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Transcutaneous Electrical Stimulation (TENS) and Transcutaneous Electrical Modulation Pain Reprocessing (TEMPR)

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Related Policies (if applicable)
SUR705.010: Temporomandibular Joint (TMJ) Disorders (TMJD)
SUR701.046: Remote Electrical Neuromodulation for Migraines

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Coverage

Transcutaneous Electrical Nerve Stimulation
Transcutaneous electrical nerve stimulation (TENS) **may be considered medically necessary** for treatment of refractory chronic pain (e.g., chronic musculoskeletal or neuropathic pain) that causes significant disruption of function, and pain is unresponsive to at least three (3) months of conservative medical therapy, including nonsteroidal anti-inflammatory medications, ice, rest, and/or physical therapy.

NOTE 1: It is recommended that the individual should have had a trial of TENS of at least 30 days to establish efficacy of the treatment and compliance in using the device on a regular basis (e.g., daily or near daily use) throughout the trial period and that the trial is monitored by a physician.

TENS **is considered experimental, investigational and/or unproven** for any other condition including, but not limited to:

- Management of acute pain (e.g., postoperative or during labor and delivery);
- Treatment of dementia;
- Headache, including prevention or treatment of migraine headaches;
- Essential tremor; and
- Management of attention deficit hyperactivity disorder.

Form-Fitting Conductive Garment

A form-fitting conductive garment (e.g., vest, gauntlet, etc.) **may be considered medically necessary** only when it has been approved for marketing by the U.S. Food and Drug Administration (FDA), has been prescribed by a physician for use in delivering TENS that is considered medically necessary (see above criteria), and meets at least **ONE** of the following criteria:

- There is a large area or number of sites to be stimulated such that it is not feasible to use conventional electrodes, adhesive tapes, and lead wires; or
- The individual has a documented skin problem or other medical condition that precludes the application of conventional electrodes, adhesive tapes, and lead wires; or
- The areas or sites to be stimulated are inaccessible with the use of conventional electrodes, adhesive tapes, and lead wires.

Form-fitting conductive garments for all other indications **are considered not medically necessary**.

Transcutaneous Electrical Modulation Pain Reprocessing

Transcutaneous electrical modulation pain reprocessing (TEMPR) (e.g., scrambler therapy) **is considered experimental, investigational and/or unproven.**

Combination Therapies

Devices capable of combination therapies (e.g., NexWave™) that provide several modalities (e.g., interferential, transcutaneous electrical nerve stimulation, and neuromuscular electrical stimulation) **are considered experimental, investigational and/or unproven.**

Transcutaneous Magnetic Stimulation (Axon Therapy)

Transcutaneous magnetic stimulation by focused low-frequency electromagnetic pulse (Axon Therapy) **is considered experimental, investigational and/or unproven** for all indications, including but not limited to, chronic pain management.

Policy Guidelines

None.

Description

Transcutaneous Electrical Nerve Stimulation (TENS)
TENS describes the application of electrical stimulation to the surface of the skin. In addition to more traditional settings such as a physician's office or an outpatient clinic, TENS can be self-administered in a patient's home.

Transcutaneous electrical nerve stimulation has been used to treat chronic intractable pain, postsurgical pain, and pain associated with active or post-trauma injury unresponsive to other standard pain therapies. It has been proposed that TENS may provide pain relief through the release of endorphins in addition to potential blockade of local pain pathways. TENS has also been used to treat dementia by altering neurotransmitter activity and increasing brain activity that is thought to reduce neural degeneration and stimulate regenerative processes.

Percutaneous electrical nerve stimulation (PENS) is similar to TENS, but uses microneedles that penetrate the skin instead of surface electrodes. Interferential stimulation uses a modulated waveform for deeper tissue stimulation, and the stimulation is believed to improve blood flow to the affected area.

Regulatory Status
<u>TENS</u>
TENS devices consist of an electrical pulse generator, usually battery-operated, connected by wire to 2 or more electrodes, which are applied to the surface of the skin at the site of the pain. Since 1977, a large number of devices have received marketing clearance through the U.S. Food and Drug Administration (FDA) 510(k) process. Marketing clearance via the 510(k) process does not require data regarding clinical efficacy; as a result, these cleared devices are considered substantially equivalent to predicate devices marketed in interstate commerce before May 1976, the enactment date of the Medical Device Amendments. The cleared devices are also equivalent to devices that have been reclassified and do not require approval of a premarket approval application (PMA). FDA product code: GZJ.

