimulation is efficacious as an add-on to pharmacological therapy in complex regional pain syndrome (CRPS) type I. Journal of Pain. 2010; 11(11):1203-10

282. Plazier M, Dekelver I, Vanneste S, Stassijns G, Menovsky T, Thimineur M et al. Occipital nerve stimulation in fibromyalgia: a double-blind placebo-controlled pilot study with a six-month follow-up. Neuromodulation. 2014; 17(3):256-64

283. Powers A, Madan A, Hilbert M, Reeves ST, George M, Nash MR et al. Effects of combining a brief cognitive intervention with transcranial direct current stimulation on pain tolerance: A randomized controlled pilot study. Pain Medicine. 2018; 19(4):677-685

284. Rayegani S, Bahrami M, Samadi B, Sedighipour L, Mokhtarirad M, Eliaspoor D. Comparison of the effects of low energy laser and ultrasound in treatment of shoulder myofascial pain syndrome: a randomized single-blinded clinical trial. European journal of physical & rehabilitation medicine. 2011; 47(3):381-9

285. Reid P, Pridmore S. Improvement in chronic pain with transcranial magnetic stimulation. Australian and New Zealand Journal of Psychiatry. 2001; 35(2):252

286. Renzenbrink GJ, MJ IJ. Percutaneous neuromuscular electrical stimulation (P-NMES) for treating shoulder pain in chronic hemiplegia. Effects on shoulder pain and quality of life. Clinical Rehabilitation. 2004; 18(4):359-65

287. Riberto M, Marcon Alfieri F, Monteiro de Benedetto Pacheco K, Dini Leite V, Nemoto Kaihami H, Fregni F et al. Efficacy of transcranial direct current stimulation coupled with a multidisciplinary rehabilitation program for the treatment of fibromyalgia. Open Rheumatol J. 2011; 5:45-50

288. Rigby JH, Draper DO. Effects of long duration low intensity ultrasound for active trapezius trigger points: A randomized clinical trial.[retraction in j sport rehabil. 2017 apr;26(2):189; pmid: 28414267]. Journal of Sport Rehabilitation. 2017:1-17

289. Rohlig BG, Kipirdi S, Meric U, Capan N, Keskin H. Masticatory muscle pain and low-level laser therapy: a double-blind and placebo-controlled study. Turkish Journal of Physical Medicine and Rehabilitation. 2011; 57(1):31-37

290. Roizenblatt S, Fregni F, Gimenez R, Wetzel T, Rigonatti SP, Tufik S et al. Site-specific effects of transcranial direct current stimulation on sleep and pain in fibromyalgia: a randomized, sham-controlled study. Pain Practice. 2007; 7(4):297-306

291. Rollnik JD, Wustefeld S, Dauper J, Karst M, Fink M, Kossev A et al. Repetitive transcranial magnetic stimulation for the treatment of chronic pain - a pilot study. European Neurology. 2002; 48(1):6-10

292. Rowe E, Smith C, Laverick L, Elkabir J, O'N Witherow R, Patel A. A prospective, randomized, placebo controlled, double-blind study of pelvic electromagnetic therapy for the treatment of chronic pelvic pain syndrome with 1 year of followup. Journal of Urology. 2005; 173(6):2044-2047

293. Ruiz-Lopez I, Martinez-Fuentes J. Efficacy of spinal cord stimulation in type I complex regional pain syndrome: Literature review. Revista de la Sociedad Espanola del Dolor. 2017; 24(4):169-178

294. Ryan CG, King R, Robinson V, Punt TD, Dinse HR, Grunenberg C et al. Transcutaneous electrical nerve stimulation using an LTP-like repetitive stimulation protocol for patients with upper limb complex regional pain syndrome: A feasibility study. Hand Therapy. 2017; 22(2):52-63

295. Sahin N, Albayrak I, Ugurlu H. Effect of different transcutaneous electrical stimulation modalities on cervical myofascial pain syndrome. Journal of Musculoskeletal Pain. 2011; 19(1):18-23

296. Sahin N, Ozcan E, Sezen K, Karatas O, Issever H. Efficacy of acupunture in patients with chronic neck pain--a randomised, sham controlled trial. Acupuncture and Electro-Therapeutics Research. 2010; 35(1-2):17-27

297. Sakrajai P, Janyacharoen T, Jensen MP, Sawanyawisuth K, Auvichayapat N, Tunkamnerdthai O et al. Pain reduction in myofascial pain syndrome by anodal transcranial direct current stimulation combined with standard treatment: a randomized controlled study. Clinical Journal of Pain. 2014; 30(12):1076-83

298. Salazar AP, Stein C, Marchese RR, Plentz RD, Pagnussat AS. Electric stimulation for pain relief in patients with fibromyalgia: A systematic review and meta-analysis of randomized controlled trials. Pain Physician. 2017; 20(2):15-25

299. Saltychev M, Laimi K. Effectiveness of repetitive transcranial magnetic stimulation in patients with fibromyalgia: a meta-analysis. International Journal of Rehabilitation Research. 2017; 40(1):11-18

300. Samson D. Percutaneous intradiscal radiofrequency thermocoagulation for chronic discogenic low back pain. Chicago, IL, USA. Blue Cross Blue Shield Association (BCBS), 2004.

301. Sancakli E, Gokcen-Rohlig B, Balik A, Ongul D, Kipirdi S, Keskin H. Early results of low-level laser application for masticatory muscle pain: a double-blind randomized clinical study. BMC Oral Health. 2015; 15:131

302. Santos V, Zortea M, Alves RL, Naziazeno C, Saldanha JS, Carvalho S et al. Cognitive effects of transcranial direct current stimulation combined with working memory training in fibromyalgia: a randomized clinical trial. Scientific Reports. 2018; 8(1):12477

303. Sator-Katzenschlager SM, Scharbert G, Kozek-Langenecker SA, Szeles JC, Finster G, Schiesser AW et al. The short- and long-term benefit in chronic low back pain through adjuvant electrical versus manual auricular acupuncture. Anesthesia and Analgesia. 2004; 98(5):1359-64

304. Sator-Katzenschlager SM, Szeles JC, Scharbert G, Michalek-Sauberer A, Kober A, Heinze G et al. Electrical stimulation of auricular acupuncture points is more effective than conventional manual auricular acupuncture in chronic cervical pain: a pilot study. Anesthesia and Analgesia. 2003; 97(5):1469-73

305. Sattayut S, Bradley P. A study of the influence of low intensity laser therapy on painful temporomandibular disorder patients. Laser Therapy. 2012; 21(3):183-92

306. Sayilir S. The short-term effects of TENS plus therapeutic ultrasound combinations in chronic neck pain. Complementary Therapies in Clinical Practice. 2018; 31:278-281

307. Sayilir S, Yildizgoren MT. The medium-term effects of diadynamic currents in chronic low back pain; TENS versus diadynamic currents: A randomised, follow-up study. Complementary Therapies in Clinical Practice. 2017; 29:16-19

308. Schabrun SM, Cannan A, Mullens R, Dunphy M, Pearson T, Lau C et al. The effect of interactive neurostimulation therapy on myofascial trigger points associated with mechanical neck pain: a preliminary randomized, sham-controlled trial. Journal of Alternative and Complementary Medicine. 2012; 18(10):946-52

309. Shafik A. Re: A Prospective, Randomized, Placebo Controlled, Double-Blind Study of Pelvic Electromagnetic Therapy for the Treatment of Chronic Pelvic Pain Syndrome With 1 Year of Followup. E. Rowe, C. Smith, L. Laverick, J. Elkabir, R. O. Witherow and A. Patel. Journal of Urology. 2006; 175(5):1964-1965

310. Shimoji K, Takahashi N, Nishio Y, Koyanagi M, Aida S. Pain relief by transcutaneous electric nerve stimulation with bidirectional modulated sine waves in patients with chronic back pain: a randomized, double-blind, sham-controlled study. Neuromodulation. 2007; 10(1):42-51

311. Shirani AM, Gutknecht N, Taghizadeh M, Mir M. Low-level laser therapy and myofacial pain dysfunction syndrome: a randomized controlled clinical trial. Lasers in Medical Science. 2009; 24(5):715-20

312. Shobha R, Narayanan VS, Jagadish Pai BS, Jaishankar HP, Jijin MJ. Low-level laser therapy: A novel therapeutic approach to temporomandibular disorder - A randomized, double-blinded, placebo-controlled trial. Indian Journal of Dental Research. 2017; 28(4):380-387

313. Short EB, Borckardt J, Beam W, Anderson B, Nahas Z, George MS. Transcranial magnetic stimulation for fibromyalgia. Biological Psychiatry. 2010; 67(9 Suppl):151S

314. Short EB, Borckardt JJ, Anderson BS, Frohman H, Beam W, Reeves ST et al. Ten sessions of adjunctive left prefrontal rTMS significantly reduces fibromyalgia pain: a randomized, controlled pilot study. Pain. 2011; 152(11):2477-84

315. Silva AF, Zortea M, Carvalho S, Leite J, Torres IL, Fregni F et al. Anodal transcranial direct current stimulation over the left dorsolateral prefrontal cortex modulates attention and pain in fibromyalgia: randomized clinical trial. Scientific Reports. 2017; 7(1):135

316. Simons DG, Dommerholt J. A randomized controlled study on the effect of two different treatments (FREMS and TENS) in myofascial pain syndrome. Journal of Musculoskeletal Pain. 2006; 14(1):59-60

317. Simpson EL, Duenas A, Holmes MW, Papaioannou D, Chilcott J. Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin: systematic review and economic evaluation. Health Technology Assessment. 2009; 13(17)

318. Skorupska E, Lisinski P, Samborski W. The effectiveness of the conservative versus myofascial pain physiotherapy in tennis elbow patients: Double-blind randomized trial of 80 patients. Journal of Musculoskeletal Pain. 2012; 20(1):41-50

319. Skrinjar I, Brzak BL, Vidranski V, Boras VV, Rogulj AA, Pavelic B. Salivary cortisol levels and burning symptoms in patients with burning mouth syndrome before and after low level laser therapy: A double blind controlled randomized clinical trial. Acta Stomatologica Croatica. 2020; 54(1):44-50

320. Slattery K, Amy R, Pinto J, Gonzales G, Shanks S. Treatment of chronic neck and shoulder pain with 635 nm low level laser therapy. A randomized, multi-centre, double-blind clinical study on 100 patients. Proceedings of the North American Association of Laser Therapy. 2002:23

321. Smania N, Corato E, Fiaschi A, Pietropoli P, Aglioti SM, Tinazzi M. Therapeutic effects of peripheral repetitive magnetic stimulation on myofascial pain syndrome. Clinical Neurophysiology. 2003; 114(2):350-8

322. Smania N, Corato E, Fiaschi A, Pietropoli P, Aglioti SM, Tinazzi M. Repetitive magnetic stimulation: a novel therapeutic approach for myofascial pain syndrome. Journal of Neurology. 2005; 252(3):307-14

323. Snyder-Mackler L, Bork C, Bourbon B, Trumbore D. Effect of helium-neon laser on musculoskeletal trigger points. Physical Therapy. 1986; 66(7):1087-1090

324. Soysal ANO, Aslan UB. Treatment of chronic neck pain by two combined physiotherapy programs: Comparison of phonophoresis and ultrasound. Asian Biomedicine. 2013; 7(6):821-827

325. Spanemberg JC, Lopez Lopez J, de Figueiredo MA, Cherubini K, Salum FG. Efficacy of low-level laser therapy for the treatment of burning mouth syndrome: a randomized, controlled trial. Journal of Biomedical Optics. 2015; 20(9):098001

326. Spanemberg JC, Segura-Egea JJ, Rodriguez-de Rivera-Campillo E, Jane-Salas E, Salum FG, Lopez-Lopez J. Low-level laser therapy in patients with Burning Mouth Syndrome: A double-blind, randomized, controlled clinical trial. Journal of Clinical & Experimental Dentistry. 2019; 11(2):e162-e169

327. Srbely JZ, Dickey JP. Randomized controlled study of the antinociceptive effect of ultrasound on trigger point sensitivity: novel applications in myofascial therapy? Clinical Rehabilitation. 2007; 21(5):411-7

328. Stonnington HH, Stillwell GK, Ebersold MJ, Thorsteinsson G, Laws ER. Transcutaneous electrical stimulation for chronic pain relief. A pilot study. Minnesota Medicine. 1976; 59(10):681-683

329. Sugaya NN, Silva EF, Kato IT, Prates R, Gallo CB, Pellegrini VD. Low Intensity laser therapy in patients with burning mouth syndrome: a randomized, placebo-controlled study. Pesquisa Odontologica Brasileira. 2016; 30(1):e108

330. Sunshine W, Field TM, Quintino O, Fierro K, Kuhn C, Burman I et al. Fibromyalgia benefits from massage therapy and transcutaneous electrical stimulation. JCR: Journal of Clinical Rheumatology. 1996; 2(1):18-22

331. Sutton CJG, Pooley AS, Ewen SP, Haines P. Follow-up report on a randomized controlled trial of laser laparoscopy in the treatment of pelvic pain associated with minimal to moderate endometriosis. Fertility and Sterility. 1997; 68(6):1070-1074

332. Takla MKN. Low-frequency high-intensity versus medium-frequency low-intensity combined therapy in the management of active myofascial trigger points: A randomized controlled trial. Physiotherapy Research International. 2018; 23(4):e1737

333. Takla MKN, Rezk-Allah SS. Immediate effects of simultaneous application of transcutaneous electrical nerve stimulation and ultrasound phonophoresis on active myofascial trigger points: A randomized controlled trial. American Journal of Physical Medicine and Rehabilitation. 2018; 97(5):332-338

334. Tanwar S, Mattoo B, Jain S, Kumar U, Dada R, Bhatia R. Transcranial magnetic stimulation in reducing chronic pain and the related symptoms in patients with fibromyalgia. Indian Journal of Physiology and Pharmacology. 2016; 60(5 Suppl 1):67-68

335. Taube S, Ylipaavalniemi P, Könönen M, B S. The effect of pulsed ultrasound on myofascial pain. A placebo controlled study. Proceedings of the Finnish Dental Society. 1988; 84:241-6

336. Taylor AG, Anderson JG, Riedel SL, Lewis JE, Bourguignon C. A randomized, controlled, double-blind pilot study of the effects of cranial electrical stimulation on activity in brain pain processing regions in individuals with fibromyalgia. Explore: The Journal of Science & Healing. 2013; 9(1):32-40

337. Taylor K, Newton RA, Personius WJ, Bush FM. Effects of interferential current stimulation for treatment of subjects with recurrent jaw pain. Physical Therapy. 1987; 67(3):346-50

338. Taylor RS, Taylor RJ, Van Buyten JP, Buchser E, North R, Bayliss S. The cost effectiveness of spinal cord stimulation in the treatment of pain: a systematic review of the literature. Journal of Pain and Symptom Management. 2004; 27(4):370-8

339. Tekin A, Ozdil E, Guleken MD, Iliser R, Bakim B, Oncu J et al. Efficacy of high frequency [10 Hz] repetitive transcranial magnetic stimulation of the primary motor cortex in patients with fibromyalgia syndrome: A randomized, double blind, sham-controlled trial. Journal of Musculoskeletal Pain. 2014; 22(1):20-26

340. Thorsteinsson G, Stonnington HH, Stillwell GK, Elveback LR. Transcutaneous electrical stimulation: a double blind trial of its efficacy for pain. Archives of Physical Medicine and Rehabilitation. 1977; 58(1):8-13

341. Tieppo Francio V, Dima RS, Towery C, Davani S. Prolotherapy and low level laser therapy: A synergistic approach to pain management in chronic osteoarthritis. Anesthesiology & Pain Medicine. 2017; 7(5):e14470

342. Tirlapur SA, Vlismas A, Ball E, Khan KS. Nerve stimulation for chronic pelvic pain and bladder pain syndrome: a systematic review. Acta Obstetricia et Gynecologica Scandinavica. 2013; 92(8):881-7

343. To WT, James E, Ost J, Hart J, Jr., De Ridder D, Vanneste S. Differential effects of bifrontal and occipital nerve stimulation on pain and fatigue using transcranial direct current stimulation in fibromyalgia patients. Journal of Neural Transmission. 2017; 124(7):799-808

344. Uemoto L, Garcia MA, Gouvea CV, Vilella OV, Alfaya TA. Laser therapy and needling in myofascial trigger point deactivation. Journal of Oral Science. 2013; 55(2):175-81

345. Umezaki Y, Badran BW, DeVries WH, Moss J, Gonzales T, George MS. The efficacy of daily prefrontal repetitive transcranial magnetic stimulation (rtms) for burning mouth syndrome (bms): A randomized controlled single-blind study. Brain Stimulation. 2016; 9(2):234-42

346. Valenzuela S, Lopez-Jornet P. Effects of low-level laser therapy on burning mouth syndrome. Journal of Oral Rehabilitation. 2017; 44(2):125-132

347. Valle A, Roizenblatt S, Botte S, Zaghi S, Riberto M, Tufik S et al. Efficacy of anodal transcranial direct current stimulation (tDCS) for the treatment of fibromyalgia: results of a randomized, sham-controlled longitudinal clinical trial. Journal of Pain Management. 2009; 2(3):353-361

348. Van Der Windt DAWM, Van Der Heijden GJMG, Van Den Berg SGM, Ter Riet G, De Winter AF, Bouter LM. Ultrasound therapy for musculoskeletal disorders: A systematic review. Pain. 1999; 81(3):257-271

349. Vance C, Dailey D, Rakel B, Geasland K, Darghosian L, Alemo Munters L et al. A novel method to obtain higher intensity TENS stimulation in clinical application. Journal of Pain. 2015; 1:S93

350. Vas J, Perea-Milla E, Mendez C, Sanchez Navarro C, Leon Rubio JM, Brioso M et al. Efficacy and safety of acupuncture for chronic uncomplicated neck pain: a randomised controlled study. Pain. 2006; 126(1-3):245-55

351. Vaseghi B, Zoghi M, Jaberzadeh S. Does anodal transcranial direct current stimulation modulate sensory perception and pain? A meta-analysis study. Clinical Neurophysiology. 2014; 125(9):1847-58

352. Vaseghi B, Zoghi M, Jaberzadeh S. A meta-analysis of site-specific effects of cathodal transcranial direct current stimulation on sensory perception and pain. PloS One. 2015; 10(5):e0123873

353. Vayvay ES, Tok D, Turgut E, Tunay VB. The effect of Laser and taping on pain, functional status and quality of life in patients with fibromyalgia syndrome: A placebo-randomized controlled clinical trial. Journal of Back and Musculoskeletal Rehabilitation. 2016; 29(1):77-83

354. Venancio Rde A, Camparis CM, Lizarelli Rde F. Low intensity laser therapy in the treatment of temporomandibular disorders: a double-blind study. Journal of Oral Rehabilitation. 2005; 32(11):800-7

355. Venezian GC, da Silva MA, Mazzetto RG, Mazzetto MO. Low level laser effects on pain to palpation and electromyographic activity in TMD patients: a double-blind, randomized, placebo-controlled study. Cranio. 2010; 28(2):84-91

356. Viana R, Pereira S, Mehta S, Miller T, Teasell R. Evidence for therapeutic interventions for hemiplegic shoulder pain during the chronic stage of stroke: a review. Topics in Stroke Rehabilitation. 2012; 19(6):514-22

357. Visnjevac O, Costandi S, Patel BA, Azer G, Agarwal P, Bolash R et al. A comprehensive outcome-specific review of the use of spinal cord stimulation for complex regional pain syndrome. Pain Practice. 2017; 17(4):533-545

358. Vitiello AL, Bonello R, Pollard H. The effectiveness of ENAR for the treatment of chronic neck pain in Australian adults: a preliminary single-blind, randomised controlled trial. Chiropractic & Osteopathy. 2007; 15:9

359. Vrijens D, Marcelissen T, Jairam R, De Ruiter B, Van Koeveringe G, Van Kerrebroeck P. Neuromodulation in chronic pelvic pain: A systematic review. Neurourology and Urodynamics. 2017; 36(Suppl 3):S460-S461

360. Vukoja D, Alajbeg I, Vucicevic Boras V, Brailo V, Alajbeg IZ, Andabak Rogulj A. Is effect of low-level laser therapy in patients with burning mouth syndrome result of a placebo? Photomedicine and Laser Surgery. 2011; 29(9):647-651

361. Walker JB, Akhanjee LK, Cooney MM, Goldstein J, Tamayoshi S, Segal-Gidan F. Laser therapy for pain of trigeminal neuralgia. Clinical Journal of Pain. 1987; 3(4):183-187

362. Wang H, Xie Y, Zhang Q, Xu N, Zhong H, Dong H et al. Transcutaneous electric acupoint stimulation reduces intra-operative remifentanil consumption and alleviates postoperative side-effects in patients undergoing sinusotomy: a prospective, randomized, placebo-controlled trial. British Journal of Anaesthesia. 2014; 112(6):1075-82

363. Wang X, Yang Z, Zhang W, Yi X, Liang C, Li X. Efficacy evaluation of low-level laser therapy on temporomandibular disorder. West China Journal of Stomatology. 2011; 29(4):393-5, 399

364. Wang X, Zhao W, Wang Y, Hu J, Chen Q, Yu J et al. A self-administered method of acute pressure block of sciatic nerves for short-term relief of dental pain: a randomized study. Pain Medicine. 2014; 15(8):1304-11

365. Waschl S, Morrissey MC, Rugelj D. The efficacy of ultrasound-facilitated electrical stimulation as an adjunct to exercise in treating chronic neck and shoulder pain. Journal of Musculoskeletal Pain. 2014; 22(1):78-88

366. WCB Evidence Based Practice Group. Spinal cord stimulation: use in patients with complex regional pain syndrome. Richmond, BC. WorkSafe BC, 2003.

367. Weisstanner C, Mordasini L, Thalmann GN, Rummel C, Verma RK, Abela E et al. Cortical reorganization of pain processing in patients with chronic pelvic pain syndrome. Neuroradiology. 2014; 1:231-232

368. Weisstanner C, Mordasini L, Thalmann GN, Verma RK, Rummel C, Federspiel A et al. Therapy-related longitudinal brain perfusion changes in patients with chronic pelvic pain syndrome. Swiss Medical Weekly. 2017; 147:w14454

369. Weng CS, Tsai YS, Shu SH, Chen Cc, Sun MF. The treatment of upper back pain by two modulated frequency modes of acupuncture-like TENS. Journal of Medical and Biological Engineering. 2005; 25(1):21-25

370. White A, Foster NE, Cummings M, Barlas P. Acupuncture treatment for chronic knee pain: A systematic review. Rheumatology. 2007; 46(3):384-390

371. White P, Bishop FL, Prescott P, Scott C, Little P, Lewith G. Practice, practitioner, or placebo? A multifactorial, mixed-methods randomized controlled trial of acupuncture. Pain. 2012; 153(2):455-62

372. White PF, Craig WF, Vakharia AS, Ghoname E, Ahmed HE, Hamza MA. Percutaneous neuromodulation therapy: does the location of electrical stimulation effect the acute analgesic response? Anesthesia and Analgesia. 2000; 91(4):949-54

373. Wiffen PJ. Evidence-based pain management and palliative care in issue two for 2005 of the Cochrane library. Journal of Pain and Palliative Care Pharmacotherapy. 2005; 19(4):67-70

374. Wilson RD, Gunzler DD, Bennett ME, Chae J. Peripheral nerve stimulation compared with usual care for pain relief of hemiplegic shoulder pain: a randomized controlled trial. American Journal of Physical Medicine and Rehabilitation. 2014; 93(1):17-28

375. Yagci I, Agirman M, Ozturk D, Eren B. Is the transcranial magnetic stimulation an adjunctive treatment in fibromyalgia patients? Turkiye Fiziksel Tip ve Rehabilitasyon Dergisi. 2014; 60(3):206-211

376. Yang Y, Fu J, Xu X, Shi C. Ultrasound-guided pulsed radiofrequency therapy of suprascapular nerve versus suprascapular nerve block for the treatment of chronic refractory shoulder pain: analysis of curative effect. Journal of Interventional Radiology. 2018; 27(7):665-668

377. Yatci I, Atirman M, Ozturk D, Eren B. Effect of low-frequency transcranial magnetic stimulation of the motor cortex area in fibromyalgia patients. Turkiye Fiziksel Tip ve Rehabilitasyon Dergisi. 2013; 59(Suppl 1):232

378. Yesil H, Hepguler S, Dundar U, Taravati S, Isleten B. Does the use of analgesic current therapies increase the effectiveness of neck stabilization exercises for improving pain, disability, mood, and quality of life in chronic neck pain? a randomized, controlled, single-blind study (a pilot study). Annals of the Rheumatic Diseases. 2017; 76(Suppl 2):475-476

379. Yesil H, Hepguler S, Dundar U, Taravati S, Isleten B. Does the Use of Electrotherapies Increase the Effectiveness of Neck Stabilization Exercises for Improving Pain, Disability, Mood, and Quality of life in Chronic Neck Pain? A Randomized, Controlled, Single Blind Study. Spine. 2018; 43(20):E1174-E1183

380. Yildirim MA, Ones K, Goksenoglu G. Effectiveness of ultrasound therapy on myofascial pain syndrome of the upper trapezius: Randomized, single-blind, placebo-controlled study. Archives of Rheumatology. 2018; 33(4):418-423

381. Yoshimizu M, Teo AR, Ando M, Kiyohara K, Kawamura T. Relief of chronic shoulder and neck pain by electro-acupuncture and transcutaneous electrical nervous stimulation: A randomized crossover trial. Medical Acupuncture. 2012; 24(2):97-103

382. Young RF, Chambi VI. Pain relief by electrical stimulation of the periaqueductal and periventricular gray matter. Evidence for a non-opioid mechanism. Journal of Neurosurgery. 1987; 66(3):364-71

383. Yuksel M, Ayas S, Cabioglu MT, Yilmaz D, Cabioglu C. Quantitative data for transcutaneous electrical nerve stimulation and acupuncture effectiveness in treatment of fibromyalgia syndrome. Evidence-Based Complementary & Alternative Medicine: eCAM. 2019; 2019:9684649

384. Zhu CE, Yu B, Zhang W, Chen WH, Qi Q, Miao Y. Effiectiveness and safety of transcranial direct current stimulation in fibromyalgia: A systematic review and meta-analysis. Journal of Rehabilitation Medicine. 2017; 49(1):2-9

385. Zhu XM, Polus B. A controlled trial on acupuncture for chronic neck pain. American Journal of Chinese Medicine. 2002; 30(1):13-28

Appendices

Appendix A: Review protocols

Review protocol for electrical physical modalities

ID	Field	Content
0.	PROSPERO registration number	Not registered.
1.	Review title	What is the clinical and cost effectiveness of electrical physical modalities for the management of chronic primary pain?
2.	Review question	What is the clinical and cost effectiveness of electrical physical modalities for the management of chronic primary pain?
3.	Objective	To determine the clinical and cost effectiveness of electrical physical modalities for the management of chronic primary pain.
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • CINAHL, Current Nursing and Allied Health Literature Searches will be restricted by: • English language • Human studies • Letters and comments are excluded. Other searches:

		• Inclusion lists of relevant systematic reviews will be checked by the reviewer. The searches may be re-run 6 weeks before final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review.
5.	Condition or domain being studied	Chronic pain in one or more anatomical regions that is characterized by significant emotional distress (anxiety, anger/frustration or depressed mood) and functional disability (interference in daily life activities and reduced participation in social roles). The diagnosis is appropriate independently of identified biological or psychological contributors unless another diagnosis would better account for the presenting symptoms.
6.	Population	Inclusion: People, aged 16 years and over, with chronic primary pain (whose pain management is not addressed by existing NICE guidance) (chronic widespread pain, complex regional pain syndrome, chronic visceral pain, chronic orofacial pain, chronic primary musculoskeletal pain other than orofacial) Exclusion: Those whose pain management is addressed by existing NICE guidance.
7.	Intervention/Exposure/Test	Interventions: • transcutaneous electrical nerve stimulation (TENS) • percutaneous electrical nerve stimulation (PENS) • interferential therapy • laser therapy • therapeutic ultrasound • transcranial magnetic stimulation (TMS) • transcranial direct current stimulation (TDCS)
8.	Comparator/Reference standard/Confounding factors	Comparators: • each other • placebo/sham • usual care • physical therapies in this guideline.
9.	Types of study to be included	Randomised controlled trials (RCTs) and systematic reviews of RCTs

		Cross-over RCTs will be considered if no non-cross-over RCT evidence is identified.
10.	Other exclusion criteria	Non-English language studies. Studies comparing combinations of interventions.
11.	Context	A clear understanding of the evidence for the effectiveness of chronic primary pain treatments: • improves the confidence of healthcare professionals in their conversations about pain, and • helps healthcare professionals and patients to have realistic expectations about outcomes of treatment.
12.	Primary outcomes (critical outcomes)	• Pain reduction (any validated scale) • health related quality of life (including meaningful activity) • physical function (5 minute walk, sit to stand, Roland Morris Disability Questionnaire, Oswestry Disability Index, Canadian Occupational Performance Measure) • psychological distress (depression/anxiety) (preferably Hospital Anxiety and Depression Scale) • pain interference (brief pain inventory interference subscale) • pain self-efficacy (pain self-efficacy questionnaire). Outcomes will be extracted at the longest time point up to 3 months and at the longest time point after 3 months.
13.	Secondary outcomes (important outcomes)	• Use of healthcare services • sleep • discontinuation. Outcomes will be extracted at the longest time point up to 3 months and at the longest time point after 3 months.
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two

		reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. EviBASE will be used for data extraction. Study investigators may be contacted for missing data where time and resources allow.	
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the Cochrane Risk of Bias (2.0) tool. Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.	
16.	Strategy for data synthesis	Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome.	
17.	Analysis of sub-groups	Proposed sensitivity / subgroup analysis to be explored where there is heterogeneity: • chronic widespread pain • complex regional pain syndrome • chronic visceral pain • chronic orofacial pain • chronic primary musculoskeletal pain • cognitive impairment • learning difficulties • first language not English • sensory impairment • homeless	
18.	Type and method of review	☒	Intervention
		☐	Diagnostic

		☐	Prognostic
		☐	Qualitative
		☐	Epidemiologic
		☐	Service Delivery
		☐	Other (please specify)
19.	Language	English	
20.	Country	England	
21.	Anticipated or actual start date	NA – not registered on PROSPERO	
22.	Anticipated completion date	19/08/2020	
23.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail Chronicpain@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre	
24.	Review team members	From the National Guideline Centre: Serena Carville, Guideline Lead Maria Smyth, Senior Systematic Reviewer Rebecca Boffa, Senior Systematic Reviewer	

		Margaret Constanti, Senior Health Economist Joseph Runicles, Information Specialist Katie Broomfield, Project Manager
25.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
26.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
27.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10069
28.	Other registration details	NA
29.	Reference/URL for published protocol	NA
30.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.

31.	Keywords	-
32.	Details of existing review of same topic by same authors	NA
33.	Additional information	-
34.	Details of final publication	www.nice.org.uk

Table 13: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2002. Abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[258] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).

	• OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2002 or later but that depend on unit costs and resource data entirely or predominantly from before 2002 will be rated as 'Not applicable'. • Studies published before 2002 will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[258]

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

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 20 May 2020	Exclusions Randomised controlled trials Systematic review studies
Embase (OVID)	1974 – 20 May 2020	Exclusions Randomised controlled trials Systematic review studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2020 Issue 5 of 12 CENTRAL to 2020 Issue 5 of 12	None

Medline (Ovid) search terms

1.	Chronic pain/
2.	((chronic or persist* or idiopathic or atypical or a-typical) adj4 pain).ti,ab.
3.	exp Complex Regional Pain Syndromes/
4.	(complex regional pain syndrome* or CRPS or causalgia).ti,ab.
5.	((reflex or sympathetic) adj2 dystroph*).ti,ab.
6.	fibromyalgia/
7.	(fibromyalgia* or fibrositis or myofascial pain syndrome).ti,ab.
8.	vulvodynia/
9.	(vulvodynia or vestibulodynia or dyspareunia or vulvar vestibulitis or vulvitis).ti,ab.
10.	interstitial cystitis/
11.	(interstitial adj2 cystitis).ti,ab.
12.	algodystrophy/
13.	(algodystroph* or sudek or sudeck*).ti,ab.
14.	exp myofascial pain syndromes/
15.	cystitis, interstitial/
16.	(loin pain adj (haematuria or hematuria) adj syndrome*).ti,ab.
17.	(LPHS or prostatodynia or CPPS or atypic* odontalgia or a-typic* odontalgia or burning mouth syndrome* or phantom tooth pain or neuropathic orofacial pain or "myofascial pain" or MPS).ti,ab.

18.	((pelvic or pelvis) adj pain syndrome*).ti,ab.
19.	((non-cardiac or noncardiac) adj3 chest adj3 pain).ti,ab.
20.	(temporomandibular adj3 joint adj3 pain).ti,ab.
21.	((prostate or vulv* or bladder or perineal) adj3 pain).ti,ab.
22.	(functional pain syndrome* or non-cancer pain or noncancer pain).ti,ab.
23.	((pelvic or pelvis or abdominal) adj3 pain adj3 (unknown or un-known or idiopathic or atypic* or a-typic*)).ti,ab.
24.	or/1-23
25.	letter/
26.	editorial/
27.	news/
28.	exp historical article/
29.	Anecdotes as Topic/
30.	comment/
31.	case report/
32.	(letter or comment*).ti.
33.	or/25-32
34.	randomized controlled trial/ or random*.ti,ab.
35.	33 not 34
36.	animals/ not humans/
37.	exp Animals, Laboratory/
38.	exp Animal Experimentation/
39.	exp Models, Animal/
40.	exp Rodentia/
41.	(rat or rats or mouse or mice).ti.
42.	or/35-41
43.	24 not 42
44.	limit 43 to English language
45.	Transcutaneous Electric Nerve Stimulation/
46.	(TENS or PENS or ALTENS or TNS or TENMS or TMS or TDCS).ti,ab.
47.	(electroanalges* or electro analges*).ti,ab.
48.	Electric Stimulation Therapy/
49.	electrotherap*.ti,ab.
50.	((transcutaneous or transcranial or percutaneous or cutaneous or transderm* or peripheral or microamperage) adj3 (stimulat* or electr*)).ti,ab.
51.	electrostimulat*.ti,ab.
52.	(interferential adj2 current*).ti,ab.
53.	((electric* or electro or interferential) adj2 (stimulat* or therap* or acupuncture)).ti,ab.
54.	Laser Therapy, Low-Level/
55.	(laser adj2 (therap* or treat* or phototherap* or irradiat* or biostimulat* or stimulat*)).ti,ab.
56.	Ultrasonic Therapy/ or Extracorporeal Shockwave Therapy/
57.	((ultrasound or ultra sound or ultrasonic or ultra sonic) adj3 (contin* or therap* or treat* or stimulat* or intervention*)).ti,ab.
58.	or/45-57
59.	randomized controlled trial.pt.
60.	controlled clinical trial.pt.
61.	randomi#ed.ti,ab.

62.	placebo.ab.
63.	randomly.ti,ab.
64.	Clinical Trials as topic.sh.
65.	trial.ti.
66.	or/59-65
67.	Meta-Analysis/
68.	exp Meta-Analysis as Topic/
69.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
70.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
71.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
72.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
73.	(search* adj4 literature).ab.
74.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
75.	cochrane.jw.
76.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
77.	or/67-76
78.	44 and 58 and (66 or 77)

Embase (Ovid) search terms

1.	Chronic pain/
2.	((chronic or persist* or idiopathic or atypical or a-typical) adj4 pain).ti,ab.
3.	exp Complex regional pain syndrome/
4.	(complex regional pain syndrome* or CRPS or causalgia).ti,ab.
5.	((reflex or sympathetic) adj2 dystroph*).ti,ab.
6.	fibromyalgia/
7.	(fibromyalgia* or fibrositis or myofascial pain syndrome).ti,ab.
8.	vulvodynia/
9.	(vulvodynia or vestibulodynia or dyspareunia or vulvar vestibulitis or vulvitis).ti,ab.
10.	interstitial cystitis/
11.	(interstitial adj2 cystitis).ti,ab.
12.	algodystrophy/
13.	(algodystroph* or sudek or sudeck*).ti,ab.
14.	myofascial pain/
15.	noncardiac chest pain/
16.	cystalgia/
17.	Pelvis pain syndrome/
18.	(loin pain adj (haematuria or hematuria) adj syndrome*).ti,ab.
19.	(LPHS or prostatodynia or CPPS or atypic* odontalgia or a-typic* odontalgia or burning mouth syndrome* or phantom tooth pain or neuropathic orofacial pain or "myofascial pain" or MPS).ti,ab.
20.	((pelvic or pelvis) adj pain syndrome*).ti,ab.
21.	((non-cardiac or noncardiac) adj3 chest adj3 pain).ti,ab.
22.	(temporomandibular adj3 joint adj3 pain).ti,ab.
23.	((prostate or vulv* or bladder or perineal) adj3 pain).ti,ab.
24.	(functional pain syndrome* or non-cancer pain or noncancer pain).ti,ab.

25.	((pelvic or pelvis or abdominal) adj3 pain adj3 (unknown or un-known or idiopathic or atypic* or a-typic*)).ti,ab.
26.	or/1-25
27.	letter.pt. or letter/
28.	note.pt.
29.	editorial.pt.
30.	case report/ or case study/
31.	(letter or comment*).ti.
32.	or/27-31
33.	randomized controlled trial/ or random*.ti,ab.
34.	32 not 33
35.	animal/ not human/
36.	nonhuman/
37.	exp Animal Experiment/
38.	exp Experimental Animal/
39.	animal model/
40.	exp Rodent/
41.	(rat or rats or mouse or mice).ti.
42.	or/34-41
43.	26 not 42
44.	limit 43 to English language
45.	transcutaneous nerve stimulation/
46.	electrostimulation therapy/
47.	(TENS or PENS or ALTENS or TNS or TENMS or TMS or TDCS).ti,ab.
48.	(electroanalges* or electro analges*).ti,ab.
49.	electrotherap*.ti,ab.
50.	((transcutaneous or transcranial or percutaneous or cutaneous or transderm* or peripheral or microamperage) adj3 (stimulat* or electr*)).ti,ab.
51.	electrostimulat*.ti,ab.
52.	(interferential adj2 current*).ti,ab.
53.	((electric* or electro or interferential) adj2 (stimulat* or therap* or acupuncture)).ti,ab.
54.	(laser adj2 (therap* or treat* or phototherap* or irradiat* or biostimulat* or stimulat*)).ti,ab.
55.	Ultrasonic Therapy/
56.	((ultrasound or ultra sound or ultrasonic or ultra sonic) adj3 (contin* or therap* or treat* or stimulat* or intervention*)).ti,ab.
57.	low level laser therapy/
58.	electroanalgesia/
59.	or/45-58
60.	44 and 59
61.	random*.ti,ab.
62.	factorial*.ti,ab.
63.	(crossover* or cross over*).ti,ab.
64.	((doubl* or singl*) adj blind*).ti,ab.
65.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
66.	crossover procedure/
67.	single blind procedure/
68.	randomized controlled trial/

69.	double blind procedure/
70.	or/61-69
71.	systematic review/
72.	meta-analysis/
73.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
74.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
75.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
76.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
77.	(search* adj4 literature).ab.
78.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
79.	cochrane.jw.
80.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
81.	or/71-80
82.	60 and (70 or 81)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Chronic Pain] explode all trees
#2.	((chronic or persist* or idiopathic or atypical or a-typical) near/4 pain):ti,ab
#3.	MeSH descriptor: [Complex Regional Pain Syndromes] explode all trees
#4.	(complex regional pain syndrome* or CRPS or causalgia):ti,ab
#5.	((reflex or sympathetic) near/2 dystroph*):ti,ab
#6.	MeSH descriptor: [Fibromyalgia] explode all trees
#7.	(fibromyalgia* or fibrositis or myofascial pain syndrome):ti,ab
#8.	MeSH descriptor: [Vulvodynia] explode all trees
#9.	(vulvodynia or vestibulodynia or dyspareunia or vulvar vestibulitis or vulvitis):ti,ab
#10.	MeSH descriptor: [Cystitis, Interstitial] explode all trees
#11.	(interstitial near/2 cystitis):ti,ab
#12.	MeSH descriptor: [Reflex Sympathetic Dystrophy] explode all trees
#13.	(algodystroph* or sudek or sudeck*):ti,ab
#14.	MeSH descriptor: [Myofascial Pain Syndromes] explode all trees
#15.	(loin pain near (haematuria or hematuria) near syndrome*):ti,ab
#16.	(LPHS or prostatodynia or CPPS or atypic* odontalgia or a-typic* odontalgia or burning mouth syndrome* or phantom tooth pain or neuropathic orofacial pain or "myofascial pain" or MPS):ti,ab
#17.	((pelvic or pelvis) near pain syndrome*):ti,ab
#18.	((non-cardiac or noncardiac) near/3 chest near/3 pain):ti,ab
#19.	(temporomandibular near/3 joint near/3 pain):ti,ab
#20.	((prostate or vulv* or bladder or perineal) near/3 pain):ti,ab
#21.	(functional pain syndrome* or non-cancer pain or noncancer pain):ti,ab
#22.	((pelvic or pelvis or abdominal) near/3 pain near/3 (unknown or un-known or idiopathic or atypic* or a-typic*)):ti,ab
#23.	(or #1-#22)
#24.	MeSH descriptor: [Transcutaneous Electric Nerve Stimulation] explode all trees
#25.	(TENS or PENS or ALTENS or TNS or TENMS or TMS or TDCS):ti,ab
#26.	(electroanalges* or electro analges*):ti,ab
#27.	MeSH descriptor: [Electric Stimulation Therapy] explode all trees

#28.	electrotherap*:ti,ab
#29.	((transcutaneous or transcranial or percutaneous or cutaneous or transderm* or peripheral or microamperage) near/3 (stimulat* or electr*)):ti,ab
#30.	electrostimulat*:ti,ab
#31.	(interferential near/2 current*):ti,ab
#32.	((electric* or electro or interferential) near/2 (stimulat* or therap* or acupuncture)):ti,ab
#33.	MeSH descriptor: [Laser Therapy] explode all trees
#34.	(laser near/2 (therap* or treat* or phototherap* or irradiat* or biostimulat* or stimulat*)):ti,ab
#35.	MeSH descriptor: [Ultrasonic Therapy] explode all trees
#36.	MeSH descriptor: [Extracorporeal Shockwave Therapy] explode all trees
#37.	((ultrasound or ultra sound or ultrasonic or ultra sonic) near/3 (contin* or therap* or treat* or stimulat* or intervention*)):ti,ab
#38.	(or #24-#37)
#39.	#23 and #38

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to a Chronic Pain population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics and economic modelling.

Table 14: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 20 May 2020	Exclusions Health economics studies Health economics modelling studies
Embase	2014 – 20 May 2020	Exclusions Health economics studies Health economics modelling studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 20 May 2020 NHSEED - Inception to March 2015	None

Medline search terms

1.	chronic pain/ or pain, intractable/
2.	((persist* or intract* or chronic or longstanding or long standing or longterm or long term or refractory or prolong* or long last* or sustain* or linger* or syndrome*) adj3 pain*).ti,ab.
3.	((chronic or persist* or idiopathic or atypical or a-typical) adj4 pain).ti,ab.
4.	exp Complex Regional Pain Syndromes/
5.	(complex regional pain syndrome* or CRPS or causalgia).ti,ab.

6.	fibromyalgia/
7.	((reflex or sympathetic) adj2 dystroph*).ti,ab.
8.	vulvodynia/
9.	(vulvodynia or vestibulodynia or dyspareunia or vulvar vestibulitis or vulvitis).ti,ab.
10.	interstitial cystitis/
11.	(interstitial adj2 cystitis).ti,ab.
12.	algodystrophy/
13.	(algodystroph* or sudek or sudeck*).ti,ab.
14.	exp myofascial pain syndromes/
15.	cystitis, interstitial/
16.	(loin pain adj (haematuria or hematuria) adj syndrome*).ti,ab.
17.	(LPHS or prostatodynia or CPPS or atypic* odontalgia or a-typic* odontalgia or burning mouth syndrome* or phantom tooth pain or neuropathic orofacial pain or "myofascial pain" or MPS).ti,ab.
18.	((pelvic or pelvis) adj pain syndrome*).ti,ab.
19.	((non-cardiac or noncardiac) adj3 chest adj3 pain).ti,ab.
20.	(temporomandibular adj3 joint adj3 pain).ti,ab.
21.	((prostate or vulv* or bladder or perineal) adj3 pain).ti,ab.
22.	(functional pain syndrome* or non-cancer pain or noncancer pain).ti,ab.
23.	((pelvic or pelvis or abdominal) adj3 pain adj3 (unknown or un-known or idiopathic or atypic* or a-typic*)).ti,ab.
24.	(fibromyalgia* or fibrositis or myofascial pain syndrome).ti,ab.
25.	or/1-24
26.	letter/
27.	editorial/
28.	news/
29.	exp historical article/
30.	Anecdotes as Topic/
31.	comment/
32.	case report/
33.	(letter or comment*).ti.
34.	or/26-33
35.	randomized controlled trial/ or random*.ti,ab.
36.	34 not 35
37.	animals/ not humans/
38.	exp Animals, Laboratory/
39.	exp Animal Experimentation/
40.	exp Models, Animal/
41.	exp Rodentia/
42.	(rat or rats or mouse or mice).ti.
43.	or/36-42
44.	25 not 43
45.	Economics/
46.	Value of life/
47.	exp "Costs and Cost Analysis"/
48.	exp Economics, Hospital/
49.	exp Economics, Medical/
50.	Economics, Nursing/

51.	Economics, Pharmaceutical/
52.	exp "Fees and Charges"/
53.	exp Budgets/
54.	budget*.ti,ab.
55.	cost*.ti.
56.	(economic* or pharmaco?economic*).ti.
57.	(price* or pricing*).ti,ab.
58.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
59.	(financ* or fee or fees).ti,ab.
60.	(value adj2 (money or monetary)).ti,ab.
61.	or/45-60
62.	exp models, economic/
63.	*Models, Theoretical/
64.	*Models, Organizational/
65.	markov chains/
66.	monte carlo method/
67.	exp Decision Theory/
68.	(markov* or monte carlo).ti,ab.
69.	econom* model*.ti,ab.
70.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
71.	or/62-70
72.	44 and (61 or 71)

Embase (Ovid) search terms

1.	chronic pain/ or pain, intractable/
2.	((persist* or intract* or chronic or longstanding or long standing or longterm or long term or refractory or prolong* or long last* or sustain* or linger* or syndrome*) adj3 pain*).ti,ab.
3.	((chronic or persist* or idiopathic or atypical or a-typical) adj4 pain).ti,ab.
4.	exp Complex regional pain syndrome/
5.	(complex regional pain syndrome* or CRPS or causalgia).ti,ab.
6.	((reflex or sympatheti) adj2 dystroph*).ti,ab.
7.	fibromyalgia/
8.	(fibromyalgia* or fibrositis or myofascial pain syndrome).ti,ab.
9.	vulvodynia/
10.	(vulvodynia or vestibulodynia or dyspareunia or vulvar vestibulitis or vulvitis).ti,ab.
11.	interstitial cystitis/
12.	(interstitial adj2 cystitis).ti,ab.
13.	algodystrophy/
14.	(algodystroph* or sudek or sudeck*).ti,ab.
15.	myofascial pain/
16.	noncardiac chest pain/
17.	cystalgia/
18.	Pelvis pain syndrome/
19.	(loin pain adj (haematuria or hematuria) adj syndrome*).ti,ab.
20.	(LPHS or prostatodynia or CPPS or atypic* odontalgia or a-typic* odontalgia or burning mouth syndrome* or phantom tooth pain or neuropathic orofacial pain or "myofascial pain" or MPS).ti,ab.

21.	((pelvic or pelvis) adj pain syndrome*).ti,ab.
22.	((non-cardiac or noncardiac) adj3 chest adj3 pain).ti,ab.
23.	(temporomandibular adj3 joint adj3 pain).ti,ab.
24.	((prostate or vulv* or bladder or perineal) adj3 pain).ti,ab.
25.	(functional pain syndrome* or non-cancer pain or noncancer pain).ti,ab.
26.	((pelvic or pelvis or abdominal) adj3 pain adj3 (unknown or un-known or idiopathic or atypic* or a-typic*)).ti,ab.
27.	or/1-26
28.	letter.pt. or letter/
29.	note.pt.
30.	editorial.pt.
31.	case report/ or case study/
32.	(letter or comment*).ti.
33.	or/28-32
34.	randomized controlled trial/ or random*.ti,ab.
35.	33 not 34
36.	animal/ not human/
37.	nonhuman/
38.	exp Animal Experiment/
39.	exp Experimental Animal/
40.	animal model/
41.	exp Rodent/
42.	(rat or rats or mouse or mice).ti.
43.	or/35-42
44.	27 not 43
45.	health economics/
46.	exp economic evaluation/
47.	exp health care cost/
48.	exp fee/
49.	budget/
50.	funding/
51.	budget*.ti,ab.
52.	cost*.ti.
53.	(economic* or pharmaco?economic*).ti.
54.	(price* or pricing*).ti,ab.
55.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
56.	(financ* or fee or fees).ti,ab.
57.	(value adj2 (money or monetary)).ti,ab.
58.	or/45-57
59.	statistical model/
60.	exp economic aspect/
61.	59 and 60
62.	*theoretical model/
63.	*nonbiological model/
64.	stochastic model/
65.	decision theory/
66.	decision tree/

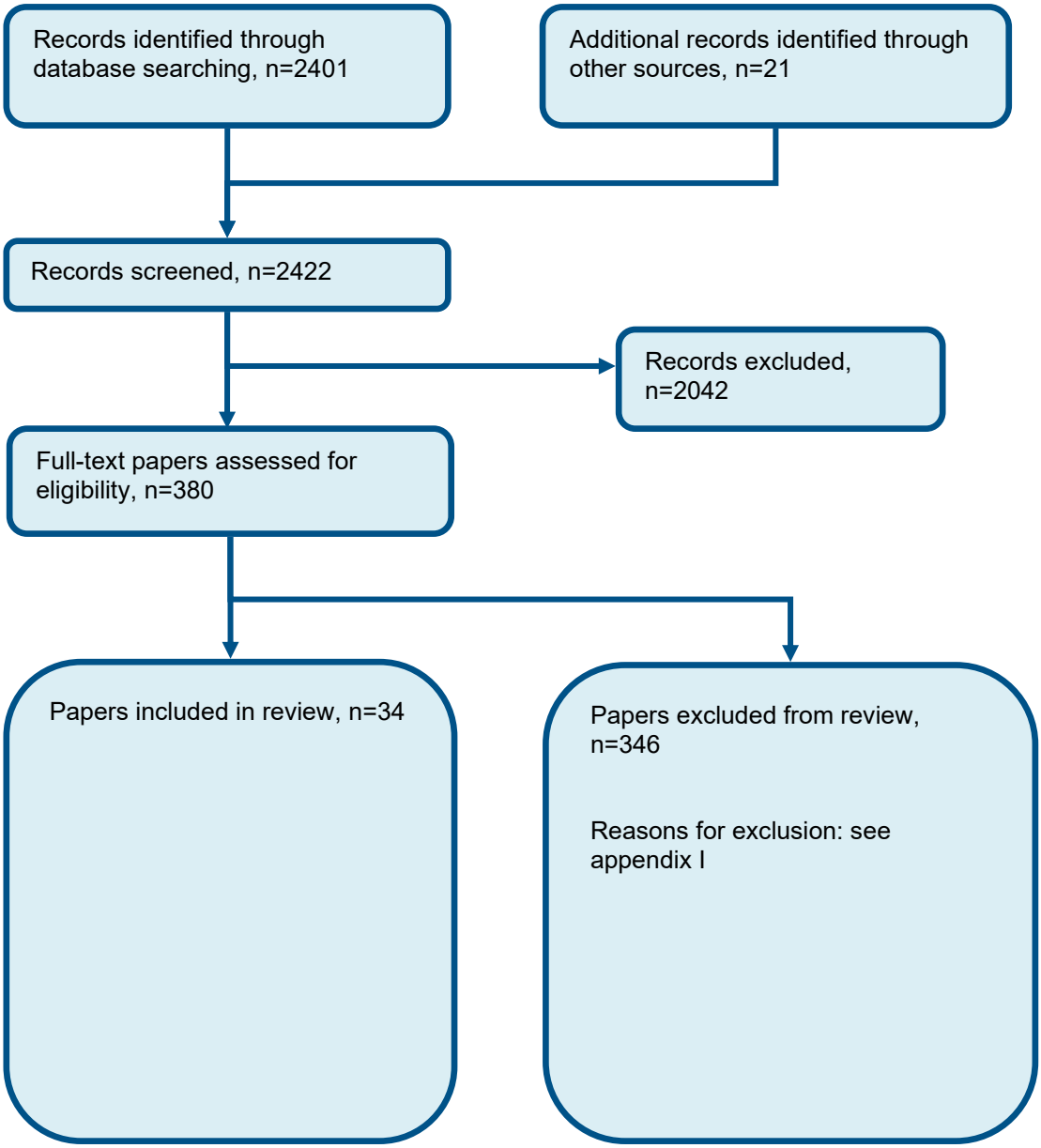
67.	monte carlo method/
68.	(markov* or monte carlo).ti,ab.
69.	econom* model*.ti,ab.
70.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
71.	or/61-70
72.	44 and (58 or 71)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Chronic Pain EXPLODE ALL TREES
#2.	(((persist* or intract* or chronic or longstanding or long standing or longterm or long term or refractory or prolong* or long last* or sustain* or linger* or syndrome*) adj3 pain*))
#3.	(((chronic or persist* or idiopathic or atypical or a-typical) adj4 pain))
#4.	MeSH DESCRIPTOR Complex Regional Pain Syndromes EXPLODE ALL TREES
#5.	((complex regional pain syndrome* or CRPS or causalgia))
#6.	MeSH DESCRIPTOR Fibromyalgia EXPLODE ALL TREES
#7.	(((reflex or sympathetic) adj2 dystroph*))
#8.	MeSH DESCRIPTOR Vulvodynia EXPLODE ALL TREES
#9.	((vulvodynia or vestibulodynia or dyspareunia or vulvar vestibulitis or vulvitis))
#10.	MeSH DESCRIPTOR Cystitis, Interstitial EXPLODE ALL TREES
#11.	((interstitial adj2 cystitis))
#12.	MeSH DESCRIPTOR Reflex Sympathetic Dystrophy EXPLODE ALL TREES
#13.	((algodystroph* or sudek or sudeck*))
#14.	MeSH DESCRIPTOR Myofascial Pain Syndromes EXPLODE ALL TREES
#15.	((loin pain adj (haematuria or hematuria) adj syndrome*))
#16.	((LPHS or prostatodynia or CPPS or atypic* odontalgia or a-typic* odontalgia or burning mouth syndrome* or phantom tooth pain or neuropathic orofacial pain or "myofascial pain" or MPS))
#17.	(((pelvic or pelvis) adj pain syndrome*))
#18.	(((non-cardiac or noncardiac) adj3 chest adj3 pain))
#19.	((temporomandibular adj3 joint adj3 pain))
#20.	(((prostate or vulv* or bladder or perineal) adj3 pain))
#21.	((functional pain syndrome* or non-cancer pain or noncancer pain))
#22.	(((pelvic or pelvis or abdominal) adj3 pain adj3 (unknown or un-known or idiopathic or atypic* or a-typic*)))
#23.	((fibromyalgia* or fibrositis or myofascial pain syndrome))
#24.	(#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 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23)

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of electrical physical modalities



Appendix D: Clinical evidence tables

Study	Altan 2005[19]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=53)
Countries and setting	Conducted in Turkey; Setting: Not stated
Line of therapy	Unclear
Duration of study	Intervention + follow up: 2 weeks + 3 months
Method of assessment of guideline condition	Unclear method of assessment/diagnosis: Only state inclusion criteria, not assessment method
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	1. Localised pain and taut bands in the neck for a minimum of the previous 3 months; 2. Bilateral and significantly more tenderness in the three cervical trigger points (midpoint and the upper border of the trapezius muscle, origin of the supraspinatus muscle, and insertion of the sub occipital muscle) compared to the control point (a non0tender point over deltoid muscle). These three trigger points are among the 18 described for FMS according to 1990 American College of Rheumatology criteria; 3. Existence of no other criterion for FMS diagnosis; 4. No history or finding of cervical arthrosis, discal hernia, cervical vertebral fracture, radiculopathy, or myelopathy; 5. No pathological finding in blood count, urinalysis, sedimentation or cervical X-ray.
Exclusion criteria	Only inclusion criteria stated.
Recruitment/selection of patients	Not stated
Age, gender and ethnicity	Age - Mean (SD): Laser group 43.48 (2.42) ; Placebo group 43.32 (2.1). Gender (M:F): 16/32. Ethnicity: Not stated
Further population details	Chronic primary musculoskeletal pain

Extra comments	Duration of symptoms in years, mean (SD): Laser group 4.74 (1.3) Placebo group 4.38 (1.21).
Indirectness of population	No indirectness
Interventions	(n=26) Intervention 1: Electrical Physical Modalities - Laser therapy. GaAs laser treatment was applied over the three trigger points bilaterally and also one point in the taut bands in trapezius muscle bilaterally with a frequency of 1000 Hz for 2 min over each point once a day for 10 weekdays during a period of 2 weeks. The head of the instrument was held perpendicularly to and in slight contact with the skin. The infrared-27 GaAs diode laser instrument (Roland Serie Elettronica Pagani) with a wavelength of 904 nm, frequency range of 5-7000 Hz, and maximum power of 27 W, 50 W, or 27x4 W was used. Duration 2 weeks (10 sessions). Concurrent medication/care: All patients were instructed not to take nonsteroidal anti-inflammatory drugs (NSAID) or any other analgesic during the treatment and control periods. All patients in both groups were instructed to perform daily isometric exercises and stretching just short of pain 2 weeks at home. Indirectness: No indirectness. (n=27) Intervention 2: Placebo/Sham. A placebo laser treatment was given by using the same instrument in the same way over the same points as in the intervention group but not turning it on. Duration 2 weeks (10 sessions). Concurrent medication/care: All patients were instructed not to take nonsteroidal anti-inflammatory drugs (NSAID) or any other analgesic during the treatment and control periods. All patients in both groups were instructed to perform daily isometric exercises and stretching just short of pain 2 weeks at home. Indirectness: No indirectness
Funding	Funding not stated

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

Protocol outcome 1: Pain reduction
- Actual outcome: Pain intensity (VAS) at 2 weeks (end of treatment); Group 1: mean 4.13 (SD 0.58); n=23, Group 2: mean 3.92 (SD 0.42); n=25; Visual analogue scale (VAS) 0-10 Top=High is poor outcome; Comments: Baselines, mean (SD):
Laser group 6.85 (0.35)
Placebo group 6.24 (0.32)
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: VAS baselines, mean (SD):
Laser group 6.85 (0.35)
Placebo group 6.24 (0.32); Group 1 Number missing: 3, Reason: Not available for treatment stage.; Group 2 Number missing: 2, Reason: Not available for

treatment stage. - Actual outcome: Pain intensity (VAS) at 14 weeks; Group 1: mean 3.17 (SD 0.58); n=23, Group 2: mean 3.8 (SD 0.51); n=25; Visual analogue scale (VAS) 0-10 Top=High is poor outcome; Comments: Baselines, mean (SD): Laser group 6.85 (0.35) Placebo group 6.24 (0.32) Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: VAS baselines, mean (SD): Laser group 6.85 (0.35) Placebo group 6.24 (0.32); Group 1 Number missing: 3, Reason: Not available for treatment stage.; Group 2 Number missing: 2, Reason: Not available for treatment stage.	
Protocol outcomes not reported by the study	Quality of life ; Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Arbabi-kalati 2015[28]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=20)
Countries and setting	Conducted in Iran; Setting: Zahedan University of Medical Sciences
Line of therapy	Unclear
Duration of study	Intervention time: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Burning mouth patients referred from Zahedan Faculty of Dentistry
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnosis criteria: 1) burning sensation in all or a part of the oral cavity with or without symptoms such as a change in taste sensation for at least 4 months; 2) normal oral mucosa without any lesion; 3) absence of any local or systemic factors which produce the same symptoms.
Exclusion criteria	Any known systemic condition; patients under 18; pregnancy; smoking; patients with oral legions; patients not signing the informed consent form.
Recruitment/selection of patients	Referred from Zahedan Faculty of Dentistry
Age, gender and ethnicity	Age - Mean (SD): Laser group 47.2(+-5.3) ; Placebo group 46.6(+-4.6). Gender (M:F): 0/20. Ethnicity: Not reported
Further population details	1. Chronic orofacial pain
Extra comments	Duration of disease in months, mean+-SD: Laser group 13.4+-7.4(6-30) ; 15.5+-0.1(6-36)
Indirectness of population	No indirectness
Interventions	(n=10) Intervention 1: Electrical Physical Modalities - Laser therapy. Low Level Laser Therapy (LLLT), wavelength 630 nm, power of 30 mW for 10 seconds, using an Iodine-Gallium-Aresnide laser of Mustange laser device (Russia). Laser dose 1 j/cm2. Applied to 10 areas on the oral mucosa, 2 areas on the tongue, 2 areas on the floor of the mouth, 1 area on the soft palate and 1 area on the soft palate. Duration Twice a week for 2 weeks.

	Concurrent medication/care: None stated. Indirectness: No indirectness. (n=10) Intervention 2: Placebo/Sham. Silent/off laser therapy carried out for the same period and at the same points as the laser treatment group. Participants wore protective glasses, blinding them to the type of treatment modality used. Duration Twice a week for 2 weeks. Concurrent medication/care: None stated. Indirectness: No indirectness
Funding	Academic or government funding (Zahedan University of Medical Sciences)

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

Protocol outcome 1: Quality of life
- Actual outcome: Quality of life questionnaire at After treatment (2 weeks); Group 1: mean 12.8 (SD 11.4); n=10, Group 2: mean 28.6 (SD 11.5); n=10; Quality of life questionnaire (Persian version of Oral Health Impact Profile) 0-40 Top=High is poor outcome; Comments: Baseline, mean (SD):
Laser group 27.8 (12)
Placebo group 28.3 (11.9)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness; Baseline details: Outcome baselines comparable; Group 1 Number missing; Group 2 Number missing

Protocol outcome 2: Pain reduction
- Actual outcome: Pain on numeric rating scale at After treatment (2 weeks); Group 1: mean 3.6 (SD 3); n=10, Group 2: mean 8 (SD 1.5); n=10; Numeric rating scale (for severity of burning sensation) 0-10 Top=High is poor outcome; Comments: Baselines, mean (SD):
Laser group 8 (2.3)
Placebo group 8.2 (1.7)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Baseline details: Outcome baselines comparable.; Group 1 Number missing; Group 2 Number missing

Protocol outcomes not reported by the study	Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Armagan 2006[31]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=32)
Countries and setting	Conducted in Turkey; Setting: Physical Therapy and Rehabilitation department of Osmangazi University hospital
Line of therapy	Unclear
Duration of study	Intervention + follow up: 10 day intervention and 6 month follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for fibromyalgia
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Widespread pain for at least 3 months located on both sides of the body and above and below the waist, the presence of at least 11 of 18 tender points on digital palpation
Exclusion criteria	Inflammatory causes of pain, inability to interrupt therapy with medications, presence of other conditions that could influence pain or response to treatment or ability to take part in treatment, pregnancy, major psychiatric disorders.
Recruitment/selection of patients	Not specified
Age, gender and ethnicity	Age - Mean (SD): 38.25 (5.36) years. Gender (M:F): All women. Ethnicity: Not specified
Further population details	Chronic widespread pain
Extra comments	Mean duration of pain 5.8 (3.2) years
Indirectness of population	No indirectness
Interventions	(n=16) Intervention 1: Electrical Physical Modalities - Laser therapy. Gal-Al-As diode laser device used with a power output of 50mW and a wavelength of 830nm. Diameter of laser beam 1mm, and laser was set to deliver a continuous form of energy, for 1 minute periods at each tender point (2 joules per tender joint). Once a day, 5 days a week for a total duration of 10 days and all participants treated by the same physician. Duration 10 days. Concurrent medication/care: Not specified. Indirectness: No indirectness

	(n=16) Intervention 2: Placebo/Sham. Placebo laser therapy. The same treatment protocol and the laser device appeared to patients to be working, but no laser beam was transferred to the treated area, and all painful points were irradiated. Duration 10 days. Concurrent medication/care: Not specified. Indirectness: No indirectness.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus PLACEBO/SHAM Protocol outcome 1: Quality of life - Actual outcome: FIQ at 10 days; Group 1: mean 58.5 (SD 10.33); n=16, Group 2: mean 63.63 (SD 9.59); n=16; FIQ 0-100 Top=High is poor outcome; Comments: Baseline: 65.5(9.01);65.38(9.44) Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing; Group 2 Number missing - Actual outcome: FIQ at 6 months; Group 1: mean 62.06 (SD 8.99); n=16, Group 2: mean 66.94 (SD 8.44); n=16; FIQ 0-100 Top=High is poor outcome; Comments: Baseline: 65.5(9.01);65.38(9.44) Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Pain reduction ; Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Bardellini 2019[37]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=90)
Countries and setting	Conducted in Italy; Setting: Department of oral medicine
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 10 weeks + 1 month
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: complaint of oral pain or burning for more than 6 months
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	Patients who had complained of oral pain or burning for more than 6 months
Exclusion criteria	age under 18 years, pregnancy, oral mucosal lesions, systemic disease (hypertension, diabetes, anaemia, vitamin B12 or folic acid deficiency.), gastro-esophageal reflux, Sjogren's syndrome, allergies, and hyposalivation; positivity to Candidida or other microorganisms
Recruitment/selection of patients	consecutive meeting the inclusion criteria
Age, gender and ethnicity	Age - Mean (SD): laser group: 59.76 (9.51) years, sham group: 60.86 (10.02) years . Gender (M:F): all female. Ethnicity: not reported

Further population details	1. Chronic orofacial pain: Chronic orofacial pain 2. Chronic primary musculoskeletal pain: Pain other than chronic primary musculoskeletal pain 3. Chronic visceral pain: Pain other than chronic visceral pain 4. Chronic widespread pain: Pain other than chronic widespread pain 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: Pain other than complex regional pain syndrome 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. Sensory impairment : Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=45) Intervention 1: Electrical Physical Modalities - Laser therapy. The laser instrument used for this trial was K Laser Cube 3®. The laser was applied by a trained dentist and irradiated the most painful areas in the oral cavity, with discontinuous combined wavelengths between 660-970 nm, medium power 3.2 W (6.4 W pulsed at 50%), treatment time 3'51", frequency 1-20000Hz, spot size 1cm². Treatment was once a week for 10 weeks. Duration 10 weeks . Concurrent medication/care: Not reported . Indirectness: No indirectness; Indirectness comment: NA Comments: NA (n=45) Intervention 2: Placebo/Sham. The device was turned on but the hand piece did not work. Laser/sham therapy was dispensed once a week for ten weeks. Duration 10 weeks . Concurrent medication/care: Not reported . Indirectness: No indirectness; Indirectness comment: NA Comments: NA
Funding	Funding not stated

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

Protocol outcome 1: Quality of life
- Actual outcome: Oral Health Impact Profile questionnaire (OHIP-14)
at 10 weeks ; Group 1: mean 7.09 (SD 2.59); n=43, Group 2: mean 10.64 (SD 4.13); n=42; OHIP-14 (Italian version) 0-56 Top=High is poor outcome; Comments: Baseline values: laser group 16.09 (4.2), sham group 15.26 (3.75)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement -

Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: did not complete therapy; Group 2 Number missing: 3, Reason: did not complete therapy - Actual outcome: Oral Health Impact Profile questionnaire (OHIP-14) at 14 weeks (10 weeks + 1 month follow up); Group 1: mean 7.43 (SD 3.78); n=43, Group 2: mean 10.43 (SD 2.99); n=42; OHIP-14 (Italian version) 0-56 Top=High is poor outcome; Comments: Baseline values: laser group 16.09 (4.2), sham group 15.26 (3.75) Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: did not complete therapy; Group 2 Number missing: 3, Reason: did not complete therapy	
Protocol outcomes not reported by the study	Pain reduction; Physical function; Psychological distress; Pain interference; Pain self-efficacy; Use of healthcare services; Sleep; Discontinuation

Study	Boyer 2014[53]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=38)
Countries and setting	Conducted in France; Setting: La Timone University Hospital pain centre
Line of therapy	Unclear
Duration of study	Intervention time: 10 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR FMS criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged >18 years, right handed, diagnosis of FMS according to ACR, score of at least 4 on the BPI average pain intensity scale, pain for more than 6 months, stable treatment for more than 1 month before enrolment, rTMS naive
Exclusion criteria	Other causes of pain such as inflammatory or autoimmune disorders, current primary psychiatric conditions, substance abuse, contraindications for rTMS. Concomitant treatment for pain and sleep were allowed, provided the dose administered had been stable for at least 1 month before enrolment and remained stable throughout the study
Recruitment/selection of patients	Not specified
Age, gender and ethnicity	Age - Mean (SD): 48.5(10.5) years. Gender (M:F): 1:37. Ethnicity: Not reported
Further population details	Chronic widespread pain
Extra comments	Duration of pain 3.7(4.2) years
Indirectness of population	No indirectness
Interventions	(n=19) Intervention 1: Electrical Physical Modalities - Transcranial Magnetic Stimulation (TMS). 14 sessions over 10 weeks (10 sessions over 2 weeks followed by maintenance phase of 4 sessions across 4 weeks). Duration 10 weeks. Concurrent medication/care: Not specified (n=19) Intervention 2: Placebo/Sham. Identical treatment but with a sham coil, that emitted a similar sound to

	the active coil. Duration 10 weeks. Concurrent medication/care: Not reported. Indirectness: No indirectness
Funding	Academic or government funding (Funding from Inserm and AP-HM)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCRANIAL MAGNETIC STIMULATION (TMS) versus PLACEBO/SHAM

Protocol outcome 1: Quality of life
- Actual outcome: SF-36 physical component summary score at 10 weeks; Group 1: mean 1.4 (SD 9); n=16, Group 2: mean 0.4 (SD 4.8); n=13; SF-36 0-100 Top=High is good outcome; Comments: Baseline: 29.9(7.5); 32.4(5.9)
Risk of bias: All domain - Very high, Selection - Low, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: NR; Group 2 Number missing: 6, Reason: NR
- Actual outcome: SF-36 mental component summary score at 10 weeks; Group 1: mean 5 (SD 6.9); n=16, Group 2: mean -1.6 (SD 7.6); n=13; SF-36 0-100 Top=High is good outcome; Comments: Baseline:39.6(11.4);34(9.3)
Risk of bias: All domain - Very high, Selection - Low, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: NR; Group 2 Number missing: 6, Reason: NR

Protocol outcome 2: Psychological distress
- Actual outcome: BDI at 10 weeks; Group 1: mean -1.9 (SD 2.8); n=16, Group 2: mean -0.1 (SD 4.4); n=16; BDI Not reported Top=High is poor outcome
Risk of bias: All domain - Very high, Selection - Low, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: NR; Group 2 Number missing: 6, Reason: NR
- Actual outcome: HADS anxiety at 10 weeks; Group 1: mean 0.4 (SD 1.7); n=16, Group 2: mean 0.5 (SD 2.3); n=13; HADS:A Not reported Top=High is poor outcome
Risk of bias: All domain - Very high, Selection - Low, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: NR; Group 2 Number missing: 6, Reason: NR

Protocol outcomes not reported by the study	Pain reduction ; Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	**Brietzke 2019** [54]
Study type	RCT (Patient randomised; Parallel)

Number of studies (number of participants)	(n=20)
Countries and setting	Conducted in Brazil; Setting: Not specified
Line of therapy	Unclear
Duration of study	Intervention time: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis of fibromyalgia (ACR 2011 criteria)
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnosis of fibromyalgia according to diagnostic criteria, daily disability present for the routine activities during the 3 months preceding enrolment, a score of at least 50mm on VAS 0-100mm.
Exclusion criteria	Contra-indications of the NIBS stimulation, positive history of other conditions such as rheumatoid arthritis, lupus autoimmune disease, neurological or oncological disease or cardiovascular disease.
Recruitment/selection of patients	2017-2018
Age, gender and ethnicity	Age - Mean (range):48.6 (18-59; 49.7(45-54) years. Gender (M:F): All female. Ethnicity: Not reported
Further population details	Chronic widespread pain
Extra comments	Mean duration of symptoms 5.75(1.48); 6.62(1.64)
Indirectness of population	No indirectness
Interventions	(n=10) Intervention 1: Electrical Physical Modalities – TDCS The anodal electrode was used over the left DLPFC and the cathode at the right DLPFC. Current applied at 2mA for 30 minutes for 5 consecutive days for 12 weeks. Current was delivered using 35cm2 electrodes coated with a vegetable sponge, which was moistened with saline solution before the start of the stimulation by 2 silicone cannulas coupled to the electrode. Neoprene caps were produced in small, medium and large sizes and cap size selected appropriately for each patients head. The electrode position was then accurate for the subjects to facilitate the identification and avoid incorrect placement of the electrodes, the anode was painted red and cathode black (although equipment already set up – participant could not change any part of it). Duration 3 months. Concurrent medication/care: Not specified (n=10) Intervention 2: Placebo/Sham. Identical treatment but the electrical stimulation was not applied in the

	sham group. Duration 3 months. Concurrent medication/care: Not specified
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TDCS versus PLACEBO/SHAM Protocol outcome 1: Psychological distress - Actual outcome: BDI at 3 months; Group 1: mean 11.8 (SD 5.63); n=10, Group 2: mean 21.5 (SD 6.6); n=10; BDI 0-61 Top=High is poor outcome; Comments: Baseline: 27.1(12.1); 20.5(5.63) Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 1: Sleep - Actual outcome: Pittsburgh sleep quality index at 3 months; Group 1: mean 7.9 (SD 7.44); n=10, Group 2: mean 16.7 (SD 3.74); n=10; PSQI, range not reported, Top=High is poor outcome; Comments: Baseline: 27.5(7.63); 24.6(7.57) Risk of bias: All domain – High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life; Pain reduction; Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Discontinuation

Study	Carretero 2009[61]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=26)
Countries and setting	Conducted in Spain; Setting: Trial part of wider project investigating the usefulness of LF-RTMS in major depression being carried out by Hospital Son Llatzer, Hospital Son Dureta, and the University of the Balearic Islands, Majorca.
Line of therapy	Unclear
Duration of study	Intervention + follow up: 4 weeks + 8 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Fibromyalgia diagnosed by a rheumatologist according to the criteria of the American College of Rheumatology
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Over 18 and fulfilling the diagnostic criteria for major depression (Diagnostic and Statistical Manual of Mental Disorders-IV Text Revision) and fibromyalgia (criteria of the American College of Rheumatology).
Exclusion criteria	Not stated
Age, gender and ethnicity	Age - Mean (SD): Real TMS group 47.5 (5.7) ; Sham TMS group 54.9 (4.9). Gender (M:F): 2/24. Ethnicity: Not stated
Further population details	Chronic widespread pain
Extra comments	Duration of illness in participants not stated, but assumed from fibromyalgia diagnosis (≥ 3 months).
Indirectness of population	No indirectness
Interventions	(n=14) Intervention 1: Electrical Physical Modalities - Transcranial Magnetic Stimulation (TMS). High-frequency repetitive transcranial magnetic stimulation (HF-rTMS) using DANTEC TMS equipment (Dantec Medical, Medtronic Inc., Minneapolis, MN), MagLite model. A butterfly coil with each wing of 8.5 cm in diameter was used. Stimulation parameters were 20 trains at 110% of motor threshold for 60 seconds at 1 Hz and a 45-second interval between trains. A total of 1,200 pulses was administered at each of the 20 sessions, which each took approximately 30 minutes. The stimulation area was the right dorsolateral prefrontal area, 5 cm in front of the specular point that triggered a more selective right-thumb abduction response in the left motor cortex. Duration 4 weeks (20 sessions). Concurrent medication/care: Pharmacologic therapy remained

	unchanged during the month before the study and during the study. (n=12) Intervention 2: Placebo/Sham. In the sham sessions, the coil was placed perpendicularly to the cranium at the calculated stimulation point, before being inclined 45° forward on the axis. Thus, the magnetic field did not significantly penetrate the brain, although the patient did hear the sound produced by the apparatus. It was explained to patients that two randomly selected methods for applying magnetic fields were being used, and that the researchers wanted to know which one was more useful for people in their situation. Duration 4 weeks (10 sessions). Concurrent medication/care: Pharmacologic therapy remained unchanged during the month before the study and during the study.
Funding	Academic or government funding (IUNICS Institute, Universitat Illes Balears - grant SEJ2007-62312 (MICINN-FEDER Funds))
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCRANIAL MAGNETIC STIMULATION (TMS) versus PLACEBO/SHAM Protocol outcome 1: Pain reduction - Actual outcome: Pain reduction (Likert pain scale) at 3 months; Group 1: mean 8.1 (SD 1); n=14, Group 2: mean 7.5 (SD 2.1); n=12; Likert pain scale 0-10 Top=High is poor outcome; Comments: Baselines, mean (SD): Real TMS group 8.7 (1.2) Sham TMS group 8.6 (1.9) Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness; Baseline details: Small variation in continued background psychopharmacological therapy between patients; Group 1 Number missing: 1, Reason: Did not complete the treatment cycle. Group 2 Number missing: 1, Reason: Did not complete the treatment cycle.	
Protocol outcomes not reported by the study	Quality of life ; Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Chow 2004[77]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=20)
Countries and setting	Conducted in Australia; Setting: Not specified
Line of therapy	Unclear
Duration of study	Intervention + follow up: 7 week intervention and 3 months follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis of chronic neck pain
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Over 18 years old, chronic neck pain, not experienced previous treatment with laser therapy other than laser acupuncture.
Exclusion criteria	Work related or third party injuries in which litigation or compensation was still current, abnormal neurological signs, inability to discontinue activity that exacerbated pain, conditions that could limit effectiveness of laser therapy or cause pain.
Recruitment/selection of patients	Adverts in the practice of the principle author
Age, gender and ethnicity	Age - Mean (SD): 57.7(10.9) years. Gender (M:F): 4:16. Ethnicity: Not specified
Further population details	Chronic primary musculoskeletal pain
Extra comments	Mean duration of pain 13.3 years (SE 2.48)
Indirectness of population	No indirectness
Interventions	(n=10) Intervention 1: Electrical Physical Modalities - Laser therapy. 830nm laser therapy for 7 weeks. Diolase device, 15mm length laser and 3mm width at widest, 300mW power. Laser applied for 30s per point or until the area became less tender. 30 minute sessions. Duration 7 weeks. Concurrent medication/care: Not reported. Indirectness: No indirectness (n=10) Intervention 2: Placebo/Sham. Identical treatment but laser did not emit a beam. Duration 7 weeks.