In 2014, the Cefaly® (STX-Med), which is a TENS device, was granted a de novo 510(k) classification by the FDA for the prophylactic treatment of migraine in patients 18 years of age or older. (1) The Cefaly® Acute and Cefaly® Dual devices were cleared by the FDA through the 510(k) process for the acute treatment of migraine in patients 18 years of age or older and for both the acute treatment and prophylaxis of migraines in adults, respectively, in 2017. (2, 3) Other TENS devices cleared by the FDA through the 510(k) process for the prophylactic treatment of migraine in patients include Allive (Nu Eyne Co), Relivion (Leurolief Ltd.), and HeadaTerm (EEspress) among others. (4, 5, 6) FDA product code: PCC.

In 2018, the FDA reviewed the Cala ONE™ TENS device (Cala Health) via the de novo pathway and granted approval for the device as an aid in the transient relief of hand tremors following stimulation in the affected hand of adults with essential tremor. This prescription device is contraindicated for use in patients with an implanted electrical medical device, those that have suspected or diagnosed epilepsy or other seizure disorder, those who are pregnant, and patients with swollen, infected, inflamed areas, or skin eruptions, open wounds, or cancerous lesions. In October 2020, the FDA granted breakthrough device designation to the Cala Trio™ device for the treatment of action tremors in the hands of adults with Parkinson's disease. (7) In November 2022, the Cala kIQ™ device was approved via the 510(k) pathway (K222237). The device is indicated to aid in the temporary relief of hand tremors in the treated hand following stimulation in adults with essential tremor. It was also approved to aid in the temporary relief of postural and kinetic hand tremor symptoms that impact some activities of daily living in the treated hand of adults with Parkinson's disease.

In 2019, the FDA permitted marketing of the first medical device to treat attention deficit hyperactivity disorder (ADHD) - the Monarch® external Trigeminal Nerve Stimulation (eTNS) System by NeuroSigma. (8) The FDA reviewed the system through the de novo premarket review pathway. This prescription only TENS device is indicated for patients 7 to 12 years of age who are not currently taking prescription ADHD medication. The Monarch eTNS System is intended to be used in the home under the supervision of a caregiver. The device generates a low-level electrical pulse and connects via a wire to a small patch that adheres to a patient's forehead, just above the eyebrow.

<u>Transcutaneous Electrical Modulation Pain Reprocessing (TEMPR)</u>
TEMPR is delivered in the same way as TENS, but instead of blocking pain signals, this therapy sends a “no pain” signal. Competitive Technologies, Inc. manufactures a device called Calmare® Pain Therapy Treatment, which has received 510(k) marketing clearance from the FDA as a multi-channel TENS device. The company describes the Calmare Pain Therapy Treatment as “a non-invasive method for rapid treatment of high-intensity oncologic, neuropathic, and drug-resistant pain through a biophysical rather than a biochemical manner. The method incorporates electromedical equipment for electronic nerve stimulation and uses the nerve fiber as a passive means to convey a message of normality to the central nervous system (CNS) by a procedure defined as scrambling or tricking of information, which then enables the CNS to modify the reflex adaptive responses.” (9) The supposed advantage is that this is a multiprocessor apparatus able to simultaneously treat multiple pain areas in the individual. The patient experiences longer “no pain” periods after each successive treatment. TEMPR is administered in the doctor’s office under direct supervision of the physician, who provides an initial consultation to discern the most effective path for electrode placement. Treatment applications are interactive between the patient and the provider, with the provider attending and making adjustments approximately every 10 minutes throughout the treatment session, which typically lasts an hour.

<u>Combination Therapy</u>
Combination therapy devices are classified as Class 2 devices by the FDA. This classification requires registration with the FDA prior to marketing and does require a 510(k) clearance. There are numerous combination therapy devices. The FDA describes these as devices as “stimulator, muscles, powered.” Refer to the FDA website at <www.fda.gov> for the most current listing of devices.