	Concurrent medication/care: Not specified. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus PLACEBO/SHAM Protocol outcome 1: Quality of life - Actual outcome: SF-36 physical component summary score at 3 months (including 7 week intervention); Group 1: mean 4 (SD 8.22); n=10, Group 2: mean 1.22 (SD 6.32); n=10; SF-36 0-100 Top=High is good outcome; Comments: Baseline mean (SEs): 39(3.6); 41.6(3) SDs calculated from SDs reported in the study Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: NA, Reason: NR; Group 2 Number missing: NA, Reason: NR - Actual outcome: SF-36 mental component summary score at 3 months (including 7 week intervention); Group 1: mean 1.71 (SD 3.79); n=10, Group 2: mean 0 (SD 6.01); n=10; SF-36 0-100 Top=High is good outcome; Comments: Baseline mean (SEs): 50.9(3.4);50.1(2.5) SDs calculated from SDs reported in the study Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: NA, Reason: NR; Group 2 Number missing: NA, Reason: NR Protocol outcome 2: Pain reduction - Actual outcome: VAS at 3 months (including 7 week intervention); Group 1: mean 2.1 (SD 2.84); n=10, Group 2: mean 0.7 (SD 1.58); n=10; VAS 0-10 Top=High is poor outcome; Comments: Baseline mean (SEs): 3.9(0.6); 3.2(0.5) SDs calculated from SDs reported in the study Note: change scores in study transformed to scale whereby high score is good outcome. Converted back to high score = poor outcome in the analysis Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: NA, Reason: NR; Group 2 Number missing: NA, Reason: NR	
Protocol outcomes not reported by the study	Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Chow 2006[78]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=90)
Countries and setting	Conducted in Australia; Setting: Large suburban medical centre of 17 GPs in Sydney, Australia
Line of therapy	Unclear
Duration of study	Intervention + follow up: 7 week intervention and 12 week follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Chronic neck pain with unknown cause
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	18 years and over, pain for at least 3 months
Exclusion criteria	Injury with current compensation or litigation, abnormal neurological signs in the upper limbs due to nerve abnormalities, unable to discontinue activities that exacerbate pain, pregnancy, previous surgery on the cervical spine, RA, neck pain part of a widespread pain syndrome involving other areas, known photosensitivity or illnesses unrelated to neck pain which precluded involvement in study.
Recruitment/selection of patients	2002-2003, Posters in waiting room of medical centre and local newspaper adverts.
Age, gender and ethnicity	Age - Mean (SD): 56(12.8) years. Gender (M:F): 31:59. Ethnicity: Not specified
Further population details	Chronic primary musculoskeletal pain
Extra comments	Duration of pain 15(12.6) years
Indirectness of population	No indirectness
Interventions	(n=45) Intervention 1: Electrical Physical Modalities - Laser therapy. Diolase laser devices. 7 week intervention 1 session per week. Subjects treated with laser 15mm in length and 3mm at widest with a wavelength of 830nm and power of 300mW. Subjects seated comfortably and tender points in the next were identified, and each treated for 30 seconds per point with up to 50 points being treated within the maximum half-hour allocated for treatment. Number of points dependent on severity of symptoms. Duration 7 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness

	(n=45) Intervention 2: Placebo/Sham. Sham laser therapy. Digital display of machine on and sound emitted identical to active intervention, but device did not emit laser. Duration 7 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus PLACEBO/SHAM Protocol outcome 1: Quality of life - Actual outcome: SF-36 physical component summary score at 3 months (follow up); Group 1: mean 3.2 (SD 10.78); n=45, Group 2: mean 1.3 (SD 4.28); n=45; SF-36 summary score 0-100 Top=High is good outcome; Comments: Baseline not reported Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness; Group 1 Number missing: 2, Reason: Family illness; Group 2 Number missing: 3, Reason: Family illness, asthma requiring steroid treatment, unanticipated work changes - Actual outcome: SF-36 mental component summary score at 3 months (follow up); Group 1: mean 2.4 (SD 8.99); n=45, Group 2: mean 5.4 (SD 10.98); n=45; SF-36 summary score 0-100 Top=High is good outcome; Comments: Baseline not reported Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness; Group 1 Number missing: 2, Reason: Family illness; Group 2 Number missing: 3, Reason: Family illness, asthma requiring steroid treatment, unanticipated work changes Protocol outcome 2: Pain reduction - Actual outcome: VAS at 3 months (follow up); Group 1: mean -2.7 (SD 1.99); n=45, Group 2: mean 0.3 (SD 2.33); n=45, Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 2, Reason: Family illness; Group 2 Number missing: 3, Reason: Family illness, asthma requiring steroid treatment, unanticipated work changes Protocol outcome 3: Discontinuation - Actual outcome: Discontinuation of study at 3 months (follow up); Group 1: 2/45, Group 2: 3/45 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness; Group 1 Number missing: 2, Reason: Family illness; Group 2 Number missing: 3, Reason: Family illness, asthma requiring steroid treatment, unanticipated work changes	
Protocol outcomes not reported by the study	Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Da cunha 2008[92]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in Brazil; Setting: Center of Occlusion and Temporomandibular Disorder of the Dental School of Sao Paulo State University (UNESP), Sao Jose dos Campos.
Line of therapy	Unclear
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Temporomandibular disorder diagnosed based on complete clinical examination, including patient's history, at the Center of Occlusion and Temporomandibular Disorder of the Dental School of Sao Paulo State University (UNESP).
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Sample selection was done based on complete clinical examination, including patients' history, masticatory and cervical muscle palpation, joint palpation and joint noises.
Exclusion criteria	Patients presenting asymptomatic joint clicking, major psychological problems, heart disease, psoriasis, rheumatoid arthritis, pregnancy and patients with pacemakers were not included in this study. Patients presenting myofascial trigger points and fibromyalgia were also excluded because of the particular characteristics of these entities.
Recruitment/selection of patients	One hundred and twenty patients were selected for assessment on a voluntary basis from a waiting list of those who presented for diagnosis and treatment of temporomandibular disorder.
Age, gender and ethnicity	Age - Mean: Laser group 40.15 years; Placebo group 46.6. Gender (M:F): 1/39. Ethnicity: Not stated
Further population details	1. Chronic orofacial pain
Extra comments	Before participating in this study, the selected patients had been waiting for treatment for at least six months, without any form of professional care.
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Electrical Physical Modalities - Laser therapy. The experimental group received laser treatment performed with a Ga-Al-As (Gallium-Aluminium-Arsenide) low level laser (Biolux laser - Bio-Art, Sao

	Carlos, SP, Brazil) from a probe applied perpendicularly and directly over the painful area. Duration 4 weeks. Concurrent medication/care: Patients had not received treatment or any professional care for 6 months prior to trial. Indirectness: No indirectness (n=20) Intervention 2: Placebo/Sham. The control group received a placebo treatment performed exactly in the same manner, but without energy output. Duration 4 weeks. Concurrent medication/care: Patients had not received treatment or any professional care for 6 months prior to trial. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus PLACEBO/SHAM Protocol outcome 1: Pain reduction - Actual outcome: Level of pain (VAS) at 4 weeks (end of treatment); Group 1: mean 3.62 Visual analogue scale (VAS) (SD 2.45); n=20, Group 2: mean 4.67 Visual analogue scale (VAS) (SD 1.9); n=20; Visual analogue scale (VAS) 0-10 Top=High is poor outcome; Comments: Baselines, mean (SD): Laser group 6.87 (2.12) Placebo group 6.60 (2.57) Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Mean pain baseline on VAS comparable between treatment and placebo groups.	
Protocol outcomes not reported by the study	Quality of life ; Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study (subsidiary papers)	Dailey 2019[94] (Dailey 2020[95])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=301)
Countries and setting	Conducted in USA; Setting: dual-site: University and University Medical Center
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: met ACR criteria for FM
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	female sex, age 18–70 years, FM according to the American College of Rheumatology 1990 criteria, on a stable medication regimen during the 4 weeks preceding the study, and projected to be on a stable treatment regimen for the next 2 months
Exclusion criteria	pain level of <4 on a 10-point numerical rating scale (NRS) at the first and second visits, inability to walk 6 minutes without assistance, TENS use in the last 5 years, presence of a pacemaker, history of neuropathic or autoimmune disorder, history of spinal fusion or metal implants in the spine, allergy to adhesive or nickel, pregnancy, epilepsy, and/or a serious or unstable medical or psychiatric condition that would preclude participation
Recruitment/selection of patients	recruited from the Pain Clinic, Rheumatology Clinic, Family Practice Clinic, Orthopedic Clinic, local physician offices, support groups, local physical therapy clinics, and radio and TV interviews, also from UIHC EPIC database for individuals with a diagnosis of myalgia and ResearchMatch (www.researchmatch.org). Specific recruitment strategies included mass email, posting flyers, and discussion of the project with physicians and nurses.

Age, gender and ethnicity	Age - Mean (SD): active: 44.7 (14.3), placebo: 47.2 (12.6), no TENS: 48.6 (11.8). Gender (M:F): all female . Ethnicity: White: active 92%, placebo 92%, no TENS 92%; not Hispanic: active 95%, placebo 95%, no TENS 95%
Further population details	1. Chronic orofacial pain: Pain other than chronic orofacial pain 2. Chronic primary musculoskeletal pain: Pain other than chronic primary musculoskeletal pain 3. Chronic visceral pain: Pain other than chronic visceral pain 4. Chronic widespread pain: Chronic widespread pain 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: Pain other than complex regional pain syndrome 7. First language not English: Not stated / Unclear 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. Sensory impairment : Not stated / Unclear
Extra comments	Duration of fibromyalgia, median (range) years: active 7 (3–12), placebo 7 (2–14), no TENS 7 (4–15)
Indirectness of population	No indirectness: NA
Interventions	(n=103) Intervention 1: Electrical Physical Modalities - Transcutaneous Electrical Nerve Stimulation (TENS). EMPI-Select TENS (DJO Global, Vista, CA) delivered through butterfly electrodes placed at the cervicothoracic junction and lower back. Active-TENS parameters were asymmetrical, biphasic waveform with a modulating frequency (2-125 Hz), pulse duration 200u sec, and highest tolerable stimulation intensity. TENS was applied by the TENS-Allocator in the clinic for 30 min prior to the Outcome-Assessor measuring effects on pain, fatigue, and function. Following completion of Visit-2, active-TENS was sent home with participants with an instruction manual developed by study personnel. TENS-Allocators used a standardized script to instruct participants in home use and for weekly contact. Participants were instructed to use TENS at least 2h per day during activity. TENS units monitored number of sessions, number of minutes used, and average intensity per channel. Duration 4 weeks. Concurrent medication/care: All participants continued current treatments prescribed by their health care provider and were asked not to change medications during the study. . Indirectness: No indirectness; Indirectness comment: NA (n=99) Intervention 2: Placebo/Sham. EMPI-Select TENS (DJO Global, Vista, CA) delivered through butterfly electrodes placed at the cervicothoracic junction and lower back. TENS was applied by the TENS-Allocator in the clinic for 30 min prior to the Outcome-Assessor measuring effects on pain, fatigue, and function. The placebo-TENS unit delivered current for 45s ramping down to 0 in the last 15s and the appearance was identical to the active unit. Following completion of Visit-2 placebo-TENS was sent home with participants with an instruction manual developed by study personnel.

	TENS-Allocators used a standardized script to instruct participants in home use and for weekly contact. Participants were instructed to use TENS at least 2h per day during activity. Placebo-TENS units monitored number of sessions, number of minutes used, and average intensity per channel. Duration 4 weeks . Concurrent medication/care: All participants continued current treatments prescribed by their health care provider and were asked not to change medications during the study.. Indirectness: No indirectness; Indirectness comment: NA (n=99) Intervention 3: Usual care. No TENS - used a mock-TENS during visits to blind Outcome-Assessors with electrodes that were attached to a TENS unit that provided no current intensity Duration 4 weeks . Concurrent medication/care: All participants continued current treatments prescribed by their health care provider and were asked not to change medications during the study. Indirectness: No indirectness; Indirectness comment: NA
Funding	Academic or government funding (NIH. One author received consulting fees from pharmaceutical companies. Active and placebo TENS units and electrodes were provided by DJO, Inc.)

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

Protocol outcome 1: Quality of life
- Actual outcome: SF36 mental composite at 4 weeks ; MD; 1.1 (95%CI -1.9 to 4.1) (p value : >0.99) T score SF36 0-100 Top=High is good outcome, Comments: Mean difference in T scores, adjusted for study site differences at baseline. Baseline values: TENS 88.7 (10), placebo 40.2 (10.2);
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in marital status and FIQR, but model adjusted for baseline differences ; Group 1 Number missing: 18, Reason: unclear ; Group 2 Number missing: 18, Reason: unclear
- Actual outcome: SF36 physical composite at 4 weeks ; MD; 1.2 (95%CI -0.7 to 3.1) (p value : 0.36) T scores SF36 0-100 Top=High is good outcome, Comments: Mean difference in T scores, adjusted for study site differences at baseline. Baseline values: TENS 32.7 (6.4), placebo 33.3 (6.2)
;
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in marital status and FIQR, but model adjusted for baseline differences ; Group 1 Number missing: 18, Reason: unclear ; Group 2 Number missing: 18, Reason: unclear

Protocol outcome 2: Pain reduction
- Actual outcome: Brief pain inventory - intensity at 4 weeks ; MD; -0.5 (95%CI -1 to 0) (p value : 0.036) BPI intensity 0-10 Top=High is poor outcome, Comments: Adjusted for study site differences at baseline. Baseline values: not reported ;

Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in marital status and FIQR, but model adjusted for baseline differences. Outcome values at baseline not reported ; Group 1 Number missing: 18, Reason: unclear ; Group 2 Number missing: 18, Reason: unclear

Protocol outcome 3: Physical function
- Actual outcome: 6 minute walk test at 4 weeks ; MD; 19 (95%CI -58 to 96) (p value : >0.99) number of feet walked , Comments: adjusted for study site differences at baseline. Baseline values: TENS 1386 (323), placebo 1358 (305);
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in marital status and FIQR, but model adjusted for baseline differences ; Group 1 Number missing: 18, Reason: unclear ; Group 2 Number missing: 18, Reason: unclear

Protocol outcome 4: Psychological distress
- Actual outcome: PROMIS depression at 4 weeks ; MD; -2.7 (95%CI -4.7 to -0.8) (p value : 0.002) T scores PROMIS depression 8-40 Top=High is poor outcome, Comments: Mean difference in T scores, adjusted for study site differences at baseline. Baseline values: TENS 58.1 (8.1), placebo 55.7 (8.5)
;
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in marital status and FIQR, but model adjusted for baseline differences ; Group 1 Number missing: 18, Reason: unclear ; Group 2 Number missing: 18, Reason: unclear
- Actual outcome: PROMIS anxiety at 4 weeks ; MD; -0.5 (95%CI -2.7 to 1.7) (p value : >0.99) T scores PROMIS anxiety 7-35 Top=High is poor outcome, Comments: Mean difference in T scores, adjusted for study site differences at baseline. Baseline values: TENS 58.8 (8.7), placebo 58.1 (8)
;
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in marital status and FIQR, but model adjusted for baseline differences ; Group 1 Number missing: 18, Reason: unclear ; Group 2 Number missing: 18, Reason: unclear

Protocol outcome 5: Pain interference
- Actual outcome: Brief pain inventory - interference at 4 weeks ; MD; -0.7 (95%CI -1.3 to 0.01) (p value : 0.043) NA BPI interference 0-10 Top=High is poor outcome, Comments: adjusted for study site differences at baseline. Baseline values: not reported ;
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in marital status and FIQR, but model adjusted for baseline differences. Outcome values at baseline not reported ; Group 1 Number missing: 18, Reason: unclear ; Group 2 Number missing: 18, Reason: unclear

Protocol outcome 6: Pain self-efficacy
- Actual outcome: Pain self-efficacy questionnaire at 4 weeks ; MD; 1.6 (95%CI -1.8 to 5.1) (p value : 0.75) NA Pain self-efficacy questionnaire 0-

60 Top=High is good outcome, Comments: adjusted for study site differences at baseline. Baseline values: TENS 28.2 (13.3), placebo 29.9 (13.1)
;
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in marital status and FIQR, but model adjusted for baseline differences ; Group 1 Number missing: 18, Reason: unclear ; Group 2 Number missing: 18, Reason: unclear

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

Protocol outcome 1: Quality of life
- Actual outcome: SF36 mental composite at 4 weeks ; MD; 2.4 (95%CI -0.6 to 5.3) (p value : 0.17) T scores SF36 0-100 Top=High is good outcome, Comments: mean difference in T scores, adjusted for study site differences at baseline. Baseline values: TENS 38.7 (10), no TENS 39.5 (10.6)
;
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in marital status and FIQR, but model adjusted for baseline differences ; Group 1 Number missing: 18, Reason: unclear ; Group 2 Number missing: 8, Reason: unclear
- Actual outcome: SF36 physical composite at 4 weeks ; MD; 1 (95%CI -0.8 to 2.8) (p value : 0.58) T scores SF36 0-100 Top=High is good outcome, Comments: mean difference in T scores, adjusted for study site differences at baseline. Baseline values: TENS 32.7 (6.4), no TENS 32.7 (6.6)
;
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in marital status and FIQR, but model adjusted for baseline differences ; Group 1 Number missing: 18, Reason: unclear ; Group 2 Number missing: 8, Reason: unclear

Protocol outcome 2: Pain reduction
- Actual outcome: Brief pain inventory - intensity at 4 weeks ; MD; -0.9 (95%CI -1.4 to -0.4) (p value : <0.0001) BPI intensity 0-10 Top=High is poor outcome, Comments: adjusted for study site differences at baseline. Baseline values: not reported ;
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in marital status and FIQR, but model adjusted for baseline differences. Baseline outcome values not reported ; Group 1 Number missing: 18, Reason: unclear ; Group 2 Number missing: 8, Reason: unclear

Protocol outcome 3: Physical function
- Actual outcome: 6 minute walk test at 4 weeks ; MD; 42 (95%CI -34 to 117) (p value : >0.99) number of feet walked , Comments: adjusted for study site differences at baseline. Baseline values: TENS 1386 (323), no TENS 1316 (318)
;
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in marital status and FIQR, but model adjusted for baseline differences ; Group 1 Number missing: 18, Reason: unclear ; Group 2 Number missing: 8, Reason: unclear Protocol outcome 4: Psychological distress - Actual outcome: PROMIS depression at 4 weeks ; MD; -3.2 (95%CI -5.1 to -1.3) (p value : 0.0001) T scores PROMIS depression 8-40 Top=High is poor outcome, Comments: mean difference in T scores, adjusted for study site differences at baseline. Baseline values: TENS 58.1 (8.1), no TENS 56.6 (8.1) ; Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in marital status and FIQR, but model adjusted for baseline differences ; Group 1 Number missing: 18, Reason: unclear ; Group 2 Number missing: 8, Reason: unclear - Actual outcome: PROMIS anxiety at 4 weeks ; MD; -0.4 (95%CI -2.5 to 1.7) (p value : >0.99) T scores , Comments: mean difference in T scores, adjusted for study site differences at baseline. Baseline values: TENS 58.8 (8.7), no TENS 58.3 (7.8) ; Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in marital status and FIQR, but model adjusted for baseline differences ; Group 1 Number missing: 18, Reason: unclear ; Group 2 Number missing: 8, Reason: unclear Protocol outcome 5: Pain interference - Actual outcome: Brief pain inventory - interference at 4 weeks ; MD; -0.6 (95%CI -1.3 to 0) (p value : 0.048) BPI interference 0-10 Top=High is poor outcome, Comments: adjusted for study site differences at baseline. Baseline values: not reported ; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in marital status and FIQR, but model adjusted for baseline differences. Baseline outcome values not reported ; Group 1 Number missing: 18, Reason: unclear ; Group 2 Number missing: 8, Reason: unclear Protocol outcome 6: Pain self-efficacy - Actual outcome: Pain self-efficacy questionnaire at 4 weeks ; MD; 2.3 (95%CI -1 to 5.7) (p value : 0.28) Pain self-efficacy questionnaire 0-60 Top=High is good outcome, Comments: adjusted for study site differences at baseline. Baseline values: TENS 28.2 (13.3), no TENS 29 (13.2) ; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in marital status and FIQR, but model adjusted for baseline differences ; Group 1 Number missing: 18, Reason: unclear ; Group 2 Number missing: 8, Reason: unclear	
Protocol outcomes not reported by the study	Use of healthcare services; Sleep; Discontinuation

Study	Dall'agnol 2014[96]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=24)
Countries and setting	Conducted in Brazil
Line of therapy	Unclear
Duration of study	Intervention + follow up: 10 rTMS sessions + 3 months follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Myofascial pain syndrome was diagnosed by two independent examiners with more than 10 years of clinical experience related to chronic pain.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Right-handed females aged 19 to 65 years with a diagnosis of myofascial pain syndrome in an upper body segment for at least 3 months prior to enrolment. Participants were also required to be experiencing limitation in at least one of the following areas of life: work, personal relationships, pleasure of activities, responsibilities at home, personal goals, clear thinking. MPS as defined by regional pain, normal neurologic examination, decreased range of motion, stiffness in the muscles, presence of trigger points, taut bands, tender points, palpable nodules, and pain characterized by dull, hollow, or deep that was exacerbated during stress. Must have scored ≥ 4 on the Neuropathic Pain Diagnostic Questionnaire.
Exclusion criteria	Presence of any other pain disorder, such as rheumatoid arthritis, radiculopathy, and fibromyalgia;
Age, gender and ethnicity	Age: mean (SD): 45.43(12.86) years . Gender (M:F): 0:24. Ethnicity: Not stated
Further population details	Chronic primary musculoskeletal pain
Indirectness of population	No indirectness
Interventions	(n=12) Intervention 1: Electrical Physical Modalities - Transcranial Magnetic Stimulation (TMS). TMS performed with a MagPro X100 and a figure-8 coil. The hot spot was marked on the scalp with a soft-tip pen. The subjects were comfortably seated in a reclining chair with arm rests for relaxing arms and hand positioning. The coil was placed over the left motor cortex (M1), held tangentially to the scalp with the handle pointing back and away from the midline at 45 degrees. All participants underwent rTMS delivered in trains consisting of 16 series of 10-second pulses with a high frequency of 10 Hz of biphasic magnetic stimulator (MagPro X100) and an interval of 26 seconds between each train, giving a total of 1,600 pulses per session. The stimulation intensity used was 80% of resting motor threshold (RMT). Duration 10 sessions. Concurrent

	medication/care: All of the patients were permitted to use supplementary analgesic medication (acetaminophen, ibuprofen, codeine, or tramadol) to relieve their pain if necessary. Patients were allowed to take 750mgof acetaminophen up to 4 times per day and 200 mg of ibuprofen at maximum 4 times per day as a rescue analgesic. If these drugs were ineffective, patients could use Dorflex (Sanofi Aventis, Sao Paulo, Brazil; 35 mg orphenadrine citrate combined with 300 mg dipyrone and 50 mg caffeine). If their pain persisted, patients were permitted to use 60mgof codeine up to 4 times per day or tramadol 3 times per day. The patients were asked to record their analgesic intake during the treatment period in their pain diaries, and these diaries were reviewed during each intervention session. The total analgesic dose administered during treatment was considered for the analysis. Indirectness: No indirectness (n=12) Intervention 2: Placebo/Sham. During placebo (sham stimulation), an inactive rTMS coil (MagPro X100) was used as a sham coil and was placed in the identical area as the active coil. The patient recorded identical experiences (including sound effects and somatic sensations caused by contraction of the muscles of the scalp) as during active stimulation. Duration 10 sessions. Concurrent medication/care: All of the patients were permitted to use supplementary analgesic medication (acetaminophen, ibuprofen, codeine, or tramadol) to relieve their pain if necessary. Patients were allowed to take 750mgof acetaminophen up to 4 times per day and 200 mg of ibuprofen at maximum 4 times per day as a rescue analgesic. If these drugs were ineffective, patients could use Dorflex (Sanofi Aventis, Sao Paulo, Brazil; 35 mg orphenadrine citrate combined with 300 mg dipyrone and 50 mg caffeine). If their pain persisted, patients were permitted to use 60mgof codeine up to 4 times per day or tramadol 3 times per day. The patients were asked to record their analgesic intake during the treatment period in their pain diaries, and these diaries were reviewed during each intervention session. The total analgesic dose administered during treatment was considered for the analysis. Indirectness: No indirectness
Funding	Academic or government funding (Grants and material from the Brazilian Innovation Agency, Committee for the Development of Higher Education Personnel, National Council for Scientific and Technological Development, Postgraduate Program in Medical Sciences at the School of Medicine of the Federal University of Rio Grande do Sul, Postgraduate Research Group at the Hospital de Clinicas de Porto Alegre and the Foundation for Support of Research at Rio Grande do Sul.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCRANIAL MAGNETIC STIMULATION (TMS) versus PLACEBO/SHAM

Protocol outcome 1: Pain reduction
- Actual outcome: Pain intensity (visual analogue scale) at 3 months after treatment; Group 1: mean 3.57 Pain reported on VAS (SD 2.82); n=12, Group 2: mean 5.29 Pain reported on VAS (SD 2.78); n=12; VAS 0-10 Top=High is poor outcome; Comments: Baselines, mean (SD):
Placebo 6.83 (2.45)

rTMS 6.94 (1.7) Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1, Reason: Treatment inefficacy.; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Quality of life ; Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	**Del vecchio 2019[101]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=60)
Countries and setting	Conducted in Italy; Setting: Department of Dental Sciences and Maxillo-Facial Surgery of Sapienza, University of Rome
Line of therapy	Unclear
Duration of study	Intervention time: 1 week

Method of assessment of guideline condition	Adequate method of assessment/diagnosis: TMJD diagnosis. The disorder was diagnosed by clinical and radiological examinations and according to the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD)Axis I and Axis II
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	The inclusion criteria to been rolled in the study were: the presence of pain in the joint area and/or radiating to the face, jaw, or neck for at least six months; reduced mouth opening or jaw locks; painful clicking, popping or grating when opening or closing the mouth; occlusal changes; no muscle tenderness at palpation; and no drug consumption for at least three weeks before treatment.
Exclusion criteria	None specified
Recruitment/selection of patients	Not specified
Age, gender and ethnicity	Age - Mean (SD): 42.55 (14.842) years. Gender (M:F): 12:74. Ethnicity: Not specified
Further population details	Chronic orofacial pain
Extra comments	Duration of pain not specified (minimum duration 6 months)
Indirectness of population	No indirectness
Interventions	(n=30) Intervention 1: Electrical Physical Modalities - Laser therapy. Received LLLT through the B-cureDental Pro low-level laser device, provided by BiocareEnterprise Limited (Good Energies, Haifa, Israel). This medical device emits a low-level laser beam with a wavelength of 808 nm; each application was performed at 5 J/min, 250 mW and 15 KHz for 8 m, for a total of40J each, directly over the pain area. The treatment had to be performed twice a day for seven consecutive days. A laser therapy expert examiner performed the first application at the Department of Dental Sciences and Maxillo-Facial Surgery of Sapienza, University of Rome. This first application was used as an instruction to the patients so they could perform the successive applications by themselves at home. The same examiner explained clearly to each patient how to use and safely store the devices. After the instruction, each patient performed the remaining applications at home. Duration 1 week. Concurrent medication/care: Not specified. Indirectness: No indirectness (n=30) Intervention 2: Placebo/Sham. Participants received the same instructions and followed the same protocol as the SG patients but received a sham laser device manufactured also by Biocare Enterprise Limited (Good Energies, Haifa,Israel) with the same exterior characteristics of the effective device, including the guide beam and the working sound, but devoid of the therapeutic diode source. Duration 1 week. Concurrent medication/care: Not specified. Indirectness: No indirectness

Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus PLACEBO/SHAM Protocol outcome 1: Pain reduction - Actual outcome: VAS pain reduction at 1 week; Group 1: mean 35.17 (SD 22.139); n=29, Group 2: mean 22.14 (SD 16.635); n=28; VAS 0-100 Top=High is poor outcome Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Minimal baseline details; Group 1 Number missing: 1; Group 2 Number missing: 2	
Protocol outcomes not reported by the study	Quality of life ; Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Esenyel 2000[117]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=76)
Countries and setting	Conducted in Turkey; Setting: Not specified
Line of therapy	Unclear
Duration of study	Intervention time: 10 days (with 12 week follow up)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis of myofascial pain
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Travel and Simons criteria for active myofascial trigger points in the upper trapezius muscle.
Exclusion criteria	Meeting the ACR criteria for fibromyalgia, having myofascial trigger point infections or receiving physical medicine in the year preceding this study, having a history of acute trauma, inflammatory joint or muscle disease, infection or malignancy, or evidence of neurologic deficit.
Recruitment/selection of patients	Consecutively recruited from the outpatient clinic of the physical medicine and rehab department and the pain clinic of a hospital over a 2.3 year period.
Age, gender and ethnicity	Age - Mean (SD): 30(7.7) years. Gender (M:F): 38:64. Ethnicity: Not stated
Further population details	Chronic widespread pain
Extra comments	Pain duration ranged 6 months to 7 years
Indirectness of population	No indirectness
Interventions	(n=36) Intervention 1: Electrical Physical Modalities - Therapeutic Ultrasound. Ultrasound therapy 1.5Wcm2 to trigger points for 6 minute duration for 10 sessions, as well as neck-stretching exercises. Duration 10 days. Concurrent medication/care: Not reported. Indirectness: No indirectness (n=40) Intervention 2: Usual care. Neck stretching exercises only. Duration 10 days. Concurrent medication/care: Not reported. Indirectness: No indirectness

Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: THERAPEUTIC ULTRASOUND versus USUAL CARE Protocol outcome 1: Pain reduction - Actual outcome: VAS at 3 months; Group 1: mean 3.08 (SD 2.42); n=36, Group 2: mean 5.78 (SD 0.87); n=40; VAS 0-10 Top=High is poor outcome; Comments: Baseline not reported Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Other 1 - High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life ; Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Fagerlund 2015[120]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=50)
Countries and setting	Conducted in Norway; Setting: Pain clinic, university hospital of Northern Norway
Line of therapy	Unclear
Duration of study	Intervention + follow up: 5 day intervention and 1 month follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for fibromyalgia
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Over 18 years old, diagnosed with FMS, and manual examination of patients' tender points confirmed this. If on medication, this needed to be stable for 3 months before inclusion
Exclusion criteria	Severe psychiatric conditions, neurological conditions, developmental disorders, pregnancy and drug abuse.
Recruitment/selection of patients	Commenced September 2011, from Tromso (Northern Norway) - patients treated in pain clinics in the previous 2 years and members of the national FM patient association were contacted by mail, as well as advertisements in local newspapers
Age, gender and ethnicity	Age - Mean (SD): 48.6 (9.4) years. Gender (M:F):3:47. Ethnicity: Not specified
Further population details	Chronic widespread pain
Extra comments	Duration of pain 18.1(9) years
Indirectness of population	No indirectness
Interventions	(n=25) Intervention 1: Electrical Physical Modalities - Transcranial Direct Current Stimulation (TDCS). 5 consecutive days of treatment. Direct current stimulation administered using neuroConn DC stimulator. Stimulation duration 20 minutes, intensity of 2mA. Anodes placed at C3 position and cathode placed on contralateral supraorbital area. Duration 5 days. Concurrent medication/care: Not specified. Indirectness: No indirectness (n=25) Intervention 2: Placebo/Sham. Identical treatment but sham treatment; 8 second fade in period

	followed by 30 seconds of direct current stimulation that was terminated by a 5 second fade out (mimics skin sensation of active treatment with insufficient duration to induce changes in cortical excitability). Duration 5 days. Concurrent medication/care: Not specified. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) versus PLACEBO/SHAM

Protocol outcome 1: Quality of life
- Actual outcome: SF-36 physical component at 1 month (follow up); Group 1: mean 34.78 (SD 9.42); n=24, Group 2: mean 35.92 (SD 7.34); n=24; SF-36 summary score 0-100 Top=High is good outcome; Comments: Baseline: 29.83(26.17-33.49); 34.55(31.37-37.74)

Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference at baseline more than MIDs; Group 1 Number missing: 1, Reason: NR; Group 2 Number missing: 1, Reason: NR
- Actual outcome: SF-36 mental component at 1 month (follow up); Group 1: mean 48.2 (SD 15.35); n=24, Group 2: mean 45.4 (SD 10.85); n=24; SF-36 summary score 0-100 Top=High is good outcome; Comments: Baseline: 48.16(42.54-53.78);45.88(39.92-51.83)

Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference at baseline more than MIDs; Group 1 Number missing: 1, Reason: NR; Group 2 Number missing: 1, Reason: NR

Protocol outcome 2: Pain reduction
- Actual outcome: Pain intensity (numeric rating scale) at 1 month (follow up); Group 1: mean 4.26 (SD 1.9); n=24, Group 2: mean 5.22 (SD 1.5); n=24; NRS 0-10 Top=High is poor outcome; Comments: Baseline: 4.93(1.58); 5.31(1.59)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference at baseline; Group 1 Number missing: 1, Reason: NR; Group 2 Number missing: 1, Reason: NR

Protocol outcome 3: Psychological distress
- Actual outcome: HADS anxiety at 1 month (follow up); Group 1: mean 5.47 (SD 4.16); n=24, Group 2: mean 5.82 (SD 3.36); n=24; HADS:A Not specified Top=High is poor outcome; Comments: Baseline: 6.9(3.99);6.48(3.48)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference at baseline; Group 1 Number missing: 1, Reason: NR; Group 2 Number missing: 1, Reason: NR

- Actual outcome: HADS depression at 1 month (follow up); Group 1: mean 3.76 (SD 2.77); n=24, Group 2: mean 5.41 (SD 3.37); n=24; HADS:D Not specified Top=High is poor outcome; Comments: Baseline: 5.33(3.04); 6.13(3.53) Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference at baseline; Group 1 Number missing: 1, Reason: NR; Group 2 Number missing: 1, Reason: NR	
Protocol outcomes not reported by the study	Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Fregni 2006[129]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=32)
Countries and setting	Conducted in Brazil; Setting: Not specified
Line of therapy	Unclear
Duration of study	Intervention + follow up: 1 week (and 3 week follow up)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for fibromyalgia
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Met ACR criteria for FMS, score of at least 4 on VAS and at least 20 on the total tender point score. Participants were required to maintain a stable dose of any medications they were on.
Exclusion criteria	Uncontrolled clinical disease such as thyroid or cardiovascular disease, substance abuse, pregnancy, lactation
Recruitment/selection of patients	From a specialised outpatient centre
Age, gender and ethnicity	Age - Mean (SD): 53.2(8.97) years. Gender (M:F): All female. Ethnicity: Not specified
Further population details	Chronic widespread pain
Extra comments	Mean duration of pain 8.4(9.3) years
Indirectness of population	No indirectness
Interventions	(n=11) Intervention 1: Electrical Physical Modalities - Transcranial Direct Current Stimulation (TDCS). Current transferred by a pair of saline soaked surface sponge electrodes and battery driven stimulators with maximum output of 10mA. Anodal stimulation of left DLPFC area. Constant current of 2mA intensity was applied for 20 minutes. Duration 5 days. Concurrent medication/care: Not specified. Indirectness: No indirectness (n=11) Intervention 2: Electrical Physical Modalities - Transcranial Direct Current Stimulation (TDCS). Current transferred by a pair of saline soaked surface sponge electrodes and battery driven stimulators with maximum output of 10mA. Anodal stimulation of primary motor cortex area. Constant current of 2mA intensity was

	applied for 20 minutes. Duration 5 days. Concurrent medication/care: Not specified. Indirectness: No indirectness (n=10) Intervention 3: Placebo/Sham. Identical treatment with sham stimulation of the primary motor cortex. The stimulator was turned off after 30 seconds of stimulation. The patients therefore felt the initial itching sensation but received no current for the rest of the stimulation period. Duration 5 days. Concurrent medication/care: Not specified. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) FOR DLPFC versus PLACEBO/SHAM Protocol outcome 1: Psychological distress - Actual outcome: BDI at 3 weeks; Group 1: mean 14.6 (SD 5.7); n=11, Group 2: mean 18 (SD 7.7); n=10; Comments: baseline:17.8(8.7); 20.7(8.1) Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) FOR M1 versus PLACEBO/SHAM Protocol outcome 1: Psychological distress - Actual outcome: BDI at 3 weeks; Group 1: mean 18.6 (SD 9.1); n=11, Group 2: mean 18 (SD 7.7); n=10; BDI Not reported Top=High is poor outcome; Comments: Baseline: 19.9(8.2); 20.7(8.1) Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life ; Pain reduction ; Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Gokyildiz 2012[137]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=26)
Countries and setting	Conducted in Turkey; Setting: Urogynecology Unit, Istanbul Medical School Department of Obstetrics and Gynecology, Istanbul University.
Line of therapy	Unclear
Duration of study	Intervention time: 3 months
Method of assessment of guideline condition	Method of assessment/diagnosis not stated: All the patients were evaluated through CPP history, physical examination, gynecological examination and ultrasound at Istanbul Medical School Department of Obstetrics and Gynecology, Istanbul University.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnosis of CPP; voluntary participation; pain score >5 according to the visual analogue scale (VAS); cessation of analgesic at least 2 weeks before PTNS treatment; cessation of physiotherapy or electrotherapy at least 3 months before PTNS treatment.
Exclusion criteria	Pregnancy or planning a pregnancy; heart disease or cardiac pacing; nerve damage; use of anticoagulant medicine; active or recurrent urinary tract infection (more than five in the last 12 months).
Recruitment/selection of patients	8,872 gynecology patient records in the year 2006, 10,427 in the year 2007 and 500 in the year 2008 were reviewed at Istanbul Medical School Department of Obstetrics and Gynecology, Istanbul University. Sixty-five patients who had pain in the pelvis/lower abdomen for at least 6 months were identified and these patients were called and asked whether they still had pain. Those who still did were invited to the Urogynecology Unit and 52 patients applied to the unit.
Age, gender and ethnicity	Age - Other: Ages not stated, but report that 'no significant difference between the women in the control and experimental groups in terms of age'. Gender (M:F): 0/26. Ethnicity: Not stated
Further population details	Chronic visceral pain
Extra comments	Chronic population: pain in pelvis and lower abdomen for at least 6 months.
Indirectness of population	No indirectness

Interventions	(n=13) Intervention 1: Electrical Physical Modalities - Percutaneous Electrical Nerve Stimulation (PENS). Percutaneous Tibial Nerve Stimulation (PTNS) was applied using a neuromodulation system composing a needle set and a stimulator that runs with a 9-volt battery and creates an adjustable current between 0.5 and 10 mA, 200s and 20 Hz frequency. The patients lay on their backs in a supine position with the knees abducted and flexed (frog position). The 34-gauge needle was inserted approximately 3–4 cm above the inner malleolus, by entering at the place appropriate to the posterior tibial nerve line with a 60° angle, the adhesive electrode was placed on the inner side of the heel and the set was connected to the stimulator. The stimulator was run and the current was adjusted according to the patient's tolerance. When the current is flowing correctly, if the inserted needle is in the right place, toes should have plantar flexion (moving downwards) and/or 2nd to 5th fingers should release or have plantar flexion. Each session lasted 30 minutes. Duration 3 months (12 sessions). Concurrent medication/care: None. Inclusion required cessation of analgesic at least 2 weeks before treatment and cessation of physiotherapy or electrotherapy at least 3 months before treatment. Indirectness: No indirectness (n=13) Intervention 2: Usual care. Received 'routine intervention' (normal care) for 3 months. Duration 3 months. Concurrent medication/care: None. Inclusion required cessation of analgesic at least 2 weeks before treatment and cessation of physiotherapy or electrotherapy at least 3 months before treatment. Indirectness: No indirectness
Funding	Funding not stated (State no conflict of interest.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PERCUTANEOUS ELECTRICAL NERVE STIMULATION (PENS) versus USUAL CARE

Protocol outcome 1: Quality of life
- Actual outcome: SF-36 Physical function at After treatment (3 months); Group 1: mean 74.16 (SD 31.03); n=12, Group 2: mean 52.91 (SD 23.1); n=12; SF-36 0-100 Top=High is good outcome; Comments: Baselines, mean (SD):
PENS group 56.66 (23.19)
Control group 54.58 (23.88)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Key outcome baselines comparable between experimental and control groups. Differences in baseline for SF-36 Physical role and SF-36 Social functioning. ; Group 1 Number missing: 1, Reason: Unclear ("dropped"); Group 2 Number missing: 1, Reason: Unclear ("dropped")
- Actual outcome: SF-36 Physical role at After treatment (3 months); Group 1: mean 66.66 (SD 45.64); n=12, Group 2: mean 14.58 (SD 22.5); n=12; Sf-36 0-100 Top=High is good outcome; Comments: Baselines, mean (SD):
PENS group 25.00 (35.35)
Control group 12.5 (25.00)

Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Key outcome baselines comparable between experimental and control groups. Differences in baseline for SF-36 Physical role and SF-36 Social functioning. ; Group 1 Number missing: 1, Reason: Unclear ("dropped"); Group 2 Number missing: 1, Reason: Unclear ("dropped")
- Actual outcome: SF-36 Emotional role at After treatment (3 months); Group 1: mean 61.11 (SD 44.57); n=12, Group 2: mean 13.87 (SD 26.4); n=12; SF-36 0-100 Top=High is good outcome; Comments: Baselines, mean (SD):
PENS group 27.77 (37.15)
Control group 19.42 (29.98)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Key outcome baselines comparable between experimental and control groups. Differences in baseline for SF-36 Physical role and SF-36 Social functioning. ; Group 1 Number missing: 1, Reason: Unclear ("dropped"); Group 2 Number missing: 1, Reason: Unclear ("dropped")
- Actual outcome: SF-36 Energy/fatigue at After treatment (3 months); Group 1: mean 62.91 (SD 25.97); n=12, Group 2: mean 45 (SD 16.23); n=12; SF-36 0-100 Top=High is good outcome; Comments: Baselines, mean (SD):
PENS group 49.16 (14.74)
Control group 46.25 (18.35)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Key outcome baselines comparable between experimental and control groups. Differences in baseline for SF-36 Physical role and SF-36 Social functioning. ; Group 1 Number missing: 1, Reason: Unclear ("dropped"); Group 2 Number missing: 1, Reason: Unclear ("dropped")
- Actual outcome: SF-36 Mental health at After treatment (3 months); Group 1: mean 60.66 (SD 19.35); n=12, Group 2: mean 40.33 (SD 15.48); n=12; SF-36 0-100 Top=High is good outcome; Comments: Baselines, mean (SD):
PENS group 42.00 (17.18)
Control group 42.33 (18.48)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Key outcome baselines comparable between experimental and control groups. Differences in baseline for SF-36 Physical role and SF-36 Social functioning. ; Group 1 Number missing: 1, Reason: Unclear ("dropped"); Group 2 Number missing: 1, Reason: Unclear ("dropped")
- Actual outcome: SF-36 Social functioning at After treatment (3 months); Group 1: mean 71.87 (SD 33.33); n=12, Group 2: mean 50 (SD 11.91); n=12; SF-36 0-100 Top=High is good outcome; Comments: Baselines, mean (SD):
PENS group 43.75 (25.28)
Control group 54.16 (17.94)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Key outcome baselines comparable between experimental and control groups. Differences in baseline for SF-36 Physical role and SF-36 Social functioning. ; Group 1 Number missing: 1, Reason: Unclear ("dropped"); Group 2 Number missing: 1, Reason: Unclear ("dropped")
- Actual outcome: SF-36 Pain at After treatment (3 months); Group 1: mean 60 (SD 27.96); n=12, Group 2: mean 23.33 (SD 7.78); n=12; SF-36 0-100 Top=High is good outcome; Comments: Baselines, mean (SD):

PENS group 32.5 (23.40) Control group 23.33 (7.78) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Key outcome baselines comparable between experimental and control groups. Differences in baseline for SF-36 Physical role and SF-36 Social functioning. ; Group 1 Number missing: 1, Reason: Unclear ("dropped"); Group 2 Number missing: 1, Reason: Unclear ("dropped") - Actual outcome: SF-36 General health at After treatment (3 months); Group 1: mean 50.58 (SD 12.84); n=12, Group 2: mean 47.08 (SD 9.4); n=12; SF-36 0-100 Top=High is good outcome; Comments: Baselines, mean (SD): PENS group 48.58 (13.20) Control group 46.83 (10.01) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Key outcome baselines comparable between experimental and control groups. Differences in baseline for SF-36 Physical role and SF-36 Social functioning. ; Group 1 Number missing: 1, Reason: Unclear ("dropped"); Group 2 Number missing: 1, Reason: Unclear ("dropped") Protocol outcome 2: Pain reduction - Actual outcome: Pain intensity according to VAS at After treatment (3 months); Group 1: mean 2.62 Visual analogue scale (VAS) (SD 2.7); n=12, Group 2: mean 7.87 Visual analogue scale (VAS) (SD 0.88); n=12; Visual analogue scale (VAS) 0-10 Top=High is poor outcome; Comments: Baselines, mean (SD): PENS group 8.08 (1.72) Usual care group 7.95 (1.03) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Key outcome baselines comparable between experimental and control groups.; Group 1 Number missing: 1, Reason: Unclear ("dropped"); Group 2 Number missing: 1, Reason: Unclear ("dropped")	
Protocol outcomes not reported by the study	Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Gur 2002[147]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=50)
Countries and setting	Conducted in Turkey; Setting:
Line of therapy	Unclear
Duration of study	Intervention time: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Fibromyalgia patients diagnosed according to the American College of Rheumatology (ACR) criteria for FM.
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Fibromyalgia patients fulfilled the American College of Rheumatology (ACR) criteria for FM. These criteria include (a) a history of widespread pain for at least 3 months, i.e., pain in the left or right side of the body, pain above and below the waist, axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back pain) and (b) the presence of at least 11 tender point sites.
Exclusion criteria	Major clinical conditions other than FM were excluded by physical examinations and routine blood cells and differentials, red blood cells, hematocrit and hemoglobin, baseline thyroid-stimulating hormone, and antinuclear autoantibodies. Furthermore, exclusionary criteria for FM patients and normal controls were (a) a recent or past history of psychiatric disorders, e.g., major depressive disorder, alcohol dependence, substance abuse, schizophrenic or paranoid disorder, personality disorders, and somatoform disorders, (b) immunocompromised subjects, (c) subjects with neurological, inflammatory, endocrine, or clinically significant chronic disease such as diabetes mellitus, rheumatoid arthritis, inflammatory bowel disease, and organic brain disorders, (d) abnormal liver function tests such as serum aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and gamma-glutamyl transpeptidase, and (e) pregnant females.
Recruitment/selection of patients	Recruited from Department of Physical Therapy and Rehabilitation, University Hospital of Dicle, Diyarbakyr, Turkey.
Age, gender and ethnicity	Age - Mean (SD): Laser group 30.36 (6.91) ; Placebo group 28.52 (6.28) years. Gender (M:F): 39/11. Ethnicity: Not stated
Further population details	Chronic widespread pain

Extra comments	Disease duration in years, mean (SD): Laser group 4.86 (4.67) Placebo group 4.63 (3.28).
Indirectness of population	No indirectness
Interventions	(n=25) Intervention 1: Electrical Physical Modalities - Laser therapy. Low power laser therapy of approximately 2 J/cm2 was used at each tender point, producing an energy density radiant exposure) at each point. Two physical therapist investigators used standard technique with a Ga-As laser (20 W maximum output per pulse, 904 nm, 200 ns maximum pulse duration, 2.8 kHz pulse frequency, 11.2 mW average power, and 1 cm2 surface (class IIIb Laser Product, Frank Line IR 30, Fysiomed, Belgium). The patients were treated for 3 min at each tender point daily for 2 weeks, except weekends, at the same time in the afternoon in a sitting position and at a temperature of 20C. Duration 2 weeks. Concurrent medication/care: All patients were free of any medications for at least 1 month prior to treatment. Indirectness: No indirectness (n=25) Intervention 2: Placebo/Sham. The same unit as used for the laser intervention was used for the placebo treatment, but no laser beam was emitted. Duration 2 weeks. Concurrent medication/care: All patients were free of any medications for at least 1 month prior to treatment. Indirectness: No indirectness
Funding	Funding not stated

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

Protocol outcome 1: Pain reduction
- Actual outcome: Pain intensity on Likert scale at After treatment (2 weeks); Group 1: mean 1.24 (SD 0.72); n=25, Group 2: mean 2.19 (SD 0.74); n=25; Likert scale for pain (VAS) 0-10 Top=High is poor outcome; Comments: Baselines, mean (SD):
Laser group 3.04 (0.53)
Placebo group 3.19 (0.87)
Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness; Group 1 Number missing; Group 2 Number missing

Protocol outcomes not reported by the study	Quality of life ; Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Jales 2015[167]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=20)
Countries and setting	Conducted in Brazil; Setting: Outpatient setting in the Norte Riogranense Institute of Health Research and Teaching (IPENS), Natal/RN.
Line of therapy	Unclear
Duration of study	Intervention time: 10 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosed according to criteria established by the American College of Rheumatology: 1. Widespread Pain Index (WPI) ≥7 and severity symptoms (SS) in a scale of ≥ 5 or WPI between 3 and 6 and SS with score of ≥9; 2. Symptoms are present at similar level for at least three months; 3. Patients have no other disease which could justify the sensation of widespread pain
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Inclusion criteria were patients with FMS, aged between 25 and 65 years, of both genders and living in the city of Natal/RN.
Exclusion criteria	Exclusion criteria were patients with severe cognitive deficits; illiterate; patients with previous and/or family history of seizures; patients with arrhythmias and pacemaker; pregnant and breastfeeding females.
Recruitment/selection of patients	Not stated.
Age, gender and ethnicity	Age - Mean (SD): 46.4 (10.615) years. Gender (M:F): All female. Ethnicity: Not stated
Further population details	Chronic widespread pain
Extra comments	Over 3 months pain by nature of fibromyalgia diagnosis.
Indirectness of population	No indirectness
Interventions	(n=10) Intervention 1: Electrical Physical Modalities68.5 - Transcranial Direct Current Stimulation (TDCS). For tDCS procedures, two electrodes were positioned on the scalp of patients without causing discomfort and a 1.0mA electric impulse was applied, supplied by an electronic unit with direct current control from Cerebral

	Electronic Stimulator equipment (CES). During procedures, patients remained comfortably lying down in beds, with the anodal electrode positioned on the scalp, on the superior-lateral face of the skull, the region corresponding to the left precentral gyrus (M1 or Brodman's area 4) on its medial third. The cathodic electrode was positioned on the contralateral supraorbital region. A rubber sponge was placed between the scalp and the electrode measuring 3x5cm, previously moistened with 0.9% saline. Direct 1.0mA current was applied for 20 minutes. Duration 10 weeks. Concurrent medication/care: For the duration of the treatment patients were permitted to continue their normal pharmacological and non-pharmacological therapies according to individual situations. Indirectness: No indirectness (n=10) Intervention 2: Placebo/Sham. For the sham tDCS group (control), the same procedures were adopted as for the active tDCS treatment, once a week for 20 minutes for 10 consecutive weeks, but the tDCS device was not turned on. Duration 10 weeks. Concurrent medication/care: For the duration of the treatment patients were permitted to continue their normal pharmacological and non-pharmacological therapies according to individual situations. Indirectness: No indirectness
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) versus PLACEBO/SHAM

Protocol outcome 1: Quality of life
- Actual outcome: SF-36: Functional capacity at 10 weeks (end of treatment); Group 1: mean 68.5 (SD 11.068); n=10, Group 2: mean 38 (SD 26.895); n=10; SF-36 Quality of life questionnaire 0-100 Top=High is good outcome; Comments: Baselines, mean (SD):
tDCS group 48.00 (16.364)
Sham group 31.00 (23.07)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: SF-36 baselines significantly different in some categories
- Actual outcome: SF-36: Physical aspects at 10 weeks (end of treatment); Group 1: mean 75 (SD 31.18); n=10, Group 2: mean 47.5 (SD 41.583); n=10; SF-36 Quality of life questionnaire 0-100 Top=High is good outcome; Comments: Baselines, mean (SD):
tDCS group 17.5 (23.717)
Sham group 22.5 (36.228)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: SF-36 baselines significantly different in some categories
- Actual outcome: SF-36: Pain at 10 weeks (end of treatment); Group 1: mean 43 (SD 18.288); n=10, Group 2: mean 50 (SD 23.57); n=10; SF-36 Quality of life questionnaire 0-100 Top=High is good outcome; Comments: Baseline, mean (SD):
tDCS group 55 (22.73)
Sham group 62 (13.166)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover

- Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: SF-36 baselines significantly different in some categories
- Actual outcome: SF-36: General health status at 10 weeks (end of treatment); Group 1: mean 58 (SD 11.106); n=10, Group 2: mean 63.5 (SD 9.443); n=10; SF-36 Quality of life questionnaire 0-100 Top=High is good outcome; Comments: Baselines, mean (SD):
tDCS group 63.5 (10.554)
Sham group 59 (15.42)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome:. No indirectness ; Baseline details: SF-36 baselines significantly different in some categories
- Actual outcome: SF-36: Vitality at 10 weeks (end of treatment); Group 1: mean 53.5 (SD 9.144); n=10, Group 2: mean 58 (SD 10.055); n=10; SF-36 Quality of life questionnaire 0-100 Top=High is good outcome; Comments: Baselines, mean (SD):
tDCS group 46.5 (10.014)
Sham group 54.5 (6.852)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness; Baseline details: SF-36 baselines significantly different in some categories
- Actual outcome: SF-36: General aspects at 10 weeks (end of treatment); Group 1: mean 47.5 (SD 15.366); n=10, Group 2: mean 50 (SD 16.667); n=10; SF-36 Quality of life questionnaire 0-100 Top=High is good outcome; Comments: Baselines, mean (SD):
tDCS group 51.25 (17.129)
Sham group 50 (16.667)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness; Baseline details: SF-36 baselines significantly different in some categories
- Actual outcome: SF-36: Emotional aspects at 10 weeks (end of treatment); Group 1: mean 80 (SD 35.633); n=10, Group 2: mean 60 (SD 43.886); n=10; SF-36 Quality of life questionnaire 0-100 Top=High is good outcome; Comments: Baselines, mean (SD):
tDCS group 26.67 (30.633)
Sham group 16.67 (17.566)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness; Baseline details: SF-36 baselines significantly different in some categories
- Actual outcome: SF-36: Mental health at 10 weeks (end of treatment); Group 1: mean 58.4 (SD 11.345); n=10, Group 2: mean 54 (SD 11.963); n=10; SF-36 Quality of life questionnaire 0-100 Top=High is good outcome; Comments: Baselines, mean (SD):
tDCS group 53.6 (8.044)
Sham group 51.6 (10.741)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness; Baseline details: SF-36 baselines significantly different in some categories

Protocol outcome 2: Pain reduction
- Actual outcome: Pain intensity (VAS) at 10 weeks (end of treatment); Group 1: mean 3.6 (SD 1.838); n=10, Group 2: mean 5.6 (SD 2.503); n=10; Visual analogue scale 0-10 Top=High is poor outcome; Comments: Baselines, mean (SD):
tDCS group 6.05 (2.061)
Sham group 6.70 (2.111)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover

- Low, Subgroups - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Kabay 2009[176]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=89)
Countries and setting	Conducted in Turkey; Setting: Not specified
Line of therapy	Unclear
Duration of study	Intervention time: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Chronic therapy resistant pelvic pain category IIIB pelvic pain
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnosis of category IIIB CP/CPPS as confirmed by detailed history, physical examination, ultrasound, urine flow measurement, residual urine volume measurement, and standard microbiologic cultures. CP/CPPS defined as complaints of pain for at least 6 months in the bladder, groin, genitals, or lower abdomen and or perineal or perianal pain without any obvious abnormalities.
Exclusion criteria	Chronic bacterial prostatitis or category IIIA, aged <18 years, symptoms for less than 6 months, active or recurrent UTIs, STIs, or IC. Other diagnoses such as diabetes, cardiopulmonary disease, neurological disease or other conditions that could explain pain or limit ability to take part in treatment were excluded.
Recruitment/selection of patients	May 2006 to March 2008
Age, gender and ethnicity	Age - Mean (SD): 37.7(7.4) years. Gender (M:F): Not specified. Ethnicity: Not reported
Further population details	Chronic visceral pain
Extra comments	Mean duration of symptoms 4.5(6.1) years
Indirectness of population	No indirectness
Interventions	(n=45) Intervention 1: Electrical Physical Modalities - Percutaneous Electrical Nerve Stimulation (PENS). Percutaneous posterior tibial nerve stimulation. 30 minute sessions, one a week. Needles inserted 5cm from medial malleolus and neutral electrode placed on the same leg, both connected to a stimulator. Electrical stimulation was applied unilaterally with 200-us pulses and a pulse rate of 20Hz, and intensity levels were just below the threshold determining motor contraction. Amplitude was set at maximum tolerable level, usually 1.5

	times the threshold for evoking plantar flexion of toes or toe fanning. Duration 3 months. Concurrent medication/care: Not specified (n=44) Intervention 2: Placebo/Sham. Identical treatment but the electrical stimulation was not applied in the sham group. Duration 3 months. Concurrent medication/care: Not specified
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PERCUTANEOUS ELECTRICAL NERVE STIMULATION (PENS) versus PLACEBO/SHAM Protocol outcome 1: Quality of life - Actual outcome: NIH-CPSI quality of life at 3 months; Group 1: mean 2.1 (SD 0.9); n=45, Group 2: mean 6.7 (SD 2.1); n=44; NIH-CPSI QOL 0-12 Top=High is poor outcome; Comments: Baseline: 6.7(2.2); 6.5(2.8) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 2: Pain reduction - Actual outcome: VAS pain at 3 months; Group 1: mean 4.3 (SD 0.6); n=45, Group 2: mean 7.2 (SD 0.4); n=44; VAS 0-10 Top=High is poor outcome; Comments: Baseline: 7.6(0.8);7.4(0.9) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Khedr 2017[185]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=40)
Countries and setting	Conducted in Egypt; Setting: Assiut university hospital
Line of therapy	Unclear
Duration of study	Intervention + follow up: 2 weeks intervention and 8 weeks follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for fibromyalgia
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Met FMS criteria and had score of at least 4 on VAS pain scale
Exclusion criteria	History of autoimmune or chronic inflammatory disease, substance abuse, neuropsychiatric disorders, pregnancy or lactation.
Recruitment/selection of patients	2015-2016, from outpatient clinic
Age, gender and ethnicity	Age - Mean (SD): 32.3(10.9) years. Gender (M:F): 2:34. Ethnicity: Not specified
Further population details	Chronic widespread pain
Extra comments	Duration of symptoms 6.1(2.5) years
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Electrical Physical Modalities - Transcranial Direct Current Stimulation (TDCS). 10 sessions over 2 weeks (5 days of 5 sessions x2). 2mA for 20 mins in each session. Anodal electrode with a current density of 0.08mA placed on left primary motor area, over C3, and reference electrode fixed over contralateral arm. Duration 2 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness (n=20) Intervention 2: Placebo/Sham. Identical treatment but the current applied only for 30s at the beginning and at the end of the session (considered reliable sham stimulation as sensations similar but not enough to induce response). Duration 2 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness

Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) versus PLACEBO/SHAM Protocol outcome 1: Pain reduction - Actual outcome: VAS at 8 weeks (follow up); Group 1: mean 3.9 (SD 2.1); n=18, Group 2: mean 7.3 (SD 0.9); n=18; VAS 0-10 Top=High is poor outcome; Comments: Baseline: 7.4(1.1); 8(0.8) Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness Protocol outcome 2: Psychological distress - Actual outcome: HAM-A at 8 weeks (follow up); Group 1: mean 11.6 (SD 5.9); n=18, Group 2: mean 17.1 (SD 4.2); n=18; HAM:A Not specified Top=High is poor outcome; Comments: Baseline: 19.3(4.5); 18.7(3.3) Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness - Actual outcome: HAM-D at 8 weeks (follow up); Group 1: mean 19.6 (SD 6.3); n=18, Group 2: mean 17.6 (SD 4); n=18; HAM:D Not specified Top=High is poor outcome; Comments: Baseline: 17.5(4.4); 20.3(3.2) Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life ; Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Lee 2012[205]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=22)
Countries and setting	Conducted in South Korea
Line of therapy	Unclear
Duration of study	Intervention + follow up: 10 day intervention and 1 month follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for fibromyalgia
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Chronic, persistent pain for more than 24 months
Exclusion criteria	Evidence of other inflammatory rheumatologic disease or auto-immune disease, or psychiatric disorders, or contraindications for TMS
Recruitment/selection of patients	From division of rheumatology to the neuromodulation outpatient clinic at Adan Medical Center between May 2008 and June 2009
Age, gender and ethnicity	Age - Mean (SD): 47.2(6.2) years. Gender (M:F): All women. Ethnicity: Not specified
Further population details	Chronic widespread pain
Extra comments	Duration of pain 44.7(10.3) years
Indirectness of population	No indirectness
Interventions	(n=15) Intervention 1: Electrical Physical Modalities - Transcranial Magnetic Stimulation (TMS). Randomised to low frequency stimulation (n=7) or high frequency stimulation (n=8). 1Hz or 10 Hz treatment 5 times per week for 2 weeks of TMS, performed by a physiatrist with a 70-mm air cooled figure of eight shaped coil. Applied to the right side motor cortex, approximate location at the DLPFC. Each patient received either: 1Hz, 110% intensity of resting motor threshold, 800 stimuli of each train (2 trains with 60 secs of intertrain interval and a total of 1600 stimuli per session 10Hz, 80% intensity of resting motor threshold, 2000 stimuli per session. Duration 2 weeks. Concurrent medication/care: Not specified (medications remained unchanged throughout study period). Indirectness: No

	indirectness (n=7) Intervention 2: Placebo/Sham. Identical treatment but coil angle was 90% perpendicular to the skull rather than tangential to it, so the magnetic field could not penetrate the brain, although patients could hear the sound produced. Duration 2 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCRANIAL MAGNETIC STIMULATION (TMS) versus PLACEBO/SHAM Protocol outcome 1: Quality of life - Actual outcome: FIQ at 6 weeks; Group 1: mean 51.8 (SD 13.51); n=10, Group 2: mean 53.7 (SD 27.3); n=5; FIQ 0-100 Top=High is poor outcome; Comments: Baseline: 59.3(23.4); 67.2(11.1);60.4(21.1) Mean of TMS group: weighted mean and SD calculated from LF and HF groups Risk of bias: All domain - Very high, Selection - Low, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5; Group 2 Number missing: 2 Protocol outcome 2: Pain reduction - Actual outcome: VAS at 6 weeks; Group 1: mean 60.5 (SD 22.23); n=10, Group 2: mean 72.3 (SD 25.3); n=5; VAS 0-100 Top=High is poor outcome; Comments: Baseline: 72.4(10.7); 70(8.5); 78.1(13.1) Mean of TMS group: weighted mean and SD calculated from LF and HF groups Risk of bias: All domain - Very high, Selection - Low, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 5; Group 2 Number missing: 2 Protocol outcome 3: Psychological distress - Actual outcome: BDI at 6 weeks; Group 1: mean 17.85 (SD 6.553); n=10, Group 2: mean 18.3 (SD 5.8); n=5; BDI Not reported Top=High is poor outcome; Comments: Baseline: 19.2(4.4); 25.5(6.4); 21.6(5.5) Mean of TMS group calculated from weighted mean and SDs of HF and LF groups Risk of bias: All domain - Very high, Selection - Low, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 5; Group 2 Number missing: 2 Protocol outcome 4: Discontinuation - Actual outcome: Discontinuation at 6 weeks; Group 1: 5/15, Group 2: 2/7; Comments: 1 in the intervention group discontinued due to a seizure Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA	
Protocol outcomes not reported by the study	Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Mhalla 2011[241]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=40)
Countries and setting	Conducted in France; Setting: Not specified
Line of therapy	Unclear
Duration of study	Intervention + follow up: 21 week intervention, follow up at week 25
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for fibromyalgia
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Met ACR criteria, score of at least 4 on BPI, persistent pain for more than 6 months
Exclusion criteria	Inflammatory rheumatic disease, autoimmune disease, or other painful disorders that might confound the assessment of FMS. Any psychiatric condition including major depression or major personality disorders, or history of substance abuse. All women of childbearing age included in this study had negative pregnancy tests at inclusion and were using contraception. Any contraindications for TMS such as seizures or brain trauma. Concomitant medication for pain and sleep allowed provided dose had been stable for at least 1 month before study.
Recruitment/selection of patients	Between 2008 and 2009
Age, gender and ethnicity	Age - Mean (SD): 50.2(10.8) years. Gender (M:F): All female. Ethnicity: Not specified
Further population details	Chronic widespread pain
Extra comments	Pain duration 13.55(12.4) years
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Electrical Physical Modalities - Transcranial Magnetic Stimulation (TMS). 1 session per day for 5 days followed by one weekly session for 3 weeks, 3 fortnightly sessions, and 3 monthly sessions. Patients seated in comfortable chair in relaxed position. MagPROX100 MS device used, using a figure-8 shaped coil oriented at a tangent to the scalp, with the main phase of the induced current in the anterior posterior direction. Resting motor threshold was established in each person, and each session consisted of

	15 series of 10 second pulses with a frequency of 10Hz and an interval of 50 seconds between each train, giving a total of 1500 pulses per session (and stimulation intensity used was 80% of RMT). Duration 21 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness (n=20) Intervention 2: Placebo/Sham. Sham TMS, carried out with identical coil that emitted a sound similar to that emitted by the active coil. Duration 21 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness
Funding	Academic or government funding (Fondation APICIL and the Fondation de France)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCRANIAL MAGNETIC STIMULATION (TMS) versus PLACEBO/SHAM

Protocol outcome 1: Quality of life
- Actual outcome: FIQ at 25 weeks (follow up); Group 1: mean 56 (SD 17.7); n=15, Group 2: mean 63.3 (SD 15); n=15; FIQ 0-100 Top=High is poor outcome; Comments: Baseline: 66.8(12.5);67.2(14.8)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Psychological distress
- Actual outcome: HADS:A at 25 weeks (follow up); Group 1: mean 9.2 (SD 4.9); n=15, Group 2: mean 9.4 (SD 5.7); n=15; HADS:A 0-21 Top=High is good outcome; Comments: Baseline: 11.8(4); 11.4(4.4)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome: HADS:D at 25 weeks (follow up); Group 1: mean 8.6 (SD 4.7); n=15, Group 2: mean 7.4 (SD 4); n=15; HADS:D 0-21 Top=High is poor outcome; Comments: Baseline: 8.4(4.7); 8.7(3.5)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Protocol outcome 3: Pain interference
- Actual outcome: BPI pain interference at 25 weeks (follow up); Group 1: mean 4.1 (SD 1.7); n=15, Group 2: mean 6 (SD 1.5); n=15; BPI interference Not specified Top=High is poor outcome; Comments: Baseline: 5.8(1.3); 6.1(1.7)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness

Protocol outcomes not reported by the study	Pain reduction ; Physical function ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Murina 2008[250]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=40)
Countries and setting	Conducted in Italy; Setting: Not specified
Line of therapy	Unclear
Duration of study	Intervention time: 10 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis of vestibulodynia (positive cotton-swab test with exclusions)
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	All were diagnosed as having vestibulodynia due to the coexistence of the following conditions: a history of at least 6 months of vulval pain upon tampon insertion or attempted intercourse and a positive cotton-swab test, that is, tenderness at palpation of the vestibular area with a cotton tip applicator,8 in the absence of other causes for these findings
Exclusion criteria	pregnancy, cardiac pacemakers, vaginal infections, neurological or neuromuscular disorders and diabetes
Recruitment/selection of patients	Not specified
Age, gender and ethnicity	Age - Mean (range): 28(21-44) years. Gender (M:F): All women. Ethnicity: Not specified
Further population details	Chronic visceral pain
Extra comments	Duration of symptoms 15 month (range 7-48 months)
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Electrical Physical Modalities - Transcutaneous Electrical Nerve Stimulation (TENS). TENS group received an electrical stimulation in the form of a symmetrical biphasic wave generated via a calibrated dual channel TENS unit, an YSY-EST device. The stimulation was delivered through a commercially available plastic vaginal probe (PERIPROBE VAG2ST), 20 mm in diameter and 110 mm in length, with two gold metallic transversal rings as electrodes. It was inserted into the vagina for 20 mm. Previous studies involving the use of TENS in women with chronic pain syndromes showed that the optimal analgesic effect was achieved by alternating low- and high-frequency stimulation for 15–30 minutes.12 Based

	on these experiences, frequencies of 10 and 50 Hz at 15-min intervals during each of the active TENS treatment sessions were chosen. The standard protocol for active TENS was 15 minutes of 10-Hz frequency. Duration 10 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness (n=20) Intervention 2: Placebo/Sham. The placebo group received an electrical stimulation considered to be nonactive, that is, two sets of 3-second stimulation (frequency 2 Hz, pulse duration 2 microseconds) followed by a 15-minute pause. Women of both groups underwent 20 treatment sessions on a twice per week basis. Duration 10 weeks. Concurrent medication/care: Not stated. Indirectness: No indirectness
Funding	Funding not stated

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

Protocol outcome 1: Pain reduction
- Actual outcome: VAS at 10 weeks; Group 1: mean 2.1 (SD 2.7); n=20, Group 2: mean 5.7 (SD 2.2); n=20; VAS 0-10 Top=High is poor outcome; Comments: Baseline: 6.1(1.9); 6.7(2)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA
- Actual outcome: VAS at 22 weeks (including 10 week intervention); Group 1: mean 2.8 (SD 2.5); n=20, Group 2: mean 5.6 (SD 2.1); n=20; VAS 0-10 Top=High is poor outcome; Comments: Baseline: 6.1(1.9); 6.7(2)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA

Protocol outcome 2: Discontinuation
- Actual outcome: Discontinuation at 10 weeks; Group 1: 0/20, Group 2: 0/20
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA

Protocol outcomes not reported by the study	Quality of life ; Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Panton 2013[274]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=41)
Countries and setting	Conducted in USA; Setting: Not specified
Line of therapy	Unclear
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for FMS
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	None specified but only women recruited
Exclusion criteria	Participants were excluded if they had uncontrolled hypertension (160/ 100mm Hg or higher), uncontrolled diabetes, active heart disease, known history of cancer, long-term corticosteroid use, pregnant or planning to get pregnant, endocrine disease, anticoagulant therapy, bleeding disorders, history of stroke, a chronic infection, any type of malignancy, if they were taking medications that caused sensitivity to light, if they had a physical examination or radiological findings that would contraindicate the use of light or thermal therapy, and/or currently under the care of a chiropractic physician, acupuncture physician, massage therapist, or other forms of manual therapy.
Recruitment/selection of patients	Participants received $100.00 for participating in the study. Fifty dollars ($50.00) was given after the end of pretesting and another $50.00 was given at the completion of the study.
Age, gender and ethnicity	Age - Mean (SD): 53(11.5) years. Gender (M:F): All women. Ethnicity: Not stated
Further population details	Chronic widespread pain
Extra comments	FMS duration 10.5(7.5) years
Indirectness of population	No indirectness
Interventions	(n=23) Intervention 1: Electrical Physical Modalities - Laser therapy. Delivered by chiropractors. Treatment was designed to be consistent with the laser manufacturer's recommendations and consisted of twice weekly sessions for 4 weeks for a total of 8 sessions. The duration of each session was approximately 15 minutes,

	while actual treatment time was 7 minutes. During the treatment sessions, the participants were either gowned, or wore a sports bra to expose the skin of the cervical, thoracic, and lumbar regions. Participants were positioned face down on a treatment table or a massage chair, depending upon their comfort and preference. Participants wore eye protection with an optical density rating >5.0 at 810nm and 980nm in order to protect their eyes and further obscure which treatment they received. To ensure consistency between the laser and heat and sham and heat group, the treatment targets consisted of seven tender points used as part of the diagnostic criteria to establish a diagnosis of FM (Fig. 1). Treatment was delivered to an area approximately 2.5 inches·3.5 inches or approximately 56.45cm2 to conform to LiteCure's manual ''Clinical Overview and Application of Class IV Therapy Laser'' written by Riegal and Pryor. For the laser group, treatment was rendered utilizing a LCT-1000 (LiteCure LLC, Newark, DE) solid-state GaAlAs laser delivering a continuous-wave, dual-wavelength laser with 20% 810nm, and 80% 980nm at 10W. Each 56.45cm2 treatment point was treated with laser at 10.63J/cm2 and warm air utilizing a grid scanning technique to avoid overheating tissue. Participants were instructed to expect some warmth but that the treatment should not burn and to provide verbal cues if the treatment spots became excessively warm. Each treatment point was treated for exactly 60 seconds for a total of 600J per point, for a total daily treatment dose of 4200J. The dual wavelength was used for two reasons: (1) this is what is commercially available and (2) two wavelengths allow for treatment in patients with different skin colours since different melanin concentrations will absorb light differently. Both wavelengths are in the accepted therapeutic window. The sham treatment consisted of 60 seconds of warm air alone over the seven tender points. A timer was used to ensure that each area was treated for exactly 60 seconds so that the treatment time was identical for both groups. Duration 4 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness (n=18) Intervention 2: Placebo/Sham. Delivered by chiropractors. Because of the thermal affects associated with Class IV laser, and because the laser manufacturer's website specifically mentions the ''soothing warmth'' of laser therapy, a sham and heat therapy treatment was designed to disguise true laser treatment from sham treatment. The device for the treatment was designed to force warm air, provided by a commercially available air warmer through a tube. The air warmer was mounted out of view inside a vented cart upon which the laser was mounted so as to appear as a single unit. The air warmer was mounted to a short section of insulated pipe, which was then attached to a T fitting with a gate valve attached to one side and the warm air supply hose attached to the opposite side. The gate valve was used to control the flow of warm air. The warm air supply hose was then bound together with the laser's fiber-optic cable with zip ties, and wound with white elastic tape to obscure both the tube and the fiber-optic cable. The air supply tube was routed through a hole drilled in the laser handpiece so that warm air could be delivered alone for the sham and heat therapy or in tandem with the laser for the laser and heat therapy. The same device was used for both groups, so the treatment group received both laser and warm air, and the sham group received only warm air. Although neither the skin temperature, nor the warm air output of the treatment device was measured, an effort was made to standardize the heat treatment by utilizing the same medium heat setting for each treatment preceded by a warmup period of approximately 5 minutes to provide a consistent application

	of warm air at approximately the same LASER THERAPY ON FIBROMYALGIA 447 temperature from treatment to treatment. The air flow and temperature were adjusted by way of the gate valve and the air warmer's heat settings in an attempt to mimic the warmth associated with the Class IV laser with sufficient warmth so that participants could not discern whether they received the laser treatment or the sham. Duration 4 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness
Funding	Study funded by industry (Litecure)