In 2011, the NexWave™ (Zynex Medical) received marketing clearance via the 510(k) process and was considered substantially equivalent to predicate devices. Indications for use included: interferential mode (IFC) for symptomatic relief of chronic intractable pain, post-traumatic and post-surgical pain; neuromuscular electrical stimulation mode (NMES) for muscle re-education, prevention or retardation of disuse atrophy, increasing local blood circulation, maintaining or increasing range of motion and relation of muscle spasms, as well as; transcutaneous electrical nerve stimulation mode (TENS) for management and symptomatic relief of chronic intractable pain, post-traumatic and post-surgical pain. FDA product codes: IPF, GZI, and LIH. (10)

Conductive Garments

A conductive garment is a form-fitted, lycra-spandex garment containing electrodes, wires, and connectors that greatly simplify electrical stimulation therapy. These are supplied in many forms, including sleeves for shoulder, arm, hip or leg; belts; shorts; vest; gloves; socks; or collar. These garments provide allowance for accurate placement of multiple electrodes without professional assistance, insurance that electrodes stay in position, and avoidance of skin irritation caused by adhesive on electrode pads. There are many brands and styles available; two examples are Wearable Therapy® and RS-FBG® full back garment.

Transcutaneous Magnetic Stimulation (Axon Therapy)

Transcutaneous magnetic stimulation, or Axon Therapy, applies noninvasive neuromodulation by directing magnetic stimulation designed to activate a nerve that is causing ongoing pain post trauma. Axon Therapy non-invasively delivers focused magnetic pulses through a figure-8-shaped coil, targeting the damaged A-Beta sensory nerve fibers, proximal to the neuroma. By activating A-Beta, Axon Therapy helps modulate pain fiber activity at the site of trauma. Developed by NeuraLace Medical, Inc. (San Diego, CA), the therapy was granted 510(k) clearance (K210021) in June 2021 by the FDA to stimulate peripheral nerves for relief of chronic intractable, post-traumatic, and post-surgical pain for patients ages 18 and older. FDA product code: QPL, IPF. (11)

Rationale

This medical policy was created in June 2014 and has been updated regularly with searches of the PubMed database. The most recent literature update was performed through September 23, 2023.

Medical policies assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life (QOL), and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Transcutaneous Electrical Nerve Stimulation (TENS) for Chronic Pain
A large number of systematic reviews, most conducted by Cochrane, have assessed the use of TENS in the treatment of a variety of pain conditions, including the topics of osteoarthritis, rheumatoid arthritis, pancreatitis, myofascial trigger points, temporomandibular joint pain, cancer pain, neck pain, acute pain, phantom limb pain, labor pain, and chronic back pain. (12-32) In 2010, the American Academy of Neurology (AAN) published an evidence-based review of the efficacy of TENS for the treatment of pain in neurologic disorders, including low back pain and diabetic peripheral neuropathy. (33)

<u>Clinical Context and Therapy Purpose</u>
The purpose of TENS is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with chronic pain (e.g., musculoskeletal, neuropathic, and mixed pain conditions).

The following PICO was used to select literature to inform this policy.

Populations
The relevant population of interest is individuals who suffer from chronic pain conditions (e.g., musculoskeletal, neuropathic, and mixed pain conditions).

Interventions
The therapy being considered is TENS.

Comparators
The following therapies are currently being used to treat chronic pain: physical therapy and pharmacotherapy.

Outcomes
The general outcomes of interest are reductions in symptoms and medication use, and improvements in functional outcomes and QOL. Given the different types of pain conditions, follow-up will vary, and some cases will be life-long (e.g., fibromyalgia, arthritis).

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Low Back Pain

Systematic Reviews

Wu et al. (2018) conducted a meta-analysis of RCTs comparing the efficacy of TENS with a control and other nerve stimulation therapies for the treatment of chronic back pain. (34) Reviewers searched 4 databases (PubMed, Cochrane, Google Scholar, Clinical Trials.gov) and identified 12 RCTs involving 700 patients. Analysis indicated that TENS had efficacy for providing pain relief similar to control treatment (standard mean difference [SMD] = -0.20; 95% CI, -0.5 to 0.18; p=0.293) and other types of nerve stimulation therapies were more effective than TENS (SMD=0.86; 95% CI, 0.15 to 1.57; p=0.017).

Dubinsky et al. (2010), who conducted an evidence-based review of the AAN, evaluated the efficacy of TENS for treating pain in neurologic disorders. (33) The evidence on TENS for chronic low back pain of various etiologies (some neurologic) included 2 class I studies (prospective randomized trial with masked outcome assessment in a representative population) and 3 class II studies (randomized trial not meeting class I criteria or a prospective matched group cohort study in a representative population). The class I studies compared TENS with sham TENS for 4 or 6 weeks of treatment. Although both studies were adequately powered to find a 20% or greater difference in pain reduction by visual analog scale (VAS), after correction for multiple comparisons, no significant benefit was found for TENS compared