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

Protocol outcome 1: Quality of life
- Actual outcome: FIQ at 4 weeks; Group 1: mean 55 (SD 16); n=20, Group 2: mean 55 (SD 12); n=18; FIQ 0-100 Top=High is poor outcome; Comments: Baseline: 62(21); 57(11)
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 3, Reason: Discontinued intervention; Group 2 Number missing: 0, Reason: NA

Protocol outcome 2: Pain reduction
- Actual outcome: FIQ pain at 4 weeks; Group 1: mean 6.2 (SD 2.1); n=20, Group 2: mean 6.1 (SD 1.4); n=18; FIQ pain subscale 0-10 Top=High is poor outcome; Comments: Baseline: 7.1(2.3);5.8(1.3)
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 3, Reason: Discontinued intervention; Group 2 Number missing: 0, Reason: NA

Protocol outcome 3: Discontinuation
- Actual outcome: Discontinuation at 4 weeks; Group 1: 3/23, Group 2: 0/18
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA

Protocol outcomes not reported by the study	Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Rohlig 2011[289]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=40)
Countries and setting	Conducted in Turkey; Setting: Istanbul University
Line of therapy	Unclear
Duration of study	Intervention time: 3 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis of TMD
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Presence of signs and symptoms of TMD of myogenic origin according to the research diagnostic criteria for TMD, orofacial pain lasting for more than 6 months, aged between 18 and 60 years.
Exclusion criteria	Exclusion criteria were disk displacements, arthralgia, arthritis, general inflammatory connective tissue diseases, psychiatric disorders, tumours, heart diseases, pacemakers, pregnancy, symptoms which could be referred to other disorders of the orofacial region, any medication use or treatment for TMD within the last six months, high baseline pain intensity, local skin infections over the TM area.
Recruitment/selection of patients	Selected consecutively among patients requesting orofacial pain treatment over a period of 8 months
Age, gender and ethnicity	Age - Mean (SD): 42.5(2.3) years. Gender (M:F): 16:24. Ethnicity: Not specified
Further population details	1. Chronic orofacial pain
Extra comments	Duration of pain: 10.75(2.9) years
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Electrical Physical Modalities - Laser therapy. Active laser applied every other day for 3 weeks, totalling 10 sessions. A continuous low-intensity semiconductor was used for laser irradiation, generating radiation of 820nm wavelength, with a beam diameter of 6mm and a probe angle of 45 degrees. 8J/cm2 applied to each muscle point for 10 seconds. Duration 3 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness

	(n=20) Intervention 2: Placebo/Sham. Same equipment but the device was not programmed. No further details. Duration 3 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness
Funding	Academic or government funding (Research fund of Istanbul university)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus PLACEBO/SHAM Protocol outcome 1: Pain reduction - Actual outcome: VAS at 3 weeks; Group 1: mean 30.05 (SD 7.14); n=20, Group 2: mean 49.75 (SD 9.54); n=20; VAS 0-100 Top=High is poor outcome; Comments: Baseline: 60.05(10.42); 53.3(8.79) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: NR, Reason: NR; Group 2 Number missing: NR, Reason: NR	
Protocol outcomes not reported by the study	Quality of life ; Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Short 2011[314]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=20)
Countries and setting	Conducted in USA; Setting: In the MUSC
Line of therapy	Unclear
Duration of study	Intervention time: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for fibromyalgia
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Subjects could enrol with or without a history of major depressive disorder, but the depression could not be the main reason for their functional impairment or study enrolment. Rather subjects were recruited solely for fibromyalgia pain.
Exclusion criteria	Patients were excluded if they were taking medications known to increase the risk of TMS-induced seizures (e.g., theophylline, Ritalin, high dose thyroid supplementation), if they had medication changes within the 4 weeks of starting the trial or during the trial, or if they had pacemakers, epilepsy, recent head trauma, stroke, bipolar disorder or schizophrenia
Recruitment/selection of patients	2007-2010; Medical University of South Carolina (MUSC) Rheumatology clinics and local newspaper
Age, gender and ethnicity	Age - Mean (SD): 53(13.53) years. Gender (M:F): 4:16. Ethnicity: Not specified
Further population details	Chronic widespread pain
Extra comments	Duration of pain: 11.1(10.36) years
Indirectness of population	No indirectness
Interventions	(n=10) Intervention 1: Electrical Physical Modalities - Transcranial Magnetic Stimulation (TMS). Both Active and sham groups received the same treatment sessions 5x per week 80 trains × 15 sec = 4000 pulses per

	session, 5 × per week=20,000 pulses per week, × 2weeks = 40,000 pulses. Time - 1200 sec = 20 minutes/session, all days. Resting motor threshold (rMT) was determined using a NeoPulse Neotonus® Model 3600 (with a solid focal coil) TMS machine by starting with 80% of the machine output and 1Hz stimulus frequency. The coil was positioned over the area of the skull roughly corresponding to the motor cortex and then systematically moved and adjusted until each pulse results in isolated movement of the right thumb at rest (Abductor Pollicis Brevis; APB muscle). As the left prefrontal cortex was the cortical target, a mark was made 6 cm anterior to the motor cortex target. During active and sham stimulation, the TMS coil was aligned in a parasaggital orientation, 6 cm from the area that produced right APB muscle movement for rMT testing. The length of treatment and the number of pulses on the head was the same for all subjects; whether they receive active or sham. The same stimulation frequency was used for all active subjects (chosen as a priori stimulation based on studies showing antidepressant and antinociceptive effects): 10 Hertz - Pulse train duration (on time) 5 seconds, Power (intensity)level 120% of resting motor threshold, Inter-train interval (off time) 10seconds (15 second cycle time). Duration 2 weeks. Concurrent medication/care: No further details. Indirectness: No indirectness (n=10) Intervention 2: Placebo/Sham. Both Active and sham groups received the same treatment sessions 5x per week 80 trains × 15 sec = 4000 pulses per session, 5 × per week=20,000 pulses per week, × 2weeks = 40,000 pulses. A specially designed sham TMS coil was used for all sham conditions that produces auditory signals identical to active coils but is shielded so that actual stimulation does not occur, however subjects do experience sensory stimulation that is difficult to distinguish from real TMS. Participants experienced a brief (~250 μs) electrical pulse every time the sham TMS coil clicked. The intensity of the stimulus was adjustable at the electrical generator (1 to 60 mA) and the time that the gate was let open after each TTL trigger was adjustable on the switch-box as well. Duration 2 weeks. Concurrent medication/care: No further details. Indirectness: No indirectness
Funding	Principal author funded by industry (Glaxo-Smith Kline, Jazz Pharmaceuticals, Brainsway, Cephos, and Force Protection)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCRANIAL MAGNETIC STIMULATION (TMS) versus PLACEBO/SHAM

Protocol outcome 1: Quality of life
- Actual outcome: FIQ at 4 weeks; Group 1: mean 38.99 (SD 19.44); n=10, Group 2: mean 47.93 (SD 14.7); n=10; FIQ 0-100 Top=High is poor outcome; Comments: baseline: 58.79(11.93); 54.38(13.96)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Baseline details: Number of participants on medications differed (e.g., 20% vs 0% of participants were taking muscle relaxants in the real and sham groups respectively); Group 1 Number missing, Reason: NR; Group 2 Number missing, Reason: NR

Protocol outcome 2: Pain reduction - Actual outcome: VAS at 4 weeks; Group 1: mean 4.41 (SD 1.95); n=10, Group 2: mean 5.37 (SD 2.02); n=10; VAS 0-10 Top=High is poor outcome; Comments: Baseline: 5.6(1.85); 5.34(1.82) Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Baseline details: Number of participants on medications differed (e.g., 20% vs 0% of participants were taking muscle relaxants in the real and sham groups respectively); Group 1 Number missing, Reason: NR; Group 2 Number missing, Reason: NR Protocol outcome 3: Physical function - Actual outcome: Brief pain inventory functional impairment at 4 weeks; Group 1: mean 3.6 (SD 2.18); n=10, Group 2: mean 3.79 (SD 2.69); n=10; BPI subscale 0-10 Top=High is poor outcome; Comments: Baseline: 5.57(2.58); 5.44(2.25) Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Baseline details: Number of participants on medications differed (e.g., 20% vs 0% of participants were taking muscle relaxants in the real and sham groups respectively); Group 1 Number missing, Reason: NR; Group 2 Number missing, Reason: NR Protocol outcome 4: Psychological distress - Actual outcome: Hamilton depression rating scale at 4 weeks; Group 1: mean 14.1 (SD 9.42); n=10, Group 2: mean 16.4 (SD 8.18); n=10; HDRS 0-52 Top=High is poor outcome; Comments: Baseline:21.8(7.79); 17.6(7.31) Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Baseline details: Number of participants on medications differed (e.g., 20% vs 0% of participants were taking muscle relaxants in the real and sham groups respectively); Group 1 Number missing, Reason: NR; Group 2 Number missing, Reason: NR	
Protocol outcomes not reported by the study	Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Spanemberg 2015[325]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=58)
Countries and setting	Conducted in Spain; Setting: Not specified
Line of therapy	Unclear
Duration of study	Intervention time: 3 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis of burning mouth syndrome
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Above 40 years old, burning or pain in the oral mucosa for at least 6 months with clinically normal mucosa.
Exclusion criteria	Participants who were taking antidepressants, anxiolytic or anticonvulsant drugs or those who had undergone chemotherapy or radiotherapy were excluded. Patients who showed hyposalivation, alterations in blood count, glucose serum levels, iron, folic acid, vitamin b12 were also excluded.
Recruitment/selection of patients	Not specified
Age, gender and ethnicity	Age - Mean (SD): 61.9(8.76) years. Gender (M:F): 8:51. Ethnicity: Not specified
Further population details	1. Chronic orofacial pain: Chronic orofacial pain
Extra comments	Duration of pain not specified (minimum duration 6 months)
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Electrical Physical Modalities - Laser therapy. Infrared laser therapy 3 times a week. GaA1As, 830nm wavelength, 100mW output, continuous emissions, 3.57W/cm2, 5J energy per point, 176J/cm2 radiant exposure, application time 50s per point. Total 9 sessions. Duration 3 weeks. Concurrent medication/care: Not reported. Indirectness: No indirectness (n=19) Intervention 2: Electrical Physical Modalities - Laser therapy. Red laser therapy: InGaAlP, 685nm wavelength, 35mW output power, continuous emissions, 1.25W/cm2, 2J energy per point, 72 J/cm2 radiant exposure, application time 58s per point. Total 9 sessions (3 per week). Duration 3 weeks. Concurrent

	medication/care: Not specified. Indirectness: No indirectness (n=19) Intervention 3: Placebo/Sham. 9 sessions, similar to both laser interventions but the tool received a plastic tip with rubber interior that blocked radiation emissions, checked by means of a power meter prior to the applications. Duration 3 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness
Funding	Study funded by industry (Coorednacao de Aperfeicoamento de Pesal de Nivel Superior (CAPES) - Brazil)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY (INFRARED) versus PLACEBO/SHAM Protocol outcome 1: Quality of life - Actual outcome: Oral health impact profile at 3 weeks; Group 1: mean 6.89 (SD 4.05); n=20, Group 1: mean 13.39 (SD 3.62); n=19 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 2: Pain reduction - Actual outcome: VAS at 8 weeks follow up (including 3 week intervention); Group 1: mean 25.9 (SD 19.48); n=20, Group 2: mean 62.84 (SD 26.3); n=19; VAS 0-100 Top=High is poor outcome; Comments: Baseline: 85.26(14.25); 78.9(15.25) Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 0; Group 2 Number missing: 0 RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY (RED) versus PLACEBO/SHAM Protocol outcome 1: Quality of life - Actual outcome: Oral health impact profile at 3 weeks; Group 1: mean 9.77 (SD 4.92); n=19, Group 2: mean 13.39 (SD 3.62); n=19; OHIP Not specified Top=High is poor outcome; Comments: Baseline: 14.46(7.21); 17.8(5.37) Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 2: Pain reduction - Actual outcome: VAS at 8 weeks follow up (including 3 week intervention); Group 1: mean 41.11 (SD 27.14); n=19, Group 2: mean 62.84 (SD 26.3); n=19; VAS 0-100 Top=High is poor outcome; Comments: Baseline: 85.26(14.25);80.68(18.63) Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Sugaya 2016[329]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=30)
Countries and setting	Conducted in Brazil; Setting: Not specified
Line of therapy	Unclear
Duration of study	Intervention time: 2 week intervention plus 90 days follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Met the diagnostic criteria for burning mouth syndrome
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Other diagnoses ruled out (diabetes, anemia, hypovitaminosis).
Exclusion criteria	Clinical alterations in the oral mucosa potentially associated with the burning symptoms, hyposalivation, diabetes, B hypovitaminosis, and anemia. History of malignant of benign head and neck neoplasia, pregnancy, breast feeding
Recruitment/selection of patients	Stomatology Clinic of the Sao Paulo University School of Dentistry
Age, gender and ethnicity	Age - Mean (range): 59.7(29-83) years. Gender (M:F): 2:21. Ethnicity: Not specified
Further population details	1. Chronic orofacial pain: Chronic orofacial pain
Extra comments	Mean duration of symptoms 31.7 months (range 6 to 192)
Indirectness of population	No indirectness
Interventions	(n=15) Intervention 1: Electrical Physical Modalities - Laser therapy. 4 sessions of irradiation across 2 weeks, with a 3 day interval between each session. Laser irradiation delivered in scanning mode with laser point in contact with the mucosa. The energy released was 6J/cm2, and irradiation was applied on the entire area affected by the burning sensation. Irradiation time was determined by the extension of the affected area, according to a standardised formula. Duration 2 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness

	(n=15) Intervention 2: Placebo/Sham. Identical method but no laser energy was delivered. The machine still beeped at regular intervals so it appeared active. Duration 2 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness
Funding	Academic or government funding (State of Sao Paulo research foundation)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus PLACEBO/SHAM Protocol outcome 1: Pain reduction - Actual outcome: VAS (calculated from individual patient data) at 3 months; Group 1: mean 2 (SD 1.89); n=13, Group 2: mean 2.2 (SD 1.94); n=10; VAS 0-10 Top=High is poor outcome; Comments: Baseline not reported Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 2; Group 2 Number missing: 5 - Actual outcome: VAS (calculated from individual patient data) at 16 weeks; Group 1: mean 2.08 (SD 2.25); n=13, Group 2: mean 1.8 (SD 1.89); n=10; VAS 0-10 Top=High is poor outcome; Comments: Baseline values not reported Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 2; Group 2 Number missing: 5	
Protocol outcomes not reported by the study	Quality of life ; Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Tekin 2014[339]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=52)
Countries and setting	Conducted in Turkey; Setting: Not specified
Line of therapy	Unclear
Duration of study	Intervention time: 10 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR FMS criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Right handed, 18-65 years old, no analgesic use for at least 1 month, suffered persistent pain for longer than 6 months
Exclusion criteria	Causes of pain such as inflammatory or rheumatologic diseases, other pain related diseases, psychiatric disorders other than depression, drug abuse or dependency, or patients contraindicated to electrical therapy (e.g. epilepsy or head trauma).
Recruitment/selection of patients	2012-2013, patients who were evaluated at the Sisli Etfal education and research hospital physical medicine and rehab outpatient unit
Age, gender and ethnicity	Age - Mean (SD): 44.4(8.1) years. Gender (M:F): 4:47. Ethnicity: Not specified
Further population details	Chronic widespread pain
Extra comments	Duration of pain 12.1(6.47) years
Indirectness of population	No indirectness
Interventions	(n=27) Intervention 1: Electrical Physical Modalities - Transcranial Magnetic Stimulation (TMS). Repetitive TMS conducted with Magstim biphasic stimulation device with 8 shaped coil of 70mm. Conducted by a psychiatry physician. Resting motor threshold values determined for each patient using the minimum motor threshold method. Sessions conducted as 30 sequential series, for 5s, frequency 10Hz, application intensity 100%, interval between the series was 12s (total of 1500 stimuli per day given to each patient). Duration 10 days. Concurrent medication/care: Not specified. Indirectness: No indirectness

	(n=25) Intervention 2: Placebo/Sham. Identical treatment but a placebo coil system was used which produced similar sounds to the real application but without magnetic stimulation. Duration 10 days. Concurrent medication/care: Not specified. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCRANIAL MAGNETIC STIMULATION (TMS) versus PLACEBO/SHAM Protocol outcome 1: Quality of life - Actual outcome: WHOQOL-BREF physical domain at 10 days; Group 1: mean 14.26 (SD 2.52); n=27, Group 2: mean 11.33 (SD 2.84); n=24; WHOQOL-BREF 4-20 Top=High is good outcome; Comments: baseline: 11.07(2.54); 10.83(2.79) Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 1, Reason: NR - Actual outcome: WHOQOL-BREF psychological domain at 10 days; Group 1: mean 13.89 (SD 2.47); n=27, Group 2: mean 12.71 (SD 2.49); n=24; WHOQOL-BREF 4-20 Top=High is good outcome; Comments: Baseline: 12.15(2.57); 12.29(2.85) Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 1, Reason: NR Protocol outcome 2: Pain reduction - Actual outcome: VAS at 10 days; Group 1: mean 37.96 (SD 9.83); n=27, Group 2: mean 62.08 (SD 16.68); n=24; VAS 0-100 Top=High is poor outcome; Comments: Baseline: 79.63(12.24); 81.25(12.9) Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 1, Reason: NR Protocol outcome 3: Psychological distress - Actual outcome: MADRS at 10 days; Group 1: mean 10.14 (SD 3.96); n=27, Group 2: mean 10.24 (SD 6); n=24; MADRS Not specified Top=High is poor outcome; Comments: Baseline: 12.89(4.53); 12.25(6.44) Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 1, Reason: NR Protocol outcome 4: Discontinuation - Actual outcome: Discontinuation from treatment at 10 days; Group 1: 0/27, Group 2: 1/25 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 1, Reason: NR	
Protocol outcomes not reported by the study	Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Umezaki 2016[345]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=26)
Countries and setting	Conducted in USA; Setting: MUSC
Line of therapy	Unclear
Duration of study	Intervention + follow up: 10 day treatment and 8 weeks follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis of burning mouth syndrome
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnosis of BMS confirmed by (1) daily and deep bilateral burning sensation of the oral mucosa, burning sensation for at least 4-56 months, constant intensity or increasing intensity during the day, no worsening but possible improvement on eating or drinking, no interference with sleep and normal appearing oral mucosa
Exclusion criteria	Excluded one evidence of inflammation or autoimmune disease, current psychiatric conditions or drug abuse, or other contradictions for TMS, or starting new medication or changing medication within 4 weeks of starting the trial
Recruitment/selection of patients	Recruited through local newspaper adverts, from the oral pathology division in the MUSC dental clinic and through MUSC broadcast email
Age, gender and ethnicity	Age - Mean (SD): 63.85(9.56) years. Gender (M:F): 92.31% female. Ethnicity: Not specified
Further population details	1. Chronic orofacial pain
Extra comments	Duration of illness 63.42(65.51) years
Indirectness of population	No indirectness
Interventions	(n=14) Intervention 1: Electrical Physical Modalities - Transcranial Magnetic Stimulation (TMS). Device: MagVenture MagPro x100 stimulator with figure 8 coil. Resting motor threshold determined each for each individual. Machine set at 50% maximum output and TMS coil positioned around primary motor cortex, and moved until the area that best produced contraction of abductor pollicis brevis was identified. 10 sessions of 10Hz pulse train duration 5s, power intensity levels 110% of RMT, intertrain interval 10s for 15 minutes (total

	of 30,000 pulses). Duration 1 week. Concurrent medication/care: Not specified. Indirectness: No indirectness (n=12) Intervention 2: Placebo/Sham. Identical treatment but the coil was shielded so that actual stimulation did not occur. Duration 1 week. Concurrent medication/care: Not specified. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCRANIAL MAGNETIC STIMULATION (TMS) versus PLACEBO/SHAM Protocol outcome 1: Pain reduction - Actual outcome: Pain (McGill pain questionnaire) at 8 weeks (follow up); Group 1: mean 1.33 (SD 0.78); n=12, Group 2: mean 2.88 (SD 1.36); n=8; SFMPQ Not specified Top=High is poor outcome; Comments: Baseline: 2.54(0.84); 3.63(1.51) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 2, Reason: Lost to follow up; Group 2 Number missing: 4, Reason: Lost to follow up Protocol outcome 3: Discontinuation - Actual outcome: Discontinued intervention at 1 week; Group 1: 0/14, Group 2: 0/12 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: 2, Reason: Lost to follow up; Group 2 Number missing: 4, Reason: Lost to follow up	
Protocol outcomes not reported by the study	Quality of life ; Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Valenzuela 2017[346]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=44)
Countries and setting	Conducted in Spain; Setting: Not specified
Line of therapy	Unclear
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Burning mouth syndrome diagnosis according to international classification of headaches
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	BMS diagnosis, continuous symptoms of oral burning or pain on a daily or almost daily basis during all or part of the day for more than 6 months and absence of local or systemic factors that could produce the same symptoms
Exclusion criteria	History of head and neck malignancy radiation therapy to the head and neck area, poorly managed conditions such as diabetes, thyroid disease, Sjorgrens syndrome, rheumatological diseases, anemia, analgesics or NSAID use, pregnancy.
Recruitment/selection of patients	Consecutive patients diagnosed with idiopathic burning mouth syndrome attending the department of oral medicine (FoM and Dentistry, UoM, Spain).
Age, gender and ethnicity	Age - Mean (SD): 65.5 (10.6) years. Gender (M:F): 3:41. Ethnicity: Not specified
Further population details	1. Chronic orofacial pain
Extra comments	Duration of pain not specified
Indirectness of population	No indirectness
Interventions	(n=16) Intervention 1: Electrical Physical Modalities - Laser therapy. Low level laser. 815nm wavelength, 1W output power, 4 seconds, 4J, fluence rate 133.3Jcm-2. Applied intra-orally and continuously, perpendicularly in contact with the mucosa in areas where patient reported symptoms. Spot sizes were 0.03cm3 and ten points over each area presenting symptoms were irradiated. Duration 4 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness

	(n=16) Intervention 2: Electrical Physical Modalities - Laser therapy. Low level laser. 815nm wavelength, 1W output power, 6 seconds, 6J, fluence rate 200Jcm-2. Applied intra-orally and continuously, perpendicularly in contact with the mucosa in areas where patient reported symptoms. Spot sizes were 0.03cm3 and ten points over each area presenting symptoms were irradiated. Duration 4 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness (n=12) Intervention 3: Placebo/Sham. Sham: same procedure but laser turned off. Duration 4 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY (LOW INTENSITY) versus PLACEBO/SHAM

Protocol outcome 1: Quality of life
- Actual outcome: Oral health impact profile at 4 weeks; Group 1: mean 28.5 (SD 3.1); n=16, Group 2: mean 29.25 (SD 6.1); n=12; OHIP 0-70 Top=High is poor outcome; Comments: Baseline: 29.88(3.6); 29.33(5.9)
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: NR; Group 2 Number missing: NR

Protocol outcome 2: Pain reduction
- Actual outcome: VAS at 4 weeks; Group 1: mean 6.38 (SD 1.6); n=16, Group 2: mean 7.65 (SD 1.2); n=12; VAS 0-10 Top=High is poor outcome; Comments: Baseline: 7.56(1.5); 7.83(1.3)
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: NR; Group 2 Number missing: NR

Protocol outcome 3: Psychological distress
- Actual outcome: HADS:A at 4 weeks; Group 1: mean 10.44 (SD 3.9); n=16, Group 2: mean 10.33 (SD 3.5); n=12; HADS:A 0-21 Top=High is poor outcome; Comments: Baseline: 10.44(3.9); 10.25(3.5)
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing:: NR; Group 2 Number missing: NR
- Actual outcome: HADS:D at 4 weeks; Group 1: mean 7.19 (SD 4.9); n=16, Group 2: mean 7.25 (SD 4.5); n=12; HADS:D 0-21 Top=High is poor outcome; Comments: Baseline: 7.19(4.9); 7.25(4.5)
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: NR; Group 2 Number missing: NR

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY (HIGH INTENSITY) versus PLACEBO/SHAM

Protocol outcome 1: Quality of life - Actual outcome: Oral health impact profile at 4 weeks; Group 1: mean 28.25 (SD 6.1); n=16, Group 2: mean 29.25 (SD 6.3); n=12; OHIP 0-70 Top=High is poor outcome; Comments: Baseline: 29.57(5.9); 29.33(5.9) Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: NR; Group 2 Number missing: NR Protocol outcome 2: Pain reduction - Actual outcome: VAS at 4 weeks; Group 1: mean 7.06 (SD 1.8); n=16, Group 2: mean 7.65 (SD 1.2); n=12; VAS 0-10 Top=High is poor outcome; Comments: Baseline: 8.38(1.3); 7.83(1.3) Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: NR; Group 2 Number missing: NR Protocol outcome 3: Psychological distress - Actual outcome: HADS:A at 4 weeks; Group 1: mean 11.88 (SD 3.2); n=16, Group 2: mean 10.33 (SD 3.5); n=12; HADS:A 0-21 Top=High is poor outcome; Comments: Baseline: 11.75(3.4); 10.25(3.5) Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: NR; Group 2 Number missing: NR - Actual outcome: HADS:D at 4 weeks; Group 1: mean 9.88 (SD 3.3); n=16, Group 2: mean 7.25 (SD 4.5); n=12; HADS:D 0-21 Top=High is poor outcome; Comments: Baseline: 10(3.3); 7.25(4.5) Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference at baseline in outcome: 10(3.3); 7.25(4.5); Group 1 Number missing:: NR; Group 2 Number missing: NR	
Protocol outcomes not reported by the study	Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Venancio 2005[354]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=30)
Countries and setting	Conducted in Brazil; Setting: Not specified
Line of therapy	Unclear
Duration of study	Intervention + follow up: 3 weeks (with 8 week follow up)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: TMD diagnosis according to criteria of the American Academy of Orofacial pain
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Pain restricted to the joint area, associated with the absence of any muscle tenderness during palpation.
Exclusion criteria	Psychiatric disorders, heart diseases, epilepsy, pregnancy, RA, degenerative joint disease, tumours, people with pacemakers
Recruitment/selection of patients	Consecutive patients that presented for diagnosis and treatment of TMD in the OTDC clinic at a dentistry school.
Age, gender and ethnicity	Age - Mean (range): 36.25(13-63) years. Gender (M:F): 5:25. Ethnicity: Not specified
Further population details	1. Chronic orofacial pain
Extra comments	Mean duration of pain 44.8 months (range 6-120 months)
Indirectness of population	No indirectness
Interventions	(n=15) Intervention 1: Electrical Physical Modalities - Laser therapy. Twice a week for 3 weeks. Using Ga0Al-As laser at 780nm wavelength. Output of 30mW, 10s duration, at 6.3Jcm-2 at 3 points in each TMJ. Duration 3 weeks. Concurrent medication/care: Not reported (other than advice about resting joints, following a soft diet and conscious relaxation of masticatory muscles). Indirectness: No indirectness (n=15) Intervention 2: Placebo/Sham. Identical treatment but the laser device was not turned on. Duration 3 weeks. Concurrent medication/care: Not reported (other than advice about resting joints, following a soft diet

	and conscious relaxation of masticatory muscles). Indirectness: No indirectness
Funding	Academic or government funding (FAPESP Sao Paulo Research Support Foundation)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LASER THERAPY versus PLACEBO/SHAM Protocol outcome 1: Pain reduction - Actual outcome: VAS at 8 weeks; Group 1: mean 1.6 (SD 2.03); n=15, Group 2: mean 3.67 (SD 2.85); n=15; VAS 0-10 Top=High is poor outcome Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life ; Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Yagci 2014[375]
Study type	RCT (randomised; Parallel)
Number of studies (number of participants)	(n=28)
Countries and setting	Conducted in Turkey; Setting: Not specified
Line of therapy	Unclear
Duration of study	2 week intervention and 3 months follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for fibromyalgia
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 18-60 years, no improvement in symptoms regardless of using medical treatment for at least 3 months.
Exclusion criteria	Other diagnoses such as inflammatory rheumatic disease, current primary psychiatric disease, previous surgical treatment to the cranial area, pregnancy, or history of substance abuse
Recruitment/selection of patients	Not specified
Age, gender and ethnicity	Age - Mean (SD): 44.9(8.6) years. Gender (M:F): All female. Ethnicity: Not specified
Further population details	Chronic widespread pain
Extra comments	Mean duration of symptoms 53.5 (29.8) months
Indirectness of population	No indirectness
Interventions	(n=14) Intervention 1: Electrical Physical Modalities - Transcranial Magnetic Stimulation (TMS). 2 week interventions, with 10 sessions of low-frequency rTMS applied from Monday to Friday of each week. The stimulation area was the left primary motor cortex. Magnetic stimulation applied using a MagBenture machine, using a parabolic coil that was oriented at a tangent to the scalp. The resting motor threshold was determined before each session using single pulse stimulation over the left primary motor cortex, which was defined as the minimal intensity required to evoke MEPs of 50mV peak-to-peak amplitude in 5 out of 10 consecutive trials. The main stimulation parameters were 90% of motor threshold for 60 seconds at 1Hz and 45 second intervals between each trains. 1200 pulses were therefore administered in each session. Duration 2 weeks. Concurrent medication/care: Medications remained stable throughout the study. Indirectness: No indirectness

	(n=14) Intervention 2: Placebo/Sham. Sham stimulation carried out with the same parabolic coil, which was placed at 90 degree angles to the motor cortex area. No further details. Duration 2 weeks. Concurrent medication/care: Medications remained stable throughout. Indirectness: No indirectness
Funding	Not reported
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSCRANIAL MAGNETIC STIMULATION (TMS) versus PLACEBO/SHAM Protocol outcome 1: Quality of life - Actual outcome: FIQ at 3 months; Group 1: mean 36.95 (SD 24.27); n=13, Group 2: mean 48.13 (SD 16.79); n=12; VAS 0-10 Top=High is poor outcome; Comments: Baseline: 66.09(15.13); 65.1(12.92) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Beck depression inventory baseline difference; Group 1 Number missing: 1, Reason: NR; Group 2 Number missing: 2, Reason: NR Protocol outcome 2: Pain reduction - Actual outcome: VAS at 3 months; Group 1: mean 4.75 (SD 2.76); n=13, Group 2: mean 5.3 (SD 2.49); n=12; VAS 0-10 Top=High is poor outcome; Comments: Baseline: 7.75(1.54); 7.61(2.14) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Beck depression inventory baseline difference; Group 1 Number missing: 1, Reason: NR; Group 2 Number missing: 2, Reason: NR Protocol outcome 3: Psychological distress - Actual outcome: BDI at 3 months; Group 1: mean 16.75 (SD 10.6); n=13, Group 2: mean 14.15 (SD 8); n=12; Beck depression inventory 0-61 Top=High is poor outcome; Comments: Baseline: 19.58(9.33);18.53(9.7) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Beck depression inventory baseline difference; Group 1 Number missing: 1, Reason: NR; Group 2 Number missing: 2, Reason: NR	
Protocol outcomes not reported by the study	Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

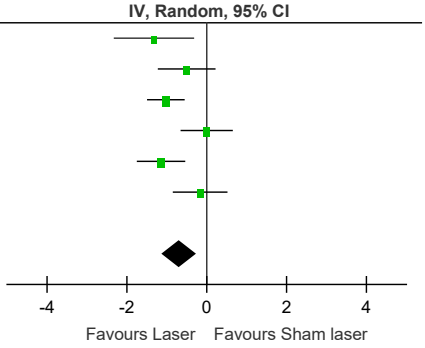
Appendix E: Forest plots

E.1 Laser therapy versus sham laser therapy

Figure 2: Quality of life at ≤3 months (Oral health impact profile, FIQ, high is poor outcome, final values)

	Laser			Sham laser				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Arbabi-Kalati 2015	12.8	11.4	10	28.6	11.5	10	11.1%	-1.32 [-2.31, -0.33]
Armagan 2006	58.5	10.33	16	63.63	9.59	16	15.8%	-0.50 [-1.21, 0.20]
Bardellini 2019	7.09	2.59	43	10.64	4.13	42	21.2%	-1.02 [-1.48, -0.57]
Panton 2013	55	16	20	55	12	18	17.2%	0.00 [-0.64, 0.64]
Spanemberg 2015	8.293	4.72	39	13.39	3.62	19	18.2%	-1.14 [-1.73, -0.55]
Valenzuela 2017	28.38	4.84	31	29.25	6.1	12	16.5%	-0.16 [-0.83, 0.50]
Total (95% CI)			**159**			**117**	**100.0%**	**-0.68 [-1.10, -0.25]**

Heterogeneity: Tau² = 0.17; Chi² = 13.07, df = 5 (P = 0.02); I² = 62%
Test for overall effect: Z = 3.12 (P = 0.002)



NB. Heterogeneity not explained by subgroup analysis

Figure 3: Quality of life at ≤3 months (SF-36 physical component summary score, 0-100, high is good outcome, change scores)

	Laser			Sham laser				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Chow 2004	4	8.22	10	1.22	6.32	10	21.8%	2.78 [-3.65, 9.21]
Chow 2006	3.2	10.78	45	1.3	4.28	45	78.2%	1.90 [-1.49, 5.29]
Total (95% CI)			**55**			**55**	**100.0%**	**2.09 [-0.91, 5.09]**

Heterogeneity: Chi² = 0.06, df = 1 (P = 0.81); I² = 0%
Test for overall effect: Z = 1.37 (P = 0.17)

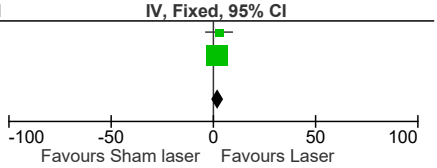
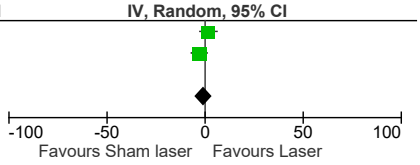


Figure 4: Quality of life at ≤3 months (SF-36 mental component summary score, 0-100, high is good outcome, change scores)

	Laser			Sham laser				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Chow 2004	1.71	3.79	10	0	6.01	10	48.0%	1.71 [-2.69, 6.11]
Chow 2006	2.4	8.2	45	5.4	10.9841	45	52.0%	-3.00 [-7.00, 1.00]
Total (95% CI)			**55**			**55**	**100.0%**	**-0.74 [-5.35, 3.87]**

Heterogeneity: Tau² = 6.48; Chi² = 2.41, df = 1 (P = 0.12); I² = 58%
Test for overall effect: Z = 0.31 (P = 0.75)



NB. Heterogeneity not explained by subgroup analysis

Figure 5: Quality of life at >3 months (FIQ, 0-100, high is poor outcome, final values)

	Laser			Sham laser				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Armagan 2006	62.06	8.99	16	66.94	8.44	16	28.4%	-0.55 [-1.25, 0.16]
Bardellini 2019	7.43	3.78	43	10.43	2.99	42	71.6%	-0.87 [-1.32, -0.43]
Total (95% CI)			**59**			**58**	**100.0%**	**-0.78 [-1.16, -0.40]**

Heterogeneity: Chi² = 0.58, df = 1 (P = 0.45); I² = 0%
Test for overall effect: Z = 4.05 (P < 0.0001)

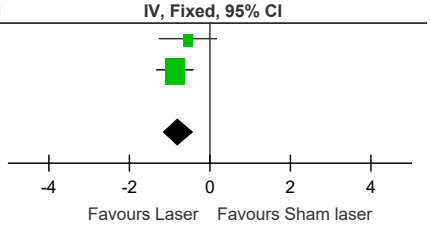
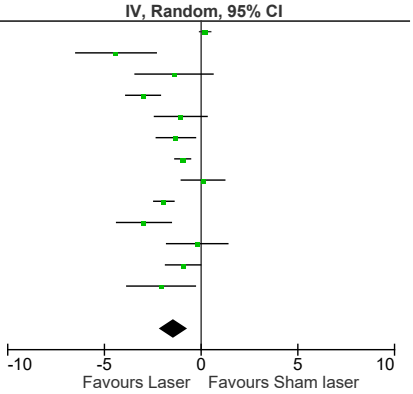


Figure 6: Pain reduction at ≤3 months (VAS, NRS, FIQ pain scale, high is poor outcome, 0-10, final values and change scores)

Study or Subgroup	Laser Mean	Laser SD	Laser Total	Sham laser Mean	Sham laser SD	Sham laser Total	Weight	Mean Difference IV, Random, 95% CI
Altan 2005	4.13	0.58	23	3.92	0.42	25	9.8%	0.21 [-0.08, 0.50]
Arbabi-Kalati 2015	3.6	3	10	8	1.5	10	5.3%	-4.40 [-6.48, -2.32]
Chow 2004	-2.1	2.84	10	-0.7	1.58	10	5.4%	-1.40 [-3.41, 0.61]
Chow 2006	-2.7	1.9971	45	0.3	2.33	45	8.6%	-3.00 [-3.90, -2.10]
da Cunha 2008	3.62	2.45	20	4.67	1.9	20	7.2%	-1.05 [-2.41, 0.31]
Del vecchio 2019	-3.517	2.2139	29	-2.214	1.6635	28	8.2%	-1.30 [-2.32, -0.29]
Gur 2002	1.24	0.72	25	2.19	0.74	25	9.7%	-0.95 [-1.35, -0.55]
Panton 2013	6.2	2.1	20	6.1	1.4	18	7.9%	0.10 [-1.02, 1.22]
Rohlig 2011	3.05	0.714	20	4.975	0.954	20	9.5%	-1.92 [-2.45, -1.40]
Spanemberg 2015	3.33	2.47	39	6.284	2.63	19	7.1%	-2.95 [-4.37, -1.54]
Sugaya 2016	2	1.89	13	2.2	1.94	10	6.6%	-0.20 [-1.78, 1.38]
Valenzuela 2017	6.72	1.74	32	7.65	1.2	12	8.5%	-0.93 [-1.84, -0.02]
Venancio 2005	1.6	2.03	15	3.67	2.85	15	6.1%	-2.07 [-3.84, -0.30]
Total (95% CI)			**301**			**257**	**100.0%**	**-1.42 [-2.12, -0.73]**

Heterogeneity: Tau² = 1.27; Chi² = 114.87, df = 12 (P < 0.00001); I² = 90%
Test for overall effect: Z = 4.00 (P < 0.0001)



NB. Heterogeneity not explained by subgroup analysis

Figure 7: Pain reduction at >3 months (VAS, high is poor outcome, 0-10, final values)

Study or Subgroup	Laser Mean	Laser SD	Laser Total	Sham laser Mean	Sham laser SD	Sham laser Total	Weight	Mean Difference IV, Fixed, 95% CI
Altan 2005	3.17	0.58	23	3.8	0.51	25	96.8%	-0.63 [-0.94, -0.32]
Sugaya 2016	2.08	2.25	13	1.8	1.89	10	3.2%	0.28 [-1.41, 1.97]
Total (95% CI)			**36**			**35**	**100.0%**	**-0.60 [-0.91, -0.30]**

Heterogeneity: Chi² = 1.07, df = 1 (P = 0.30); I² = 7%
Test for overall effect: Z = 3.86 (P = 0.0001)

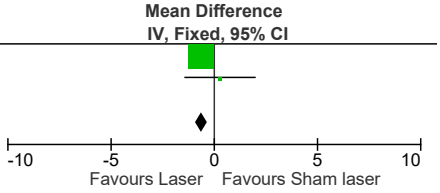


Figure 8: Psychological distress at ≤3 months (Hospital anxiety and depression rating scale, anxiety subscale, 0-21, high is poor outcome, final values)

Study or Subgroup	Laser Mean	Laser SD	Laser Total	Sham laser Mean	Sham laser SD	Sham laser Total	Weight	Mean Difference IV, Fixed, 95% CI
Valenzuela 2017	11.16	3.639	32	10.33	3.5	12	100.0%	0.83 [-1.52, 3.18]
Total (95% CI)			**32**			**12**	**100.0%**	**0.83 [-1.52, 3.18]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.69 (P = 0.49)

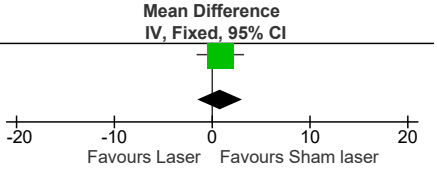


Figure 9: Psychological distress at ≤3 months (Hospital anxiety and depression rating scale, depression subscale, 0-21, high is poor outcome, final values)

Study or Subgroup	Laser Mean	Laser SD	Laser Total	Sham laser Mean	Sham laser SD	Sham laser Total	Weight	Mean Difference IV, Fixed, 95% CI
Valenzuela 2017	8.535	4.389	32	7.25	4.5	16	100.0%	1.29 [-1.39, 3.96]
Total (95% CI)			**32**			**16**	**100.0%**	**1.29 [-1.39, 3.96]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.94 (P = 0.35)

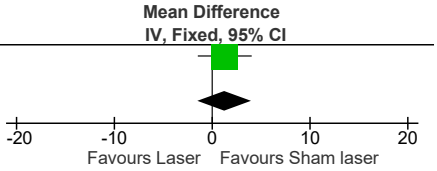
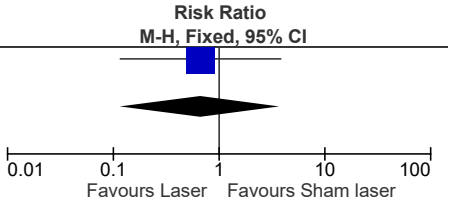


Figure 10: Discontinuation at ≤3 months

Study or Subgroup	Laser Events	Laser Total	Sham laser Events	Sham laser Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chow 2006	2	45	3	45	100.0%	0.67 [0.12, 3.80]
Total (95% CI)		**45**		**45**	**100.0%**	**0.67 [0.12, 3.80]**
Total events	2		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.46 (P = 0.65)



E.2 TMS versus sham TMS

Figure 11: Quality of life at ≤3 months (SF-36 physical summary score, 0-100, high is good outcome, change scores)

Study or Subgroup	TMS Mean	TMS SD	TMS Total	Sham TMS Mean	Sham TMS SD	Sham TMS Total	Weight	Mean Difference IV, Fixed, 95% CI
Boyer 2014	1.4	9	16	0.4	4.8	13	100.0%	1.00 [-4.12, 6.12]
Total (95% CI)			**16**			**13**	**100.0%**	**1.00 [-4.12, 6.12]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.38 (P = 0.70)

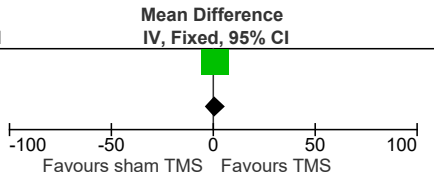


Figure 12: Quality of life at ≤3 months (SF-36 mental summary score, 0-100, high is good outcome, change scores)

Study or Subgroup	TMS Mean	TMS SD	TMS Total	Sham TMS Mean	Sham TMS SD	Sham TMS Total	Weight	Mean Difference IV, Fixed, 95% CI
Boyer 2014	5	6.9	16	-1.6	7.6	13	100.0%	6.60 [1.26, 11.94]
Total (95% CI)			**16**			**13**	**100.0%**	**6.60 [1.26, 11.94]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.42 (P = 0.02)

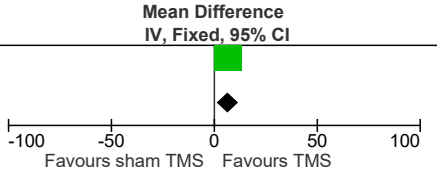


Figure 13: Quality of life at ≤3 months (WHOQOL-BREF physical domain, 4-20, high is good outcome, final values)

Study or Subgroup	TMS Mean	TMS SD	TMS Total	Sham TMS Mean	Sham TMS SD	Sham TMS Total	Weight	Mean Difference IV, Fixed, 95% CI
Tekin 2014	14.6	2.52	27	11.33	2.84	24	100.0%	3.27 [1.79, 4.75]
Total (95% CI)			**27**			**24**	**100.0%**	**3.27 [1.79, 4.75]**

Heterogeneity: Not applicable
Test for overall effect: Z = 4.33 (P < 0.0001)

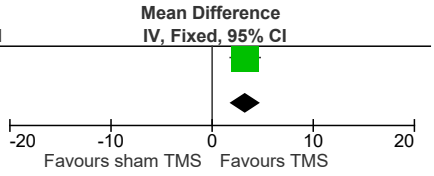


Figure 14: Quality of life at ≤3 months (WHOQOL-BREF psychological domain, 4-20, high is good outcome, final values)

Study or Subgroup	TMS Mean	TMS SD	TMS Total	Sham TMS Mean	Sham TMS SD	Sham TMS Total	Weight	Mean Difference IV, Fixed, 95% CI
Tekin 2014	13.89	2.47	27	12.71	2.49	24	100.0%	1.18 [-0.18, 2.54]
Total (95% CI)			**27**			**24**	**100.0%**	**1.18 [-0.18, 2.54]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.70 (P = 0.09)

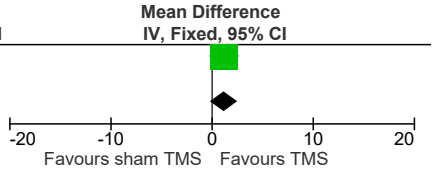


Figure 15: Quality of life at ≤3 months (FIQ, 0-100, high is poor outcome, final values)

Study or Subgroup	TMS Mean	TMS SD	TMS Total	Sham TMS Mean	Sham TMS SD	Sham TMS Total	Weight	Mean Difference IV, Fixed, 95% CI
Lee 2012	51.8	13.51	10	53.7	27.3	5	16.0%	-1.90 [-27.25, 23.45]
Short 2011	38.99	19.44	10	47.93	14.7	10	45.1%	-8.94 [-24.05, 6.17]
Yagci 2014	36.95	24.27	13	48.13	16.79	12	38.9%	-11.18 [-27.44, 5.08]
Total (95% CI)			**33**			**27**	**100.0%**	**-8.69 [-18.83, 1.46]**

Heterogeneity: Chi² = 0.37, df = 2 (P = 0.83); I² = 0%
Test for overall effect: Z = 1.68 (P = 0.09)

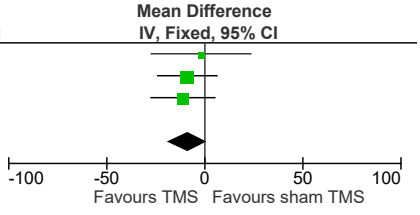


Figure 16: Quality of life at >3 months (FIQ, 0-100, high is poor outcome, final values)

Study or Subgroup	TMS Mean	TMS SD	TMS Total	Sham TMS Mean	Sham TMS SD	Sham TMS Total	Weight	Mean Difference IV, Fixed, 95% CI
Mhalla 2011	56	17.7	15	63.3	15	15	100.0%	-7.30 [-19.04, 4.44]
Total (95% CI)			**15**			**15**	**100.0%**	**-7.30 [-19.04, 4.44]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.22 (P = 0.22)

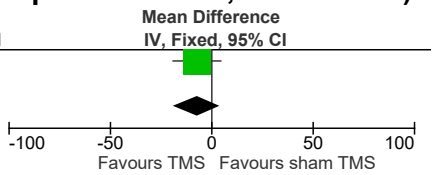
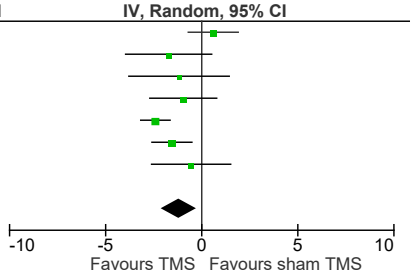


Figure 17: Pain reduction at ≤3 months (VAS, McGill Pain questionnaire, 0-10, high is poor outcome, final values)

Study or Subgroup	TMS Mean	TMS SD	TMS Total	Sham TMS Mean	Sham TMS SD	Sham TMS Total	Weight	Mean Difference IV, Random, 95% CI
Carretero 2009	8.1	1	14	7.5	2.1	12	16.7%	0.60 [-0.70, 1.90]
Dall'Agnol 2014	3.57	2.82	12	5.29	2.78	12	10.2%	-1.72 [-3.96, 0.52]
Lee 2012	6.05	2.23	10	7.23	2.53	5	8.4%	-1.18 [-3.79, 1.43]
Short 2011	4.41	1.95	10	5.37	2.02	10	13.3%	-0.96 [-2.70, 0.78]
Tekin 2014	3.796	0.983	27	6.208	1.668	24	21.2%	-2.41 [-3.18, -1.65]
Umezaki 2016	1.33	0.78	12	2.88	1.36	8	18.9%	-1.55 [-2.59, -0.51]
Yagci 2014	4.75	2.76	13	5.3	2.49	12	11.2%	-0.55 [-2.61, 1.51]
Total (95% CI)			**98**			**83**	**100.0%**	**-1.17 [-2.10, -0.24]**

Heterogeneity: Tau² = 0.91; Chi² = 16.82, df = 6 (P = 0.010); I² = 64%
Test for overall effect: Z = 2.46 (P = 0.01)



NB. Heterogeneity not explained by subgroup analysis

Figure 18: Physical function at ≤3 months (BPI functional impairment subscale, 0-10, high is poor outcome, final values)

Study or Subgroup	TMS Mean	TMS SD	TMS Total	Sham TMS Mean	Sham TMS SD	Sham TMS Total	Weight	Mean Difference IV, Fixed, 95% CI
Short 2011	3.6	2.18	10	3.79	2.69	10	100.0%	-0.19 [-2.34, 1.96]
Total (95% CI)			**10**			**10**	**100.0%**	**-0.19 [-2.34, 1.96]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.17 (P = 0.86)

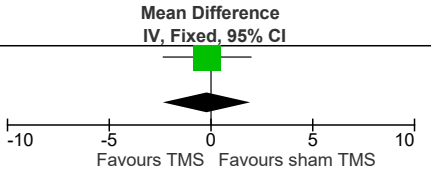


Figure 19: Psychological distress at ≤3 months (Beck depression inventory, 0-61, high is poor outcome, final values and change scores)

Study or Subgroup	TMS Mean	TMS SD	TMS Total	Sham TMS Mean	Sham TMS SD	Sham TMS Total	Weight	Mean Difference IV, Fixed, 95% CI
Boyer 2014	-1.9	2.8	16	-0.1	4.4	13	84.8%	-1.80 [-4.56, 0.96]
Lee 2012	17.85	6.553	10	18.3	5.8	5	15.2%	-0.45 [-6.96, 6.06]
Total (95% CI)			**26**			**18**	**100.0%**	**-1.59 [-4.13, 0.94]**

Heterogeneity: Chi² = 0.14, df = 1 (P = 0.71); I² = 0%
Test for overall effect: Z = 1.23 (P = 0.22)

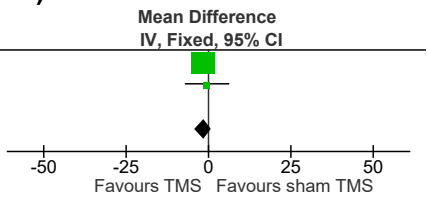


Figure 20: Psychological distress at ≤3 months (Hamilton depression rating scale, MADRS, BDI, high is poor outcome, final values)

Study or Subgroup	TMS Mean	TMS SD	TMS Total	Sham TMS Mean	Sham TMS SD	Sham TMS Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Short 2011	14.1	9.42	10	16.4	8.18	10	20.8%	-0.25 [-1.13, 0.63]
Tekin 2014	10.14	3.96	27	10.24	6	24	53.3%	-0.02 [-0.57, 0.53]
Yagci 2014	16.75	10.6	13	14.15	8	12	25.9%	0.27 [-0.52, 1.05]
Total (95% CI)			**50**			**46**	**100.0%**	**0.01 [-0.39, 0.41]**

Heterogeneity: Chi² = 0.75, df = 2 (P = 0.69); I² = 0%
Test for overall effect: Z = 0.03 (P = 0.97)

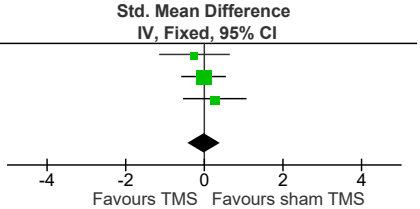


Figure 21: Psychological distress at ≤3 months (HADS anxiety, 0-21, high is poor outcome, change scores)

Study or Subgroup	TMS Mean	TMS SD	TMS Total	Sham TMS Mean	Sham TMS SD	Sham TMS Total	Weight	Mean Difference IV, Fixed, 95% CI
Boyer 2014	0.4	1.7	16	0.5	2.3	13	100.0%	-0.10 [-1.60, 1.40]
Total (95% CI)			**16**			**13**	**100.0%**	**-0.10 [-1.60, 1.40]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.13 (P = 0.90)

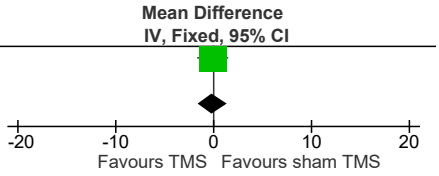


Figure 22: Psychological distress at >3 months (HADS anxiety, 0-21, high is poor outcome, change scores)

Study or Subgroup	TMS Mean	TMS SD	TMS Total	Sham TMS Mean	Sham TMS SD	Sham TMS Total	Weight	Mean Difference IV, Fixed, 95% CI
Mhalla 2011	9.2	4.9	15	9.4	5.7	15	100.0%	-0.20 [-4.00, 3.60]
Total (95% CI)			**15**			**15**	**100.0%**	**-0.20 [-4.00, 3.60]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.10 (P = 0.92)

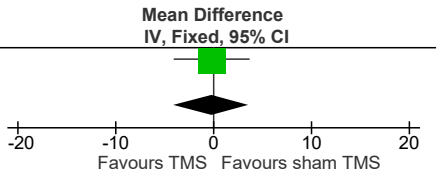


Figure 23: Psychological distress at >3 months (HADS depression, 0-21, high is poor outcome, change scores)

Study or Subgroup	TMS Mean	TMS SD	TMS Total	Sham TMS Mean	Sham TMS SD	Sham TMS Total	Weight	Mean Difference IV, Fixed, 95% CI
Mhalla 2011	8.6	4.7	15	7.4	4	15	100.0%	1.20 [-1.92, 4.32]
Total (95% CI)			**15**			**15**	**100.0%**	**1.20 [-1.92, 4.32]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.75 (P = 0.45)

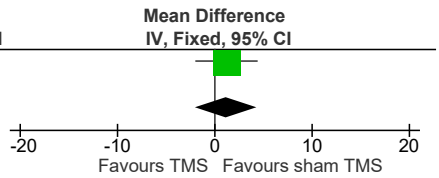


Figure 24: Pain interference at >3 months (BPI pain interference, 0-10, high is poor outcome, final values)

Study or Subgroup	TMS Mean	TMS SD	TMS Total	Sham TMS Mean	Sham TMS SD	Sham TMS Total	Weight	Mean Difference IV, Fixed, 95% CI
Mhalla 2011	4.1	1.7	15	6	1.5	15	100.0%	-1.90 [-3.05, -0.75]
Total (95% CI)			**15**			**15**	**100.0%**	**-1.90 [-3.05, -0.75]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.25 (P = 0.001)

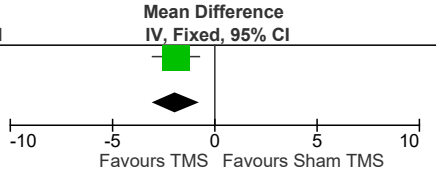
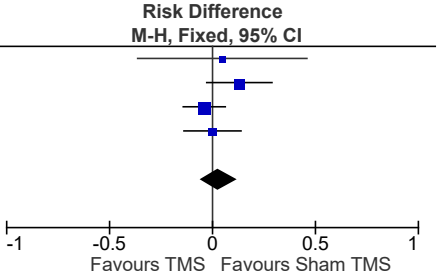


Figure 25: Discontinuation at ≤3 months

Study or Subgroup	TMS Events	TMS Total	Sham TMS Events	Sham TMS Total	Weight	Risk Difference M-H, Fixed, 95% CI
Lee 2012	5	15	2	7	13.9%	0.05 [-0.36, 0.46]
Panton 2013	3	23	0	18	29.4%	0.13 [-0.03, 0.29]
Tekin 2014	0	27	1	25	37.8%	-0.04 [-0.14, 0.06]
Umezaki 2016	0	14	0	12	18.8%	0.00 [-0.14, 0.14]
Total (95% CI)		**79**		**62**	**100.0%**	**0.03 [-0.06, 0.12]**
Total events	8		3			

Heterogeneity: Chi² = 3.53, df = 3 (P = 0.32); I² = 15%
Test for overall effect: Z = 0.65 (P = 0.51)



E.3 TDCS versus sham TDCS

Figure 26: Quality of life at ≤3 months (SF-36 mental summary score, 0-100, high is good outcome, final values)

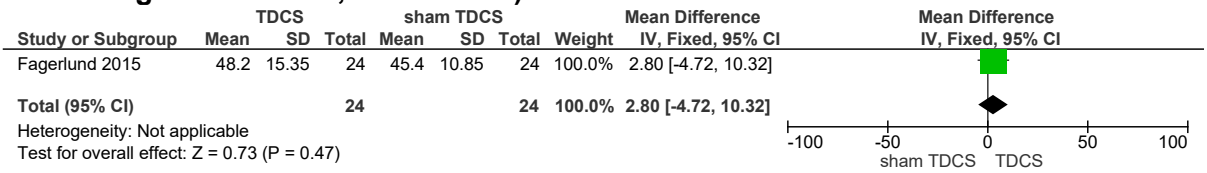


Figure 27: Quality of life at ≤3 months (SF-36 physical summary score, 0-100, high is good outcome, final values)

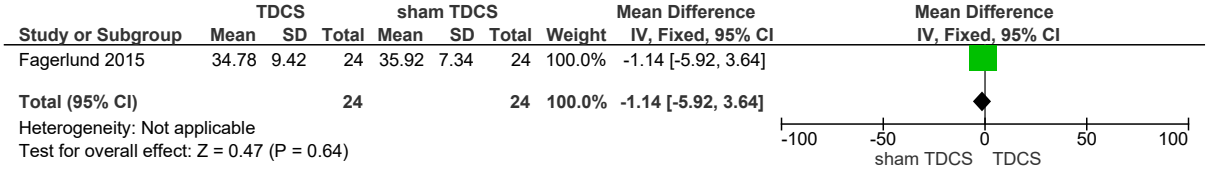


Figure 28: Quality of life at ≤3 months (SF-36 physical function subscale, 0-100, high is good outcome, final values)

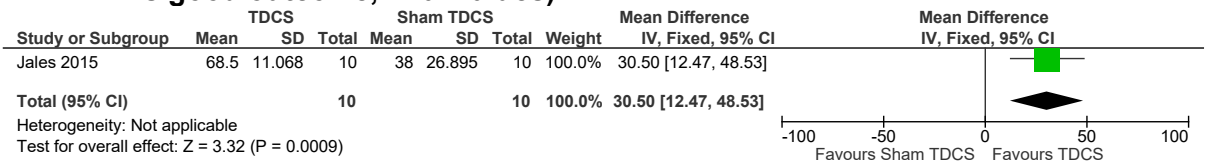


Figure 29: Quality of life at ≤3 months (SF-36 physical role subscale, 0-100, high is good outcome, final values)

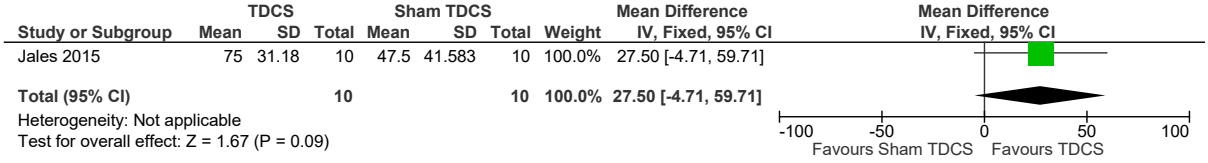


Figure 30: Quality of life at ≤3 months (SF-36 bodily pain subscale, 0-100, high is good outcome, final values)

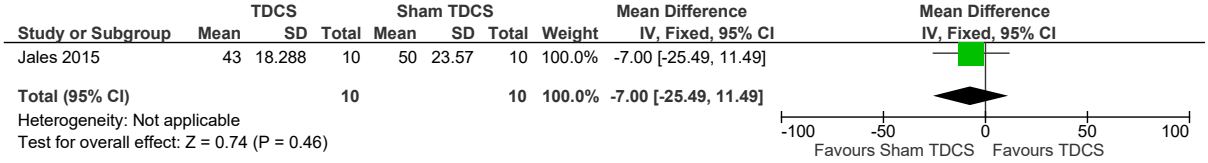


Figure 31: Quality of life at ≤3 months (SF-36 general health subscale, 0-100, high is good outcome, final values)

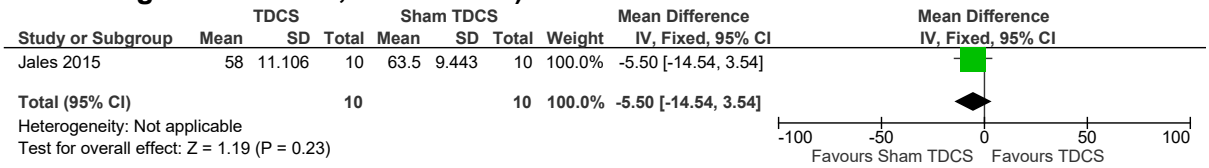


Figure 32: Quality of life at ≤3 months (SF-36 vitality subscale, 0-100, high is good outcome, final values)

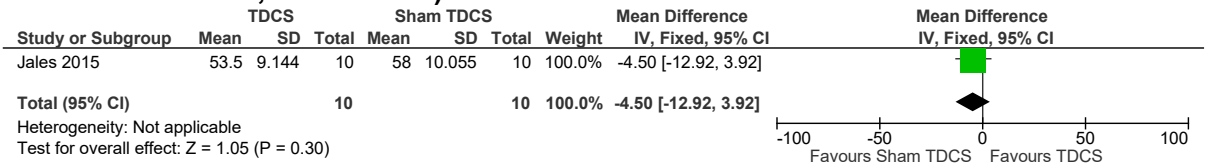


Figure 33: Quality of life at ≤3 months (SF-36 general aspects subscale, 0-100, high is good outcome, final values)

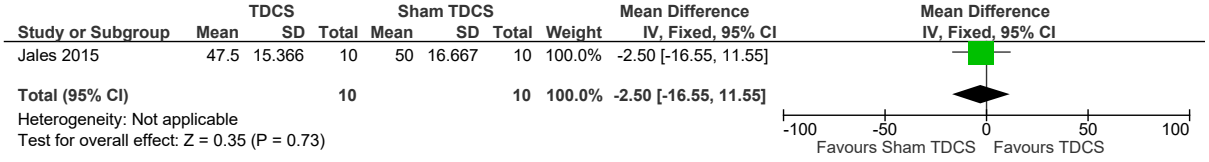


Figure 34: Quality of life at ≤3 months (SF-36 emotional role subscale, 0-100, high is good outcome, final values)

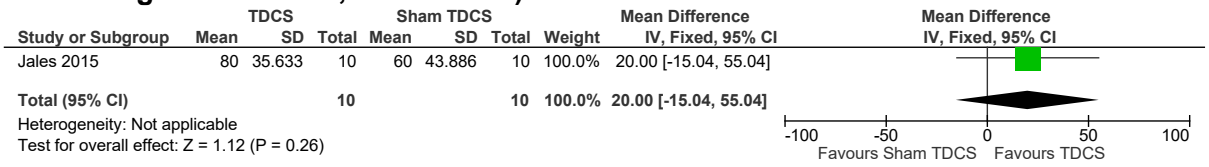


Figure 35: Quality of life at ≤3 months (SF-36 mental health subscale, 0-100, high is good outcome, final values)

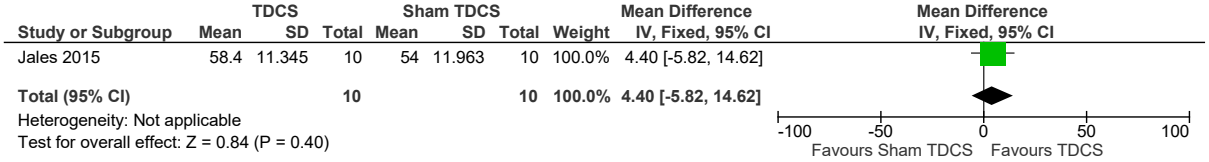
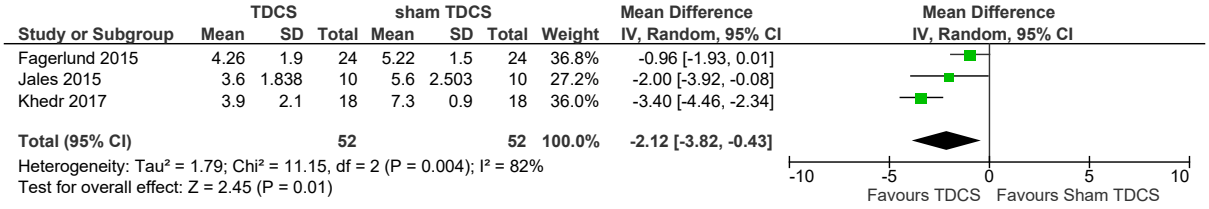
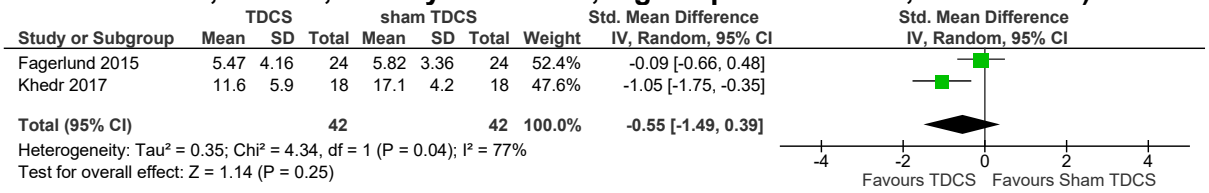


Figure 36: Pain reduction at ≤3 months (NRS, VAS, 0-10, high is poor outcome, final values)



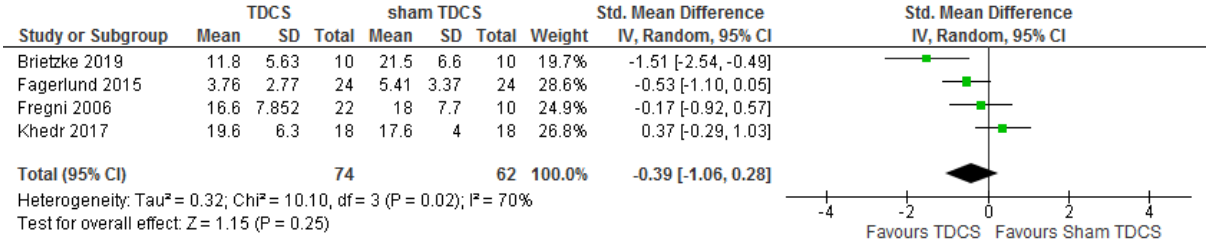
NB. Heterogeneity not explained by subgroup analysis

Figure 37: Psychological distress at ≤3 months (Hospital anxiety and depression scale, HAM-A, anxiety subscales, high is poor outcome, final values)



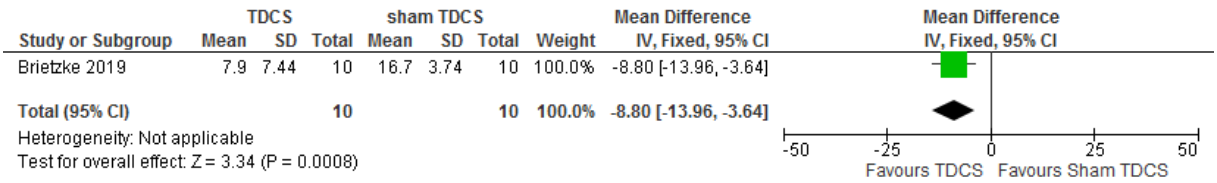
NB. Heterogeneity not explained by subgroup analysis

Figure 38: Psychological distress at ≤3 months (Hospital anxiety and depression scale, BDI, HAM-D, depression subscales, high is poor outcome, final values)



NB. Heterogeneity not explained by subgroup analysis

Figure 39: Sleep at ≤3 months (PSQI, scale range not reported, high is poor outcome, final values)



E.4 TENS versus sham TENS

Figure 40: Quality of life at ≤3 months (SF36 T scores, high is good outcome, change scores)

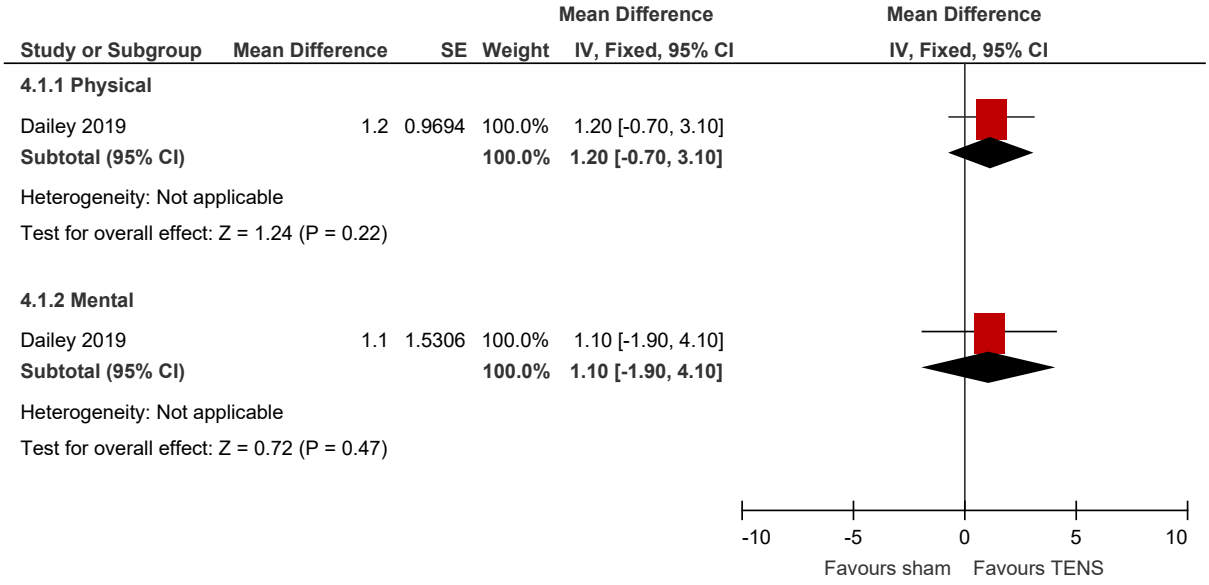
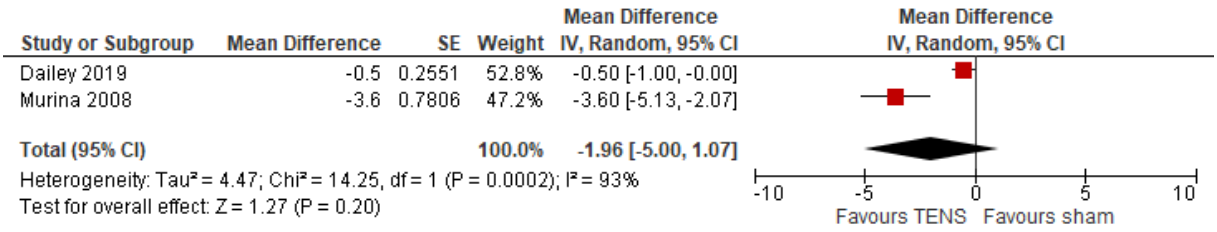


Figure 41: Pain reduction at ≤3 months (BPI, VAS, 0-10, high is poor outcome, final values and change scores)



Heterogeneity could not be explained by subgroup analysis

Figure 42: Pain reduction at >3 months (VAS, 0-10, high is poor outcome, final values)

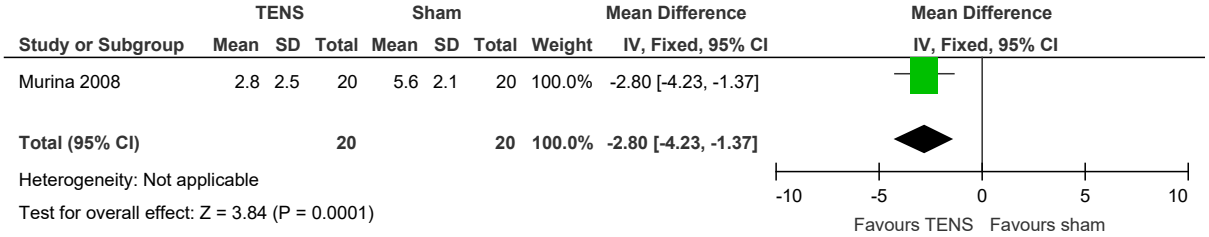


Figure 43: Physical function at ≤3 months (6 minute walk test, high is good outcome, change scores)

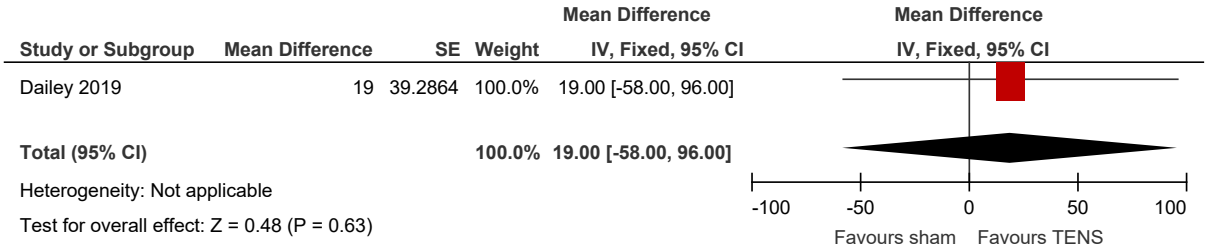


Figure 44: Psychological distress (PROMIS T scores, high is poor outcome, change scores)

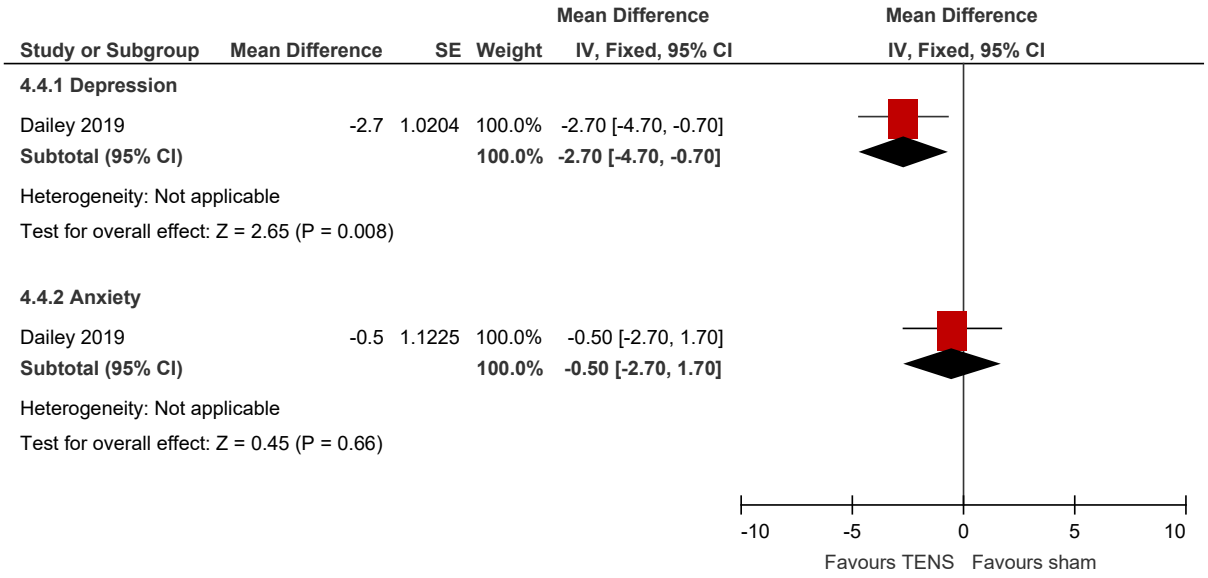


Figure 45: Pain interference at ≤3 months (BPI interference, 0-10, high is poor outcome, change scores)

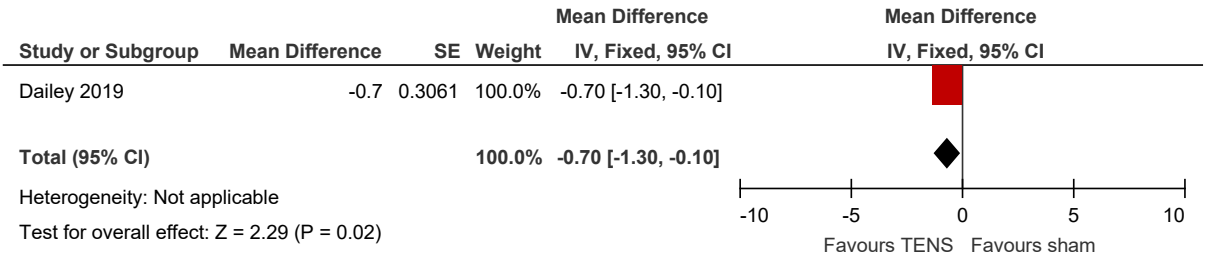


Figure 46: Pain self-efficacy at ≤3 months (Pain self-efficacy questionnaire, 0-60, high is good outcome, change scores)

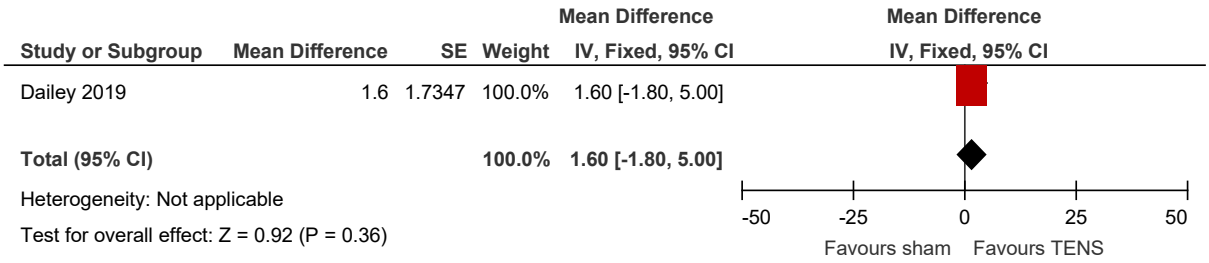
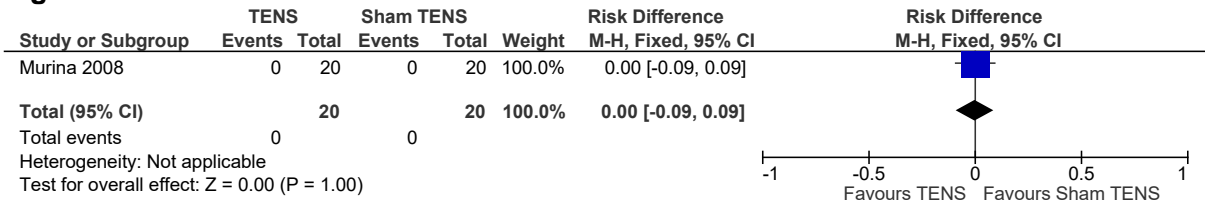


Figure 47: Discontinuation at ≤3 months



E.5 TENS versus usual care

Figure 48: Quality of life at ≤3 months (SF36 T scores, high is good outcome, change scores)

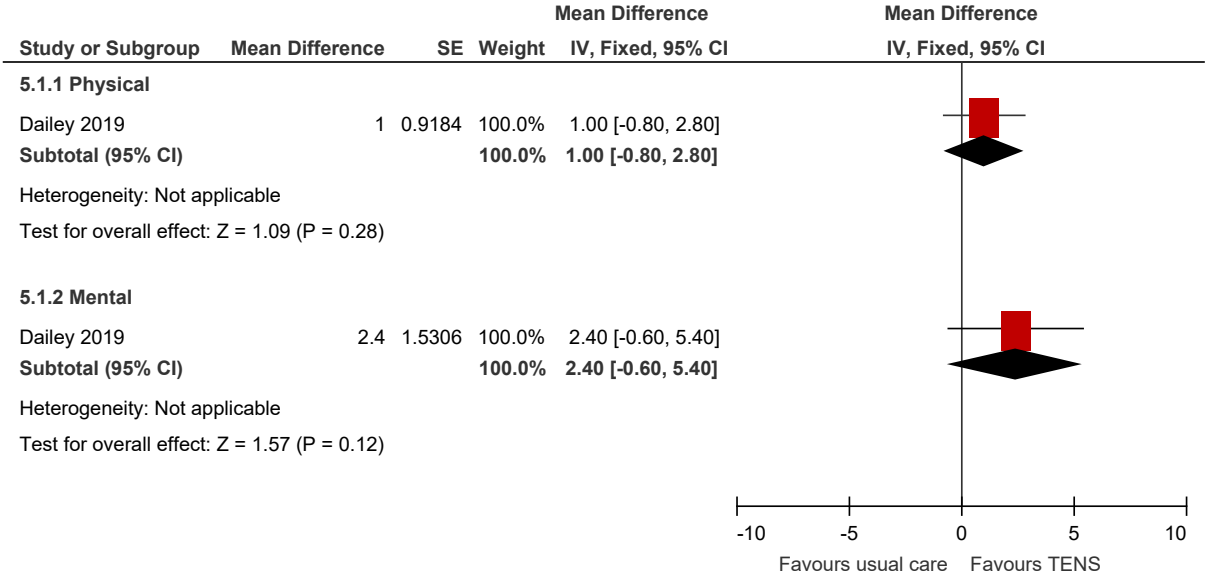


Figure 49: Pain reduction at ≤3 months (BPI, 0-10, high is poor outcome, change scores)

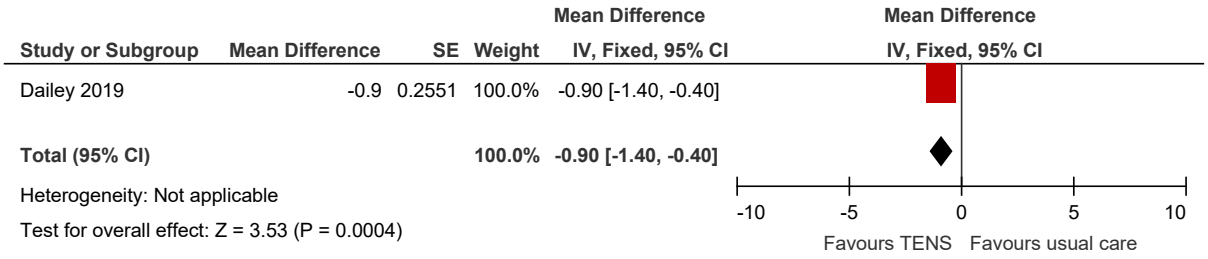


Figure 50: Physical function at ≤3 months (6 minute walk test, high is good outcome, change scores)

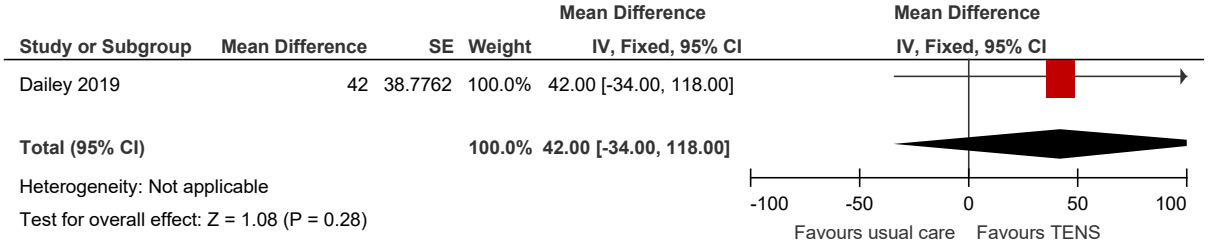


Figure 51: Psychological distress (PROMIS T scores, high is poor outcome, change scores)

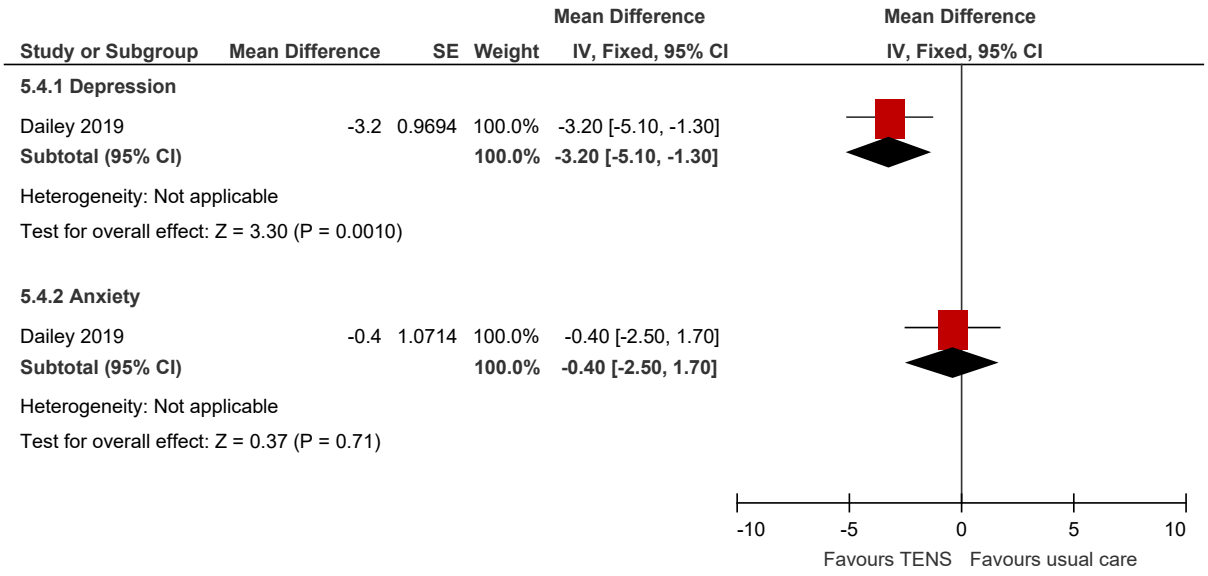


Figure 52: Pain interference at ≤3 months (BPI interference, 0-10, high is poor outcome, change scores)

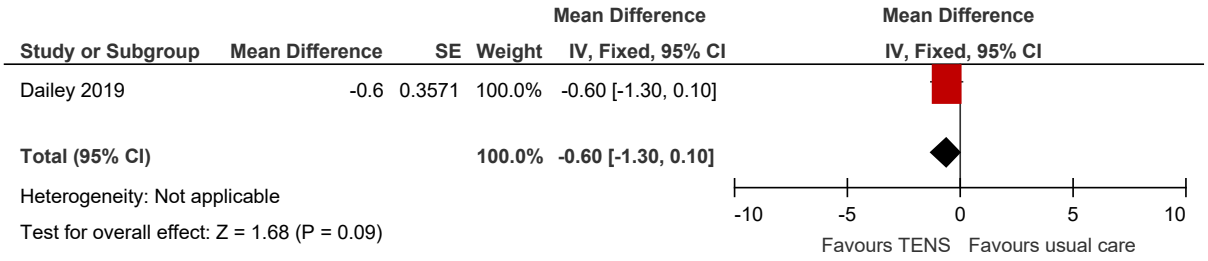
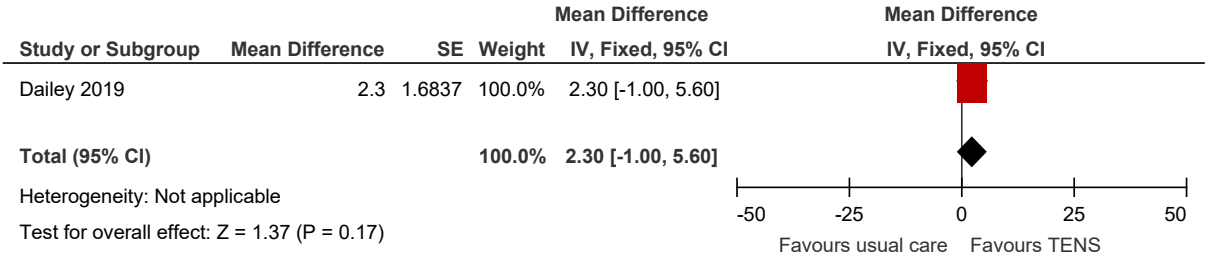


Figure 53: Pain self-efficacy at ≤3 months (Pain self-efficacy questionnaire, 0-60, high is good outcome, change scores)



E.6 PENS versus sham PENS

Figure 54: Quality of life at ≤3 months (NIH-CPSI, 0-12, high is poor outcome, final values)

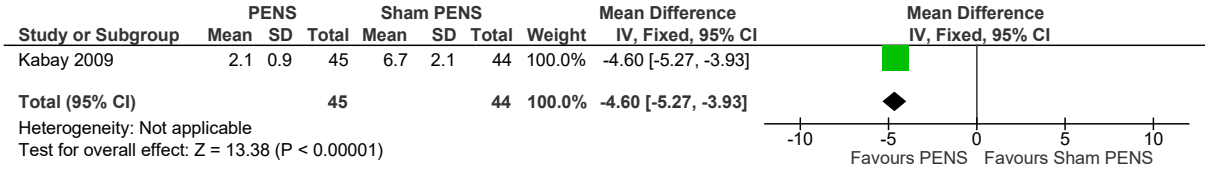
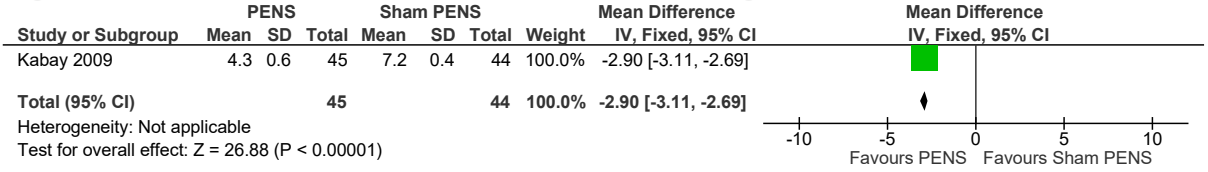


Figure 55: Pain reduction at ≤3 months (VAS, 0-10, high is poor outcome, final values)



E.7 PENS versus usual care

Figure 56: Quality of life at ≤3 months (SF-36 physical function subscale, 0-100, high is good outcome, final values)

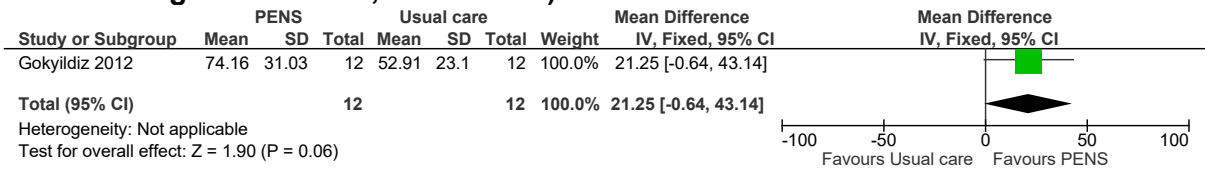


Figure 57: Quality of life at ≤3 months (SF-36 physical role subscale, 0-100, high is good outcome, final values)

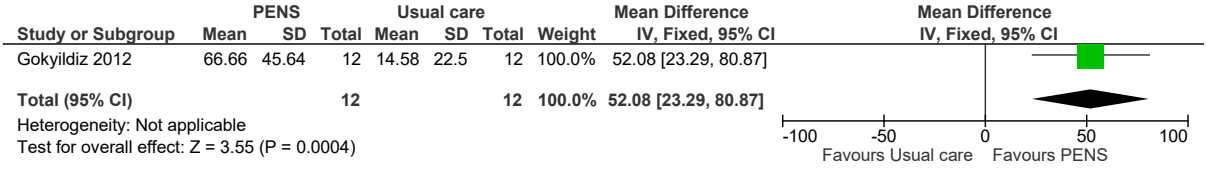


Figure 58: Quality of life at ≤3 months (SF-36 fatigue subscale, 0-100, high is good outcome, final values)

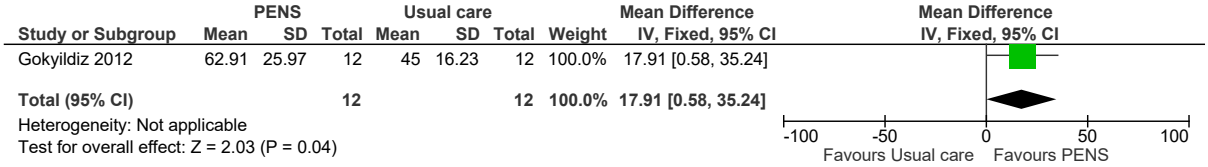


Figure 59: Quality of life at ≤3 months (SF-36 emotional role subscale, 0-100, high is good outcome, final values)

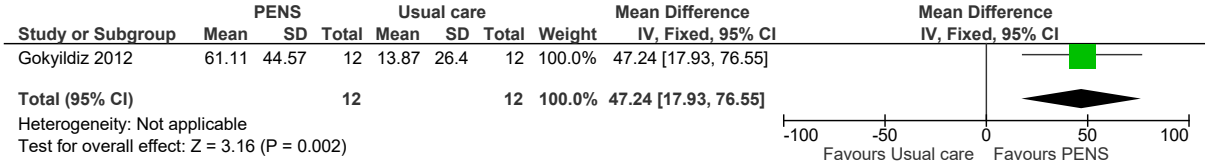


Figure 60: Quality of life at ≤3 months (SF-36 mental health subscale, 0-100, high is good outcome, final values)

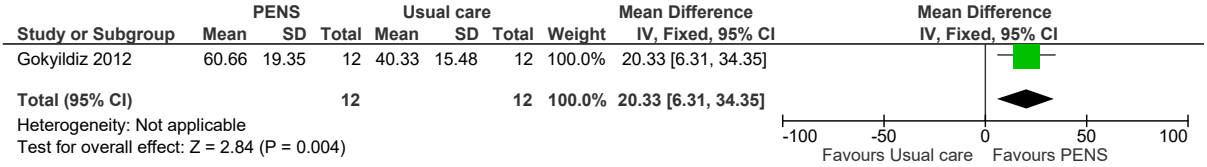


Figure 61: Quality of life at ≤3 months (SF-36 social functioning subscale, 0-100, high is good outcome, final values)

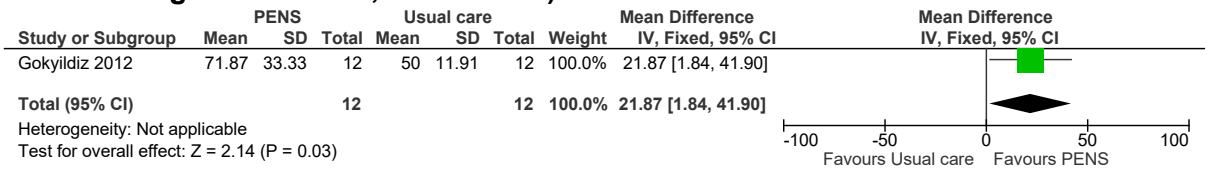


Figure 62: Quality of life at ≤3 months (SF-36 bodily pain subscale, 0-100, high is good outcome, final values)

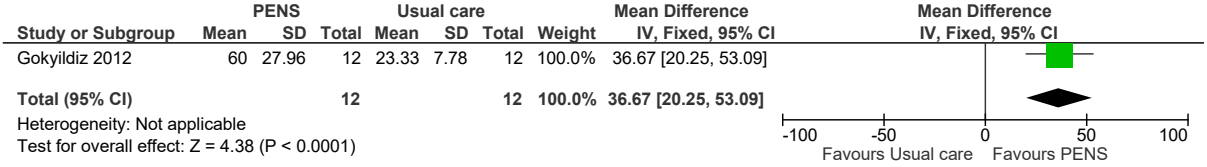
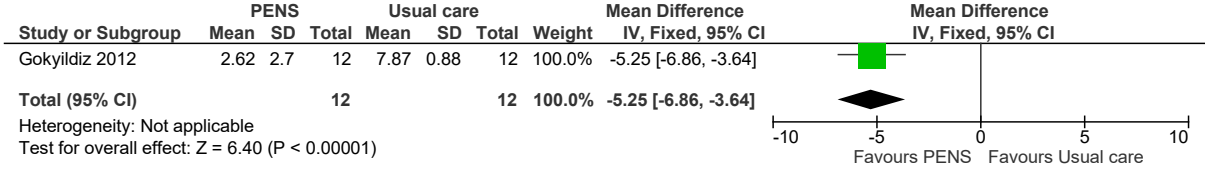
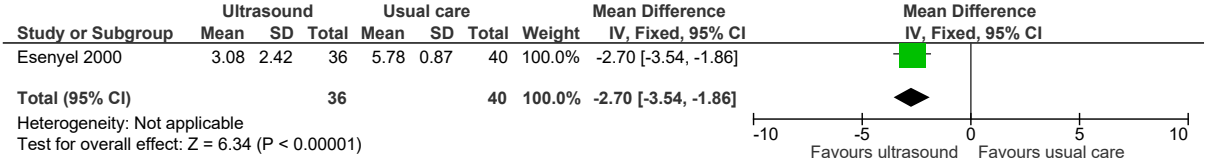


Figure 63: Pain reduction at ≤3 months (VAS, 0-10, high is poor outcome, final values)



E.8 Therapeutic ultrasound versus usual care

Figure 64: Pain reduction at 3 months (VAS, 0-10, high is poor outcome, final values)



Appendix F: GRADE tables

Table 15: Clinical evidence profile: Laser therapy versus sham laser therapy

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Laser therapy	Control	Relative (95% CI)	Absolute		
Quality of life at 2 weeks-3 months (Oral health impact profile, FIQ, high is poor outcome, final values)												
6	randomised trials	serious[3]	serious[2]	no serious indirectness	serious[1]	none	159	117	-	SMD 0.68 lower (1.1 to 0.25 lower)	⊕OOO VERY LOW	CRITICAL
Quality of life at 3 months (SF-36 physical component summary score, 0-100, high is good outcome, change scores)												
2	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	55	55	-	MD 2.09 higher (0.91 lower to 5.09 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life at 3 months (SF-36 mental component summary score, 0-100, high is good outcome, change scores)												
2	randomised trials	no serious risk of bias	serious[2]	no serious indirectness	serious[1]	none	55	55	-	MD 0.74 lower (5.35 lower to 3.87 higher)	⊕⊕OO LOW	CRITICAL
Quality of life at 24 weeks (FIQ, 0-100, high is poor outcome, final values)												
2	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[1]	none	59	58	-	SMD 0.78 lower (1.16 to 0.4 lower)	⊕⊕OO LOW	CRITICAL
Pain reduction at 1 week to 12 weeks (VAS, NRS, FIQ pain scale, high is poor outcome, 0-10, final values and change scores)												
13	randomised trials	serious[3]	serious[2]	no serious indirectness	serious[1]	none	301	257	-	MD 1.42 lower (2.12 to 0.73 lower)	⊕OOO VERY LOW	CRITICAL
Pain reduction at 14-16 weeks (VAS, high is poor outcome, 0-10, final values)												
2	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	36	35	-	MD 0.6 lower (0.91 to 0.3 lower)	⊕⊕⊕O MODERATE	CRITICAL

Psychological distress at 4 weeks (Hospital anxiety and depression rating scale, anxiety subscale, 0-21, high is poor outcome, final values)												
1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[1]	none	32	12	-	MD 0.83 higher (1.52 lower to 3.18 higher)	⊕⊕OO LOW	CRITICAL
Psychological distress at 4 weeks (Hospital anxiety and depression rating scale, depression subscale, 0-21, high is poor outcome, final values)												
1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[1]	none	32	16	-	MD 1.29 higher (1.39 lower to 3.96 higher)	⊕⊕OO LOW	CRITICAL
Discontinuation at 3 months												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	2/45 (4.4%)	6.7%	RR 0.67 (0.12 to 3.8)	22 fewer per 1000 (from 59 fewer to 188 more)	⊕⊕OO LOW	IMPORTANT

1 Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.
2 Downgraded for heterogeneity, unexplained by subgroup analysis
3 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Table 16: Clinical evidence profile: TMS versus sham TMS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**TMS**	**Control**	**Relative (95% CI)**	**Absolute**		
Quality of life at 10 weeks (SF-36 physical summary score, 0-100, high is good outcome, change scores)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	16	13	-	MD 1 higher (4.12 lower to 6.12 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life at 10 weeks (SF-36 mental summary score, 0-100, high is good outcome, change scores)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	16	13	-	MD 6.6 higher (1.26 to 11.94 higher)	⊕OOO VERY LOW	IMPORTANT
Quality of life at 2 weeks (WHOQOL-BREF physical domain, 4-20, high is good outcome, final values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	27	24	-	MD 3.27 higher (1.79 to 4.75 higher)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality of life at 2 weeks (WHOQOL-BREF psychological domain, 4-20, high is good outcome, final values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	27	24	-	MD 1.18 higher (0.18 lower to 2.54 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life at 4 weeks -3 months (FIQ, 0-100, high is poor outcome, final values)												
3	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	33	27	-	MD 8.69 lower (18.83 lower to 1.46 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life at 25 weeks (FIQ, 0-100, high is poor outcome, final values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	15	15	-	MD 7.3 lower (19.04 lower to 4.44 higher)	⊕OOO VERY LOW	CRITICAL
Pain reduction at 2 weeks -3 months (VAS, McGill Pain questionnaire, 0-10, high is poor outcome, final values)												
7	randomised trials	serious[1]	serious[3]	no serious indirectness	serious[2]	none	98	83	-	MD 1.17 lower (2.1 to 0.24 lower)	⊕OOO VERY LOW	CRITICAL
Physical function at 4 weeks (BPI functional impairment subscale, 0-10, high is poor outcome, final values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10	10	-	MD 0.19 lower (2.34 lower to 1.96 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress at 6-10 weeks (Beck depression inventory, 0-61, high is poor outcome, final values and change scores)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	26	18	-	MD 1.59 lower (4.13 lower to 0.94 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress at 2 weeks -3 months (Hamilton depression rating scale, MADRS, BDI, high is poor outcome, final values)												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	50	46	-	SMD 0.01 higher (0.39 lower to 0.41 higher)	⊕⊕⊕O MODERATE	CRITICAL
Psychological distress at 10 weeks (HADS anxiety, 0-21, high is poor outcome, change scores)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	16	13	-	MD 0.1 lower (1.6 lower to 1.4 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress at 25 weeks (HADS anxiety, 0-21, high is poor outcome, change scores)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	15	15	-	MD 0.2 lower (4 lower to 3.6 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress at 25 weeks (HADS depression, 0-21, high is poor outcome, change scores)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	15	15	-	MD 1.2 higher (1.92 lower to 4.32 higher)	⊕OOO VERY LOW	CRITICAL
Pain interference at 25 weeks (BPI pain interference, 0-10, high is poor outcome, final values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	15	15	-	MD 1.9 lower (3.05 to 0.75 lower)	⊕OOO VERY LOW	CRITICAL
Discontinuation at 2-6 weeks (follow-up 2-6 weeks)												
4	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	8/79 (10.1%)	2%	RD 0.03 (-0.06 to 0.12)	12 more per 1000 (from 25 fewer to 50 more)	⊕⊕OO LOW	IMPORTANT

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.
3 Downgraded for heterogeneity, unexplained by subgroup analysis

Table 17: Clinical evidence profile: TDCS versus sham TDCS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**TDCS**	**Control**	**Relative (95% CI)**	**Absolute**		
Quality of life at 4 weeks (SF-36 mental summary score, 0-100, high is good outcome, final values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	24	24	-	MD 2.8 higher (4.72 lower to 10.32 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life at 4 weeks (SF-36 physical summary score, 0-100, high is good outcome, final values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	24	24	-	MD 1.14 lower (5.92 lower to 3.64 higher)	⊕OOO VERY LOW	CRITICAL

Quality of life at 10 weeks (SF-36 physical function subscale, 0-100, high is good outcome, final values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	10	10	-	MD 30.5 higher (12.47 to 48.53 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life at 10 weeks (SF-36 physical role subscale, 0-100, high is good outcome, final values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10	10	-	MD 27.5 higher (4.71 lower to 59.71 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life at 10 weeks (SF-36 bodily pain subscale, 0-100, high is good outcome, final values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10	10	-	MD 7 lower (25.49 lower to 11.49 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life at 10 weeks (SF-36 general health subscale, 0-100, high is good outcome, final values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10	10	-	MD 5.5 lower (14.54 lower to 3.54 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life at 10 weeks (SF-36 vitality subscale, 0-100, high is good outcome, final values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10	10	-	MD 4.5 lower (12.92 lower to 3.92 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life at 10 weeks (SF-36 general aspects subscale, 0-100, high is good outcome, final values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10	10	-	MD 2.5 lower (16.55 lower to 11.55 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life at 10 weeks (SF-36 emotional role subscale, 0-100, high is good outcome, final values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10	10	-	MD 20 higher (15.04 lower to 55.04 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life at 10 weeks (SF-36 mental health subscale, 0-100, high is good outcome, final values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10	10	-	MD 4.4 higher (5.82 lower to 14.62 higher)	⊕OOO VERY LOW	CRITICAL
Pain reduction at 4-10 weeks (NRS, VAS, 0-10, high is poor outcome, final values)												

3	randomised trials	serious[1]	serious[3]	no serious indirectness	serious[2]	none	52	52	-	MD 2.12 lower (3.82 to 0.43 lower)	⊕OOO VERY LOW	CRITICAL
Psychological distress at 4-8 weeks (Hospital anxiety and depression scale, HAM-A, anxiety subscales, high is poor outcome, final values)												
2	randomised trials	serious[1]	serious[3]	no serious indirectness	serious[2]	none	42	42	-	SMD 0.55 lower (1.49 lower to 0.39 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress at 3-12 weeks (Hospital anxiety and depression scale, BDI, HAM-D, depression subscales, high is poor outcome, final values)												
4	randomised trials	serious[1]	serious[3]	no serious indirectness	serious[2]	none	74	62	-	SMD 0.39 lower (1.06 lower to 0.28 higher)	⊕OOO VERY LOW	CRITICAL
Sleep at ≤3 months (PSQI, scale range not reported, high is poor outcome, final values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	10	10	-	MD 8.8 lower (13.96 to 3.64 lower)	⊕⊕OO LOW	IMPORTANT

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.
3 Downgraded for heterogeneity, unexplained by subgroup analysis

Table 18: Clinical evidence profile: TENS versus sham TENS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**TENS**	**Control**	**Relative (95% CI)**	**Absolute**		
Quality of life at 4 weeks (SF36 physical T scores, high is good outcome, change scores)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	103	99	-	MD 1.2 higher (0.7 lower to 3.1 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life at 4 weeks (SF36 mental T scores, high is good outcome, change scores)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	103	99	-	MD 1.1 higher (1.9 lower to 4.1 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain reduction at 4-10 weeks (BPI, VAS, 0-10, high is poor outcome, final values and change scores)												

2	randomised trials	serious[1]	very serious inconsistency[2]	no serious indirectness	serious[3]	none	123	119	-	MD 1.96 lower (5 lower to 1.07 higher)	⊕OOO VERY LOW	CRITICAL
Pain reduction at 22 weeks (VAS, 0-10, high is poor outcome, final values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	20	20	-	MD 2.8 lower (4.23 lower to 1.37 lower)	⊕⊕⊕O MODERATE	CRITICAL
Physical function at 4 weeks (6 minute walk test, change scores)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	103	99	-	MD 19 higher (58 lower to 96 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Psychological distress at 4 weeks (PROMIS depression T scores, high is poor outcome, change scores)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	103	99	-	MD 2.7 lower (4.7 to 0.7 lower)	⊕⊕OO LOW	CRITICAL
Psychological distress at 4 weeks (PROMIS anxiety T scores, high is poor outcome, change scores)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	103	99	-	MD 0.5 lower (2.7 lower to 1.7 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain interference (Brief pain inventory interference, 0-10, high is poor outcome, change scores)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	103	99	-	MD 0.7 lower (1.3 to 0.1 lower)	⊕⊕OO LOW	CRITICAL
Pain self-efficacy (Pain self-efficacy questionnaire, 0-60, high is good outcome, change scores)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	103	99	-	MD 1.6 higher (1.8 lower to 5 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Discontinuation at 10 weeks												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	0/20 (0%)	0%	RD 0 (-0.09 to 0.09)	0 fewer per 1000 (from 90 fewer to 90 more)	⊕⊕OO LOW	CRITICAL

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

2 Downgraded for heterogeneity, unexplained by subgroup analysis

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

Table 19: Clinical evidence profile: TENS versus usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TENS	Control	Relative (95% CI)	Absolute		
Quality of life at 4 weeks (SF36 physical T scores, high is good outcome, change scores)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	103	99	-	MD 1 higher (0.8 lower to 2.8 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life at 4 weeks (SF36 mental T scores, high is good outcome, change scores)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	103	99	-	MD 2.4 higher (0.6 lower to 5.4 higher)	⊕⊕OO LOW	CRITICAL
Pain reduction at 10 weeks (BPI, 0-10, high is poor outcome, final values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	103	99	-	MD 0.9 lower (1.4 to 0.4 lower)	⊕⊕OO LOW	CRITICAL
Physical function at 4 weeks (6 minute walk test, change scores)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	103	99	-	MD 42 higher (34 lower to 118 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Psychological distress at 4 weeks (PROMIS depression T scores, high is poor outcome, change scores)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	103	99	-	MD 3.2 lower (5.1 to 1.3 lower)	⊕⊕OO LOW	CRITICAL
Psychological distress at 4 weeks (PROMIS anxiety T scores, high is poor outcome, change scores)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	103	99	-	MD 0.4 lower (2.5 lower to 1.7 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain interference (Brief pain inventory interference, 0-10, high is poor outcome, change scores)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	103	99	-	MD 0.6 lower (1.3 lower to 0.1 higher)	⊕⊕OO LOW	CRITICAL

Pain self-efficacy (Pain self-efficacy questionnaire, 0-60, high is good outcome, change scores)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	103	99	-	MD 2.3 higher (1 lower to 5.6 higher)	⊕⊕⊕⊕ HIGH	CRITICAL

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 20: Clinical evidence profile: PENS versus sham PENS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PENS	Control	Relative (95% CI)	Absolute		
Quality of life at 3 months (NIH-CPSI, 0-12, high is poor outcome, final values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	45	44	-	MD 4.6 lower (5.27 to 3.93 lower)	⊕⊕OO LOW	CRITICAL
Pain reduction at 3 months (VAS, 0-10, high is poor outcome, final values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	45	44	-	MD 2.9 lower (3.11 to 2.69 lower)	⊕⊕OO LOW	CRITICAL

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

Table 21: Clinical evidence profile: PENS versus usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PENS	Control	Relative (95% CI)	Absolute		
Quality of life at 3 months (SF-36 physical function, 0-100, high is good outcome, final values)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	12	12	-	MD 21.25 higher (0.64 lower to 43.14 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life at 3 months (SF-36 physical role, 0-100, high is good outcome, final values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	12	12	-	MD 52.08 higher (23.29 to 80.87 higher)	⊕⊕OO LOW	CRITICAL
Quality of life at 3 months (SF-36 fatigue, 0-100, high is good outcome, final values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	12	12	-	MD 17.91 higher (0.58 to 35.24 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life at 3 months (SF-36 emotional role, 0-100, high is good outcome, final values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	12	12	-	MD 47.24 higher (17.93 to 76.55 higher)	⊕⊕OO LOW	CRITICAL
Quality of life at 3 months (SF-36 mental health, 0-100, high is good outcome, final values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	12	12	-	MD 20.33 higher (6.31 to 34.35 higher)	⊕⊕OO LOW	CRITICAL
Quality of life at 3 months (SF-36 social functioning, 0-100, high is good outcome, final values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	12	12	-	MD 21.87 higher (1.84 to 41.9 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life at 3 months (SF-36 bodily pain, 0-100, high is good outcome, final values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	12	12	-	MD 36.67 higher (20.25 to 53.09 higher)	⊕⊕OO LOW	CRITICAL
Pain reduction at 3 months (VAS, 0-10, high is poor outcome, final values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	12	12	-	MD 5.25 lower (6.86 to 3.64 lower)	⊕⊕OO LOW	CRITICAL

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

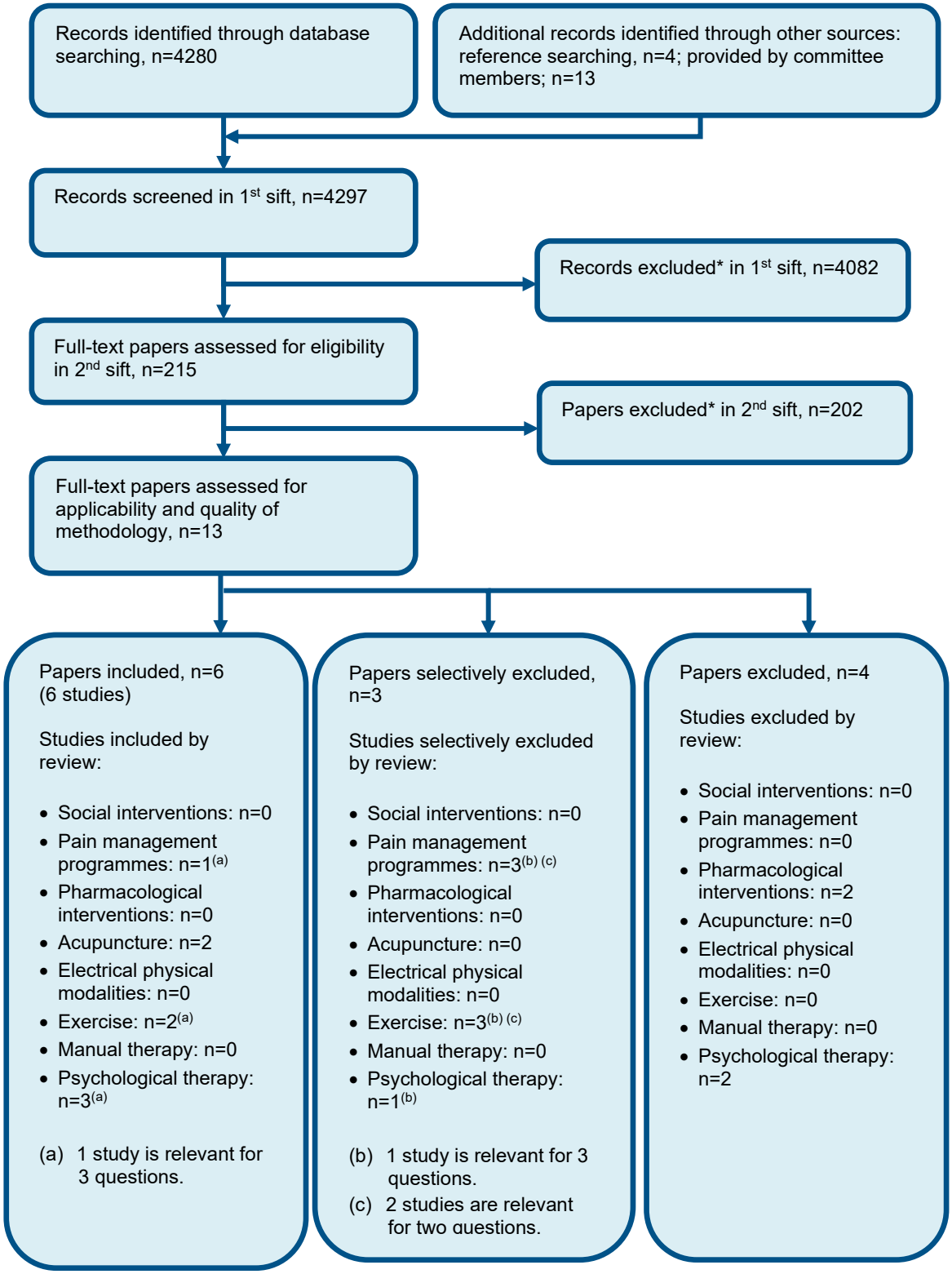
2 Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 22: Clinical evidence profile: Ultrasound versus sham ultrasound

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Therapeutic ultrasound	Control	Relative (95% CI)	Absolute		
Pain reduction at 3 months (VAS, 0-10, high is poor outcome, final values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	36	40	-	MD 2.7 lower (3.54 to 1.86 lower)	⊕⊕OO LOW	CRITICAL

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

Appendix G: Health economic evidence selection



* Non-relevant population, intervention, comparison, design or setting; non-English language

Appendix H: Health economic evidence tables

None.

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 23: Studies excluded from the clinical review

Study	Exclusion reason
Aarskog 2007[1]	Incorrect population
Abdulla 2013[2]	Incorrect study design
Abram 1976[3]	Not guideline condition. Incorrect population
Abtahi 2018[4]	Not guideline condition. Incorrect population
Acedo 2015[5]	Not guideline condition. Incorrect population
Adrian 2014[6]	Abstract
Ahmed 2011[7]	Not guideline condition. Incorrect population
Ahsin 2009[8]	Incorrect interventions. Incorrect population
Akturk 2013[9]	Incorrect study design
Akturk 2018[10]	Inappropriate comparison
Alayat 2016[13]	Incorrect interventions (combinations of interventions; intervention combined with exercise)
Alayat 2017[12]	Incorrect interventions (combinations of interventions; intervention combined with exercise)
Albornoz-cabello 2017[14]	Incorrect population. Not guideline condition
Allais 2003[15]	Not guideline condition. Incorrect population
Al-maweri 2017[11]	Incorrect study design
Almay 1985[16]	Incorrect population. Incorrect population
Almeida 2003[18]	Incorrect interventions. Combined treatments (ultrasound plus interferential current)
Almeida 2018[17]	Incorrect population. Inappropriate comparison
Altas 2019 [20]	Incorrect intervention (both interventions combined with exercise programme)
Amanat 2013[21]	Incorrect interventions. Combined treatments (laser plus pharmacological)
Anderssonn 1976[22]	Incorrect population
Andrade ortega 2014[23]	Incorrect interventions
Andre-obadia 2006[24]	Incorrect population.
Anon 2003[366]	Not article
Anon 2004[300]	Abstract
Anon 2017[119]	Incorrect study design
Anonymous 2016[56]	Incorrect interventions. Incorrect study design
Anonymous 2017[25]	Incorrect interventions. Combined treatments
Ansari 2013[26]	Abstract
Ansari 2014[27]	Abstract
Ardic 2002[29]	Not guideline condition. Incorrect population
Aridici 2016[30]	Incorrect interventions. Inappropriate comparison
Attal 2010[32]	Abstract
Avery 2015[33]	No useable outcomes
Ay 2011[34]	Incorrect population (not chronic)

Study	Exclusion reason
Azatcam 2017[35]	Incorrect population (myofascial pain, unclear duration)
Barbosa 2018[36]	Incorrect comparison
Barnhoorn 2015[38]	Incorrect interventions
Barr 1987[39]	Abstract
Barr 2004[40]	Crossover study
Bates 1980[41]	Incorrect study design: not randomised
Baudic 2013[42]	Incorrect outcome
Bergeron-vezina 2018[43]	Incorrect population
Bezuur 1988[44]	Incorrect population (not chronic pain)
Biemans 2013[45]	Incorrect population. Not primary pain
Bilgili 2016[46]	Combinations of interventions. Combined with water bath and exercise
Bingol 2005[47]	Incorrect population (not chronic pain)
Bjordal 2003[48]	Incorrect study design
Boggio 2009[49]	Crossover study
Borckardt 2011[50]	Incorrect population. Healthy population
Botelho 2018 [51]	Unclear intervention duration
Boureau 1981[52]	Incorrect interventions
Busch 2013[55]	Incorrect population. Healthy population
Canadian chiropractic 2005[57]	Incorrect study design: expert opinion/guideline
Carbonario 2013[58]	Combinations of interventions. Intervention combined with exercise
Carrasco 2008[60]	Incorrect population (not chronic pain)
Carrasco 2009[59]	Incorrect population (not chronic pain)
Castro-sanchez 2011[63]	Incorrect interventions. Inappropriate comparison. Combinations of interventions
Castro-sanchez 2020 [62]	Inappropriate comparison
Ceccherelli 1989[64]	Not guideline condition. Not primary pain
Cervigni 2018[65]	Crossover study
Cetiner 2006[66]	Incorrect population (not chronic pain)
Chabal 1998[67]	Incorrect study design (survey)
Chan 2009[68]	Incorrect interventions. Acupuncture
Chee 1986[69]	Incorrect population (not chronic pain)
Chen 2008[70]	Incorrect population. Not primary pain
Cheng 1986[72]	Incorrect interventions. Acupuncture
Cheng 2019 [71]	No useable outcomes (correlational GLM model)
Choi 2014[74]	Incorrect population. Not chronic pain
Choi 2018[73]	Incorrect population. Not primary pain
Chong 2018[75]	Incorrect interventions. Electric acupuncture
Chow 2005[76]	Incorrect population (not chronic pain)
Cohen 2012[79]	Incorrect population. Incorrect interventions. Acupuncture
Conti 1997[80]	No useable outcomes
Conti 2014[81]	No useable outcomes
Cormier 2013[82]	Incorrect population.
Correa 2016[83]	Incorrect population.
Cossins 2013[84]	Systematic review is not relevant to review question or unclear PICO

Study	Exclusion reason
Costa 2017[85]	Incorrect study design (1 day study)
Cruccu 2016[86]	Incorrect study design: expert opinion.
Cruccu 2016[87]	Incorrect study design. Systematic review is not relevant to review question or unclear PICO
Cruz 2018[88]	Incorrect population
Cummiford 2016[89]	Crossover study
Curatolo 2017[90]	No useable outcomes
Dailey 2013[93]	Crossover study
De carli 2013[97]	Incorrect population. Combinations of interventions
De giorgi 2017[98]	No useable outcomes
De souza 2018[99]	Inappropriate comparison
Defrin 2005[100]	Incorrect population. Not primary pain
Deluze 1992[102]	Incorrect interventions. Electric acupuncture
Demirkol 2015[103]	Incorrect population. Not chronic pain.
Desantana 2017[104]	Conference abstract
Di benedetto 1993[105]	Inappropriate comparison
Dibai-filho 2017[106]	Combinations of interventions
Dimitrijevic 2014[107]	Incorrect population. Not chronic pain.
Dorsher 2010[108]	Incorrect interventions. Electrical acupuncture
Dundar 2007[109]	Incorrect population. Not chronic pain.
Dundar 2014[110]	Abstract
Dundar 2015[111]	Combinations of interventions. Intervention combined with exercise
Durmus 2013[112]	Incorrect population
Eken 2018[113]	No relevant outcomes
El-Gendy 2019 [114]	Incorrect intervention. Combination of electrotherapies
Emshoff 2008[115]	Incorrect population. Not chronic pain
Escortell-mayor 2011[116]	Inappropriate comparison
Euasobhon 2018[118]	Incorrect population. Neuropathic pain
Falaki 2014[121]	Incorrect population. Not primary pain
Fernandez-rodriguez 2018[122]	Incorrect interventions. Acupuncture
Ferreira 2013[123]	Incorrect interventions. Acupuncture
Field 1992[124]	Abstract
Fikackova 2007[125]	Incorrect population. Not chronic pain
Foletti 2018[126]	Incorrect population. Not primary pain
Franco 2018[127]	Systematic review is not relevant to review question or unclear PICO
Frank 2013[128]	Incorrect population. Neuropathic pain
Fricova 2013[130]	Incorrect interventions. Not primary pain
Galhardoni 2015[131]	Systematic review is not relevant to review question or unclear PICO
Gam 1993[132]	Systematic review is not relevant to review question or unclear PICO
Gemmell 2011[133]	No relevant outcomes
Gendreau 2014[134]	Abstract
Germano maciel 2018[135]	Combinations of interventions. Intervention combined with exercise
Gibson 2017[136]	Incorrect population. Neuropathic pain

Study	Exclusion reason
Goudra 2017[138]	Systematic review is not relevant to review question or unclear PICO
Graff-radford 1989[139]	Incorrect population (myofascial pain, unclear duration)
Graham 2013[140]	Systematic review is not relevant to review question or unclear PICO
Gray 1994[141]	Incorrect population. Not chronic pain
Gross 2000[142]	Systematic review is not relevant to review question or unclear PICO
Gross 2013[143]	Incorrect population. Systematic review is not relevant to review question or unclear PICO
Guedj 2013[144]	Conference abstract
Guirro 2015[145]	No useable outcomes
Guo 2005[146]	Incorrect interventions. Acupuncture
Gur 2002[148]	No useable outcomes (not validated scales)
Gur 2013[149]	Incorrect interventions. Inappropriate comparison
Hakguder 2003[150]	Incorrect population. Not chronic pain
Hargrove 2012[151]	No relevant outcomes
Harvey 2017[152]	Incorrect population. Over 20% of the population have chronic low back pain
He 2017[153]	Combinations of interventions
Hong 1993[154]	Crossover study
Hou 2002[155]	Incorrect population. Not chronic pain
Hou 2016[156]	Combinations of interventions. Incorrect study design
Hruby 2006[157]	Incorrect study design (cystoscopy)
Hsu 2018[158]	Incorrect study design: expert opinion
Hsueh 1997[159]	Incorrect population. Not chronic pain
Hurt 2020 [160]	Incorrect intervention. Extracorporeal shockwave therapy
Ilbuldu 2004[161]	Incorrect interventions. Acupuncture
Ilter 2014[162]	Combinations of interventions. Incorrect population. Not chronic pain
Ilter 2015[163]	Incorrect population. Not chronic pain
Istek 2014[164]	Incorrect population. Not primary pain
Ito 2002[165]	No relevant outcomes
Ivanishvili 2017[166]	Incorrect population. Neuropathic pain
Janice jimenez-torres 2017[168]	Protocol
Jeans 1979[169]	Incorrect population. Not primary pain
Jeon 2012[170]	Incorrect interventions. Combinations of interventions
Jin 2015[171]	Incorrect population. Neuropathic pain
Johansson 1980[172]	Incorrect study design
Johnson 2007[173]	Systematic review is not relevant to review question or unclear PICO
Johnson 2016[175]	Protocol
Johnson 2017[174]	Cochrane review is not relevant to review question or unclear PICO
Kadhim-saleh 2013[177]	Incorrect population. Not chronic pain
Kara 2010[178]	Incorrect population. Not primary pain
Kato 2006[179]	No useable outcomes
Katsoulis 2010[180]	Incorrect interventions. Acupuncture

Study	Exclusion reason
Kavadar 2015[181]	Incorrect population. Not chronic pain
Kavvadias 2012[182]	Incorrect study design: expert opinion
Kemler 2001[183]	Incorrect interventions. Spinal cord stimulation
Kessler 2014[184]	Incorrect interventions. No relevant outcomes
Kim 2014[186]	Incorrect population (latent trigger points)
Kiraly 2018 [187]	Incorrect comparison
Knijnik 2016[188]	Systematic review is not relevant to review question or unclear PICO
Koca 2014[189]	Incorrect interventions. Inappropriate comparison
Kohutova 2017[190]	Incorrect interventions
Kriek 2015[191]	Crossover study
Kroeling 2005[193]	Incorrect population. Not chronic pain.
Kroeling 2013[192]	Systematic review is not relevant to review question or unclear PICO
Kruger 1998[194]	Incorrect study design
Kulekcioglu 2003[195]	Not guideline condition. Not chronic pain
La bianca 2017[196]	Conference abstract
Laakso 1997[197]	No useable outcomes
Lagueux 2018[198]	Combinations of interventions
Langley 1984[199]	Crossover study
Lara-palomo 2013[200]	Incorrect population.
Lassemi 2008[201]	Not guideline condition. Not chronic pain
Lauretti 2013[202]	All participants allocated to amitriptyline 25-50mg per day at least 3 weeks before randomisation
Leandri 1990[203]	Incorrect population
Lee 1997[204]	No useable outcomes
Lee 2013[206]	Abstract
Lev-sagie 2017[207]	Incorrect population
Lewis 2013[208]	Incorrect population. Not chronic pain
Lewis 2018[209]	Incorrect population. Neuropathic pain
Lichtbroun 2001[210]	No useable outcomes
Lima 2008[211]	Systematic review is not relevant to review question or unclear PICO
Lindholm 2015[212]	Crossover study
Lopez-martos 2018[213]	Incorrect interventions. Acupuncture
Luan 2019 [214]	Incorrect intervention. Extracorporeal shockwave therapy
Luedtke 2012[215]	Incorrect population
Lyskov 2005[216]	Crossover study
Macdonald 1995[217]	Not randomised
Macpherson 2017[218]	Incorrect interventions. Electric acupuncture
Madani 2020 [219]	No useable outcomes
Maestu 2013[220]	No useable outcomes
Magri 2017[221]	No useable outcomes
Magri 2018[222]	No useable outcomes
Maia 2012[223]	Incorrect study design. Systematic review is not relevant to review question or unclear PICO

Study	Exclusion reason
Majithia 2016[224]	Systematic review is not relevant to review question or unclear PICO
Majlesi 2004[225]	Not chronic pain
Maloney 2014[226]	Conference abstract
Manafnezhad 2019 [227]	Incorrect interventions
Manca 2014[228]	Not chronic pain
Manfredini 2017[229]	Inappropriate comparison. No placebo
Marchand 1991[230]	Incorrect population
Marineo 2012[231]	Incorrect interventions. Inappropriate comparison
Marini 2010[232]	Incorrect population (disc displacement)
Marlow 2013[233]	Systematic review is not relevant to review question or unclear PICO
Matsutani 2007[234]	Incorrect interventions
Mazzetto 2007[235]	Not chronic pain. Incorrect population
Medeiros 2016[236]	Combinations of interventions. rTMS combined with sham DIMST (needling)
Mekhail 2018[237]	Conference abstract
Melchior 2013[238]	Not chronic pain. Incorrect population
Mendonca 2011[239]	No useable outcomes
Mendonca 2016[240]	Combinations of interventions. Intervention combined with exercise
Moisset 2016[242]	Incorrect study design: expert opinion
Molina-torres 2016[243]	Incorrect population.
Mordasini 2014[244]	Conference abstract
Moretti 2012[245]	Combinations of interventions. Inappropriate comparison
Morin 2017[246]	Incorrect population. Episodic pain
Müller 2015[247]	Incorrect interventions. Acupuncture
Munguia 2018[248]	Systematic review is not relevant to review question or unclear PICO
Muniswamy 2016[249]	Incorrect population. Neuropathic pain
Murina 2018[251]	Combinations of interventions
Mutlu 2006[253]	Unavailable
Mutlu 2013[252]	Not guideline condition. Not chronic pain
Mysliwiec 2012[254]	Incorrect population. Not primary pain
Nadershah 2020 [255]	Unclear population. Unclear duration of pain
Nardone 2018[256]	Systematic review is not relevant to review question or unclear PICO
Naterstad 2015[257]	Incorrect population.
Nct 2009[260]	Unpublished
Niddam 2007[262]	Not randomised
Noehren 2015[263]	Abstract
Nordin 1999[264]	Incorrect study design: review of guidelines
O'connell 2011[267]	Duplicate results
O'connell 2013[265]	Incorrect population.
O'connell 2018[266]	Systematic review is not relevant to review question or unclear PICO
Ofluoglu 2013[268]	Non-English language studies
Okmen 2017[269]	Incorrect population. Chronic Not primary pain

Study	Exclusion reason
Oosterhof 2006[270]	Incorrect population
Oosterhof 2008[271]	Incorrect population (neuropathic pain, osteoarthritis)
Oosterhof 2012[272]	No useable outcomes
Oosterhof 2012[273]	Incorrect population. Not primary pain
Park 2018 [275]	Incorrect comparison (high versus low intensity)
Passard 2007[276]	No useable outcomes
Peng 1987[277]	Incorrect interventions. Electric acupuncture
Perrot 2014[278]	Systematic review is not relevant to review question or unclear PICO
Pezelj-ribaric 2013[279]	Incorrect population. Not chronic pain
Picarelli 2010[281]	Combinations of interventions. Combined with pharmacological therapy
Picarelli 2012[280]	Abstract
Plazier 2014[282]	Incorrect interventions
Powers 2018[283]	Combinations of interventions
Rayegani 2011[284]	Incorrect interventions
Reid 2001[285]	Case study
Renzenbrink 2004[286]	Incorrect population. Not primary pain
Riberto 2011[287]	Combinations of interventions. Intervention combined with exercise
Rigby 2017[288]	Incorrect population. Not chronic pain
Roizenblatt 2007[290]	No useable outcomes
Rollnik 2002[291]	Incorrect population. Not primary pain
Rowe 2005[292]	No useable outcomes
Ruiz-lopez 2017[293]	Non-English language studies
Ryan 2017[294]	Incorrect intervention (combined with a range of therapy from a physiotherapist, including but not limited to: CBT, hydrotherapy, motor imagery)
Sahin 2010[296]	No abstract/results
Sahin 2011[295]	Incorrect population (myofascial pain, duration unclear)
Sakrajai 2014[297]	Combinations of interventions. Incorrect population. Not chronic pain
Salazar 2017[298]	Combinations of interventions
Saltychev 2017[299]	Systematic review is not relevant to review question or unclear PICO
Sancakli 2015 [301]	Unclear population (no minimum duration of pain)
Santos 2018 [302]	No relevant outcomes
Sator-katzenschlager 2003[304]	Incorrect population. Incorrect interventions. Electric acupuncture.
Sator-katzenschlager 2004[303]	Incorrect interventions. Incorrect population. Electric acupuncture.
Sattayut 2012[305]	Crossover study
Sayilir 2017[307]	Incorrect population.
Sayilir 2018 [306]	Incorrect intervention (combination electrotherapy)
Schabrun 2012[308]	Incorrect population. Not chronic pain
Shafik 2006[309]	Incorrect population. Not primary pain
Shimoji 2007[310]	Incorrect population. Not primary pain
Shirani 2009[311]	Incorrect population. Not chronic pain
Shobha 2017[312]	No useable outcomes
Short 2010[313]	Abstract

Study	Exclusion reason
Silva 2017[315]	Crossover study
Simons 2006[316]	Incorrect interventions. Inappropriate comparison
Simpson 2009[317]	Unpublished
Skorupska 2012[318]	Incorrect population. Not primary pain
Skrinjar 2020 [319]	No useable outcomes
Slattery 2002[320]	Conference abstract. Unavailable
Smania 2003[321]	Incorrect population. Not primary pain
Smania 2005[322]	No useable outcomes
Snyder-mackler 1986[323]	Incorrect population. Not primary pain
Soysal 2013[324]	Combinations of interventions
Spanemberg 2019 [326]	No useable outcomes
Srbely 2007[327]	Incorrect population. Not chronic pain
Stonnington 1976[328]	Incorrect study design. Not randomised
Sunshine 1996[330]	No useable outcomes (no variability data)
Sutton 1997[331]	Endometriosis. Incorrect population
Takla 2018 [333]	Incorrect population (not chronic primary pain)
Takla 2018 [332]	No useable outcomes
Tanwar 2016[334]	Conference abstract
Taube s 1988[335]	Incorrect outcome. No useable outcomes
Taylor 1987[337]	Incorrect population (not chronic pain)
Taylor 2004[338]	Incorrect outcome. Cost-effectiveness study
Taylor 2013[336]	Incorrect interventions
Thorsteinsson 1977[340]	Incorrect population
Tieppo francio 2017[341]	Not primary pain. Osteoarthritis
Tirlapur 2013[342]	Systematic review is not relevant to review question or unclear PICO. Incorrect study design
To 2017[343]	No useable outcomes
Uemoto 2013[344]	Incorrect study design. No useable outcomes
Valle 2009[347]	No results
Van der windt 1999[348]	Systematic review is not relevant to review question or unclear PICO
Vance 2015[349]	Incorrect study design. Not randomised
Vas 2006[350]	Incorrect interventions. Acupuncture
Vaseghi 2014[351]	Systematic review is not relevant to review question or unclear PICO
Vaseghi 2015[352]	Systematic review is not relevant to review question or unclear PICO. Systematic review: study designs inappropriate
Vayvay 2016[353]	Intervention combined with exercise. Combinations of interventions
Venezian 2010[355]	Not guideline condition. Not chronic pain
Viana 2012[356]	Not primary pain. Stroke patients
Visnjevac 2017[357]	Incorrect interventions. Systematic review is not relevant to review question or unclear PICO
Vitiello 2007[358]	Incorrect population
Vrijens 2017[359]	Systematic review is not relevant to review question or unclear PICO
Vukoja 2011[360]	Incorrect study design. Letter to editor
Walker 1987[361]	Incorrect population. Neuropathic pain

Study	Exclusion reason
Wang 2011[363]	Non-English language studies
Wang 2014[362]	Incorrect population. Perioperative. Incorrect interventions. Acupuncture
Wang 2014[364]	Incorrect population. Not chronic pain
Waschl 2014[365]	Unavailable
Weisstanner 2014[367]	No relevant outcomes
Weisstanner 2017[368]	No relevant outcomes
Weng 2005[369]	Incorrect interventions
White 2000[372]	Crossover study
White 2007[370]	Incorrect interventions. Acupuncture
White 2012[371]	Incorrect interventions. Acupuncture
Wiffen 2005[373]	Incorrect population. Palliative care
Wilson 2014[374]	No useable outcomes
Yang 2018 [376]	Not in English
Yatci 2013[377]	Incorrect study design: expert opinion
Yesil 2017[378]	Incorrect interventions. Combinations of interventions
Yesil 2018[379]	Unavailable
Yildirim 2018 [380]	Incorrect population (pain for less than 6 weeks)
Yoshimizu 2012[381]	Crossover study
Young 1987[382]	Incorrect study design. Not randomised
Yuksel 2019 [383]	Incorrect comparison (healthy controls)
Zhu 2002[385]	Incorrect interventions. Acupuncture
Zhu 2017[384]	Systematic review is not relevant to review question or unclear PICO

I.2 Excluded health economic studies

None.

Appendix J: Research recommendations

J.1 Laser therapy

Research question: What is the clinical and cost-effectiveness of laser therapy for managing chronic primary pain in people aged 16 years and over?

Why this is important:

Laser therapy involves the non-invasive application of a single wavelength of light to the skin over the painful area using a probe. There are various laser devices and probe configurations in clinical use. The light is absorbed in the tissues and it is hypothesised that this results in local heating and effects on local chemical activity and cellular behaviour. It is through those effects that laser therapy is purported to have an anti-inflammatory effect and promote tissue repair.

14 studies were included in this review comparing laser to sham in a range of conditions including burning mouth syndrome (4 studies), temporomandibular pain (4 studies), fibromyalgia (3 studies), neck pain (2 studies) and myofascial pain (1).

While evidence of clinical benefit was observed there remains uncertainty regarding the efficacy and effectiveness of laser therapy, though there is some promising evidence. There is therefore a need for high quality trials into the effectiveness and cost effectiveness of laser therapy for chronic primary pain.

Criteria for selecting high-priority research recommendations:

PICO question	Population: Adults (aged >16) with Chronic Primary Pain Intervention(s): Laser therapy Comparison: Sham Outcome(s): Quality of life, Pain Interference and reduction,
Importance to patients or the population	If laser therapy offers clinically important benefits over sham laser therapy when added to care, at a reasonable cost threshold then it may be an important modality to enhance clinical outcome in this patient group.
Relevance to NICE guidance	This research will reduce the existing uncertainty regarding the effectiveness and cost-effectiveness of laser therapy and enable future guidelines to clearly recommend for or against the use of laser therapy.
Relevance to the NHS	A clear recommendation for or against laser therapy will offer clinicians clearer guidance on best care for chronic primary pain.
National priorities	None
Current evidence base	The NICE chronic pain guideline found very low to moderate quality evidence for improvement with laser therapy in quality of life in the short term and one small study showing a clinically important benefit in QOL in the long term. Although there was evidence from thirteen studies demonstrating a clinically important benefit in pain reduction in the short term, this was rated as very low quality evidence. Two further studies demonstrated clinically important benefit in pain reduction in the longer term (moderate quality evidence). However no clinically important difference was noted for psychological distress or discontinuation. Conflicting evidence was found comparing laser with sham for pain and quality of life outcomes. While evidence of clinical benefit was observed in some comparisons for pain and quality of life, there were concerns with the quality and applicability of the evidence. There remains uncertainty regarding the efficacy and effectiveness of laser therapy, though there is some promising evidence. No cost-effectiveness evidence has been identified regarding use of laser for the management of chronic primary pain. However the NICE chronic pain guideline committee noted that there

	would be resource implications, including the provision and maintenance of equipment and training therapists. There is therefore a need for a conclusive study into the clinical and cost effectiveness of laser therapy for chronic primary pain.
Equality	The recommendation is unlikely to impact on equality issues.
Study design	Randomised controlled trial with corresponding economic analysis. Post-intervention long term follow up should be included.
Feasibility	The trial is feasible and should be straightforward to carry out. There are challenges associated with the design of adequate sham controls for higher intensity laser therapy that delivers a sensation of heating that will require specific consideration when designing a trial.
Other comments	Low intensity laser therapy is easy to design sham controls for since it delivers no sensation beyond the pressure of the probe. A recommendation for laser therapy is likely to require the purchase of new equipment and staff training.
Importance	Low: the research is of interest and will fill existing evidence gaps.

J.2 Transcranial magnetic stimulation

Research question: What is the clinical and cost effectiveness of transcranial magnetic stimulation for managing chronic primary pain in people aged 16 years and over?

Why this is important:

Transcranial magnetic stimulation (TMS) has been proposed as a potential treatment option for chronic pain as stimulation of the motor cortex of the brain is known to lead to analgesia. TMS has been researched in various chronic pain conditions including those that fall within the definition of chronic primary pain. However, whether or not TMS is an effective and cost-effective treatment option for chronic primary pain remains unclear. TMS is not provided as part of current clinical practice for people with chronic primary pain and its introduction into practice would incur costs in terms of provision of the equipment and training in the use of the equipment, and therefore good quality research is required to inform this decision.

Criteria for selecting high-priority research recommendations:

PICO question	Population: Adults (aged >16) with chronic primary pain Intervention(s): TMS Comparison: Sham TMS or usual care Outcome(s): Pain reduction, health related quality of life, physical function, psychological distress, pain interference, pain self-efficacy.
Importance to patients or the population	There was a suggestion from the current evidence base that TMS may help improve pain in people with chronic primary pain. Further evidence to determine whether this benefit can be replicated in larger trials, or also has an impact on quality of life would help inform whether this should be a treatment choice for this population.
Relevance to NICE guidance	More evidence from a large RCT would help inform an update of this guideline to guide a recommendation on whether TMS should or should not be recommended for people with chronic primary pain.
Relevance to the NHS	TMS is not routinely used in current NHS practice to treat chronic primary pain, therefore good high quality evidence would be of relevance to inform whether a change in practice is warranted.
National priorities	N/A
Current evidence base	Eight studies of TMS in people with chronic primary pain were included in the guideline review. When compared to sham there was some indication of benefit in quality of life and pain interference, however this evidence was inconsistent and from relatively small sample sizes. There was more

	evidence for a reduction in pain intensity, but in the absence of consistent benefit in other outcomes, or long term benefit, this was considered insufficient to base a recommendation on.
Equality	No specific equality issues.
Study design	An adequately powered, sham controlled, RCT with a follow-up period of greater than 3 months.
Feasibility	The design of this research is feasible, although it is noted that TMS is not widely available, which may have an impact.
Other comments	None.
Importance	Low: the research is of interest and will fill existing evidence gaps.

Appendices

Appendix K: MIDs for continuous outcomes

Table 24: MIDs for continuous outcomes: Laser therapy versus sham laser therapy

Outcomes	MID
Quality of life at ≤3 months (Oral health impact profile, FIQ, high is poor outcome, final values)	0.5 (SMD)
Quality of life at >3 months (Oral health impact profile, FIQ, high is poor outcome, final values)	0.5 (SMD)
Pain reduction at ≤3 months (VAS, NRS, FIQ pain scale, high is poor outcome, 0-10, final values and change scores)	0.79
Pain reduction at >3 months (VAS, high is poor outcome, 0-10, final values)	0.6
Psychological distress at ≤3 months (Hospital anxiety and depression rating scale, anxiety subscale, 0-21, high is poor outcome, final values)	1.75
Psychological distress at ≤3 months (Hospital anxiety and depression rating scale, depression subscale, 0-21, high is poor outcome, final values)	2.25

Table 25: MIDs for continuous outcomes: TMS versus sham TMS

Outcomes	MID
Quality of life at ≤3 months (WHOQOL-BREF physical domain, 4-20, high is good outcome, final values)	1.42
Quality of life at ≤3 months (WHOQOL-BREF psychological domain, 4-20, high is good outcome, final values)	1.245
Quality of life at ≤3 months (FIQ, 0-100, high is poor outcome, final values)	8.395
Quality of life at >3 months (FIQ, 0-100, high is poor outcome, final values)	7.5
Pain reduction at ≤3 months (VAS, McGill Pain questionnaire, 0-10, high is poor outcome, final values)	1.05
Physical function at ≤3 months (BPI functional impairment subscale, 0-10, high is poor outcome, final values)	1.345
Psychological distress at ≤3 months (Beck depression inventory, 0-61, high is poor outcome, final values and change scores)	2.55
Psychological distress at ≤3 months (Hamilton depression rating scale, MADRS, BDI, high is poor outcome, final values)	0.5 (SMD)
Psychological distress at ≤3 months (HADS anxiety, 0-21, high is poor outcome, change scores)	1.15
Psychological distress at >3 months (HADS anxiety, 0-21, high is poor outcome, change scores)	2.85
Psychological distress at >3 months (HADS depression, 0-21, high is poor outcome, change scores)	2

Outcomes	MID
Pain interference at >3 months (BPI pain interference, 0-10, high is poor outcome, final values)	0.75

Table 26: MIDs for continuous outcomes: TDCS versus sham TDCS

Outcomes	MID
Pain reduction at ≤3 months (NRS, VAS, 0-10, high is poor outcome, final values)	0.75
Psychological distress at ≤3 months (Hospital anxiety and depression scale, HAM-A, anxiety subscales, high is poor outcome, final values)	0.5 (SMD)
Psychological distress at ≤3 months (Hospital anxiety and depression scale, BDI, HAM-D, depression subscales, high is poor outcome, final values)	0.5 (SMD)
Sleep at ≤3 months (PSQI, scale range not reported, high is poor outcome, final values)	1.87

Table 27: MIDs for continuous outcomes: TENS versus sham TENS

Outcomes	MID
Quality of life at ≤3 months (SF36 physical T scores, high is good outcome, change scores)	3.15
Quality of life at ≤3 months (SF36 mental T scores, high is good outcome, change scores)	5.05
Pain reduction at ≤3 months (BPI intensity, VAS, 0-10, high is poor outcome, final values and change scores)	0.94
Physical function at ≤3 months (6 minute walk test, change scores)	157
Psychological distress at ≤3 months (PROMIS depression T scores, high is poor outcome, change scores)	4.15
Psychological distress at ≤3 months (PROMIS anxiety T scores, high is poor outcome, change scores)	4.18
Pain interference at ≤3 months (BPI interference, 0-10, high is poor outcome, change scores)	1.09
Pain self-efficacy at ≤3 months (PSEQ, 0-60, high is good outcome, change scores)	6.6

Table 28: MIDs for continuous outcomes: TENS versus usual care

Outcomes	MID
Quality of life at ≤3 months (SF36 physical T scores, high is good outcome, change scores)	3.25
Quality of life at ≤3 months (SF36 mental T scores, high is good outcome, change scores)	5.15
Pain reduction at ≤3 months (BPI intensity, 0-10, high is poor outcome, change scores)	0.91
Physical function at ≤3 months (6 minute walk test, change scores)	160.25

Outcomes	MID
Psychological distress at ≤3 months (PROMIS depression T scores, high is poor outcome, change scores)	4.05
Psychological distress at ≤3 months (PROMIS anxiety T scores, high is poor outcome, change scores)	4.13
Pain interference at ≤3 months (BPI interference, 0-10, high is poor outcome, change scores)	1.27
Pain self-efficacy at ≤3 months (PSEQ, 0-60, high is good outcome, change scores)	6.63

Table 29: MIDs for continuous outcomes: PENS versus sham PENS

Outcomes	MID
Quality of life at ≤3 months (NIH-CPSI, 0-12, high is poor outcome, final values)	1.05
Pain reduction at ≤3 months (VAS, 0-10, high is poor outcome, final values)	0.2

Table 30: MIDs for continuous outcomes: PENS versus usual care

Outcomes	MID
Pain reduction at ≤3 months (VAS, 0-10, high is poor outcome, final values)	0.44

Table 31: MIDs for continuous outcomes: Therapeutic ultrasound versus usual care

Outcomes	MID
Pain reduction at ≤3 months (VAS, 0-10, high is poor outcome, final values)	0.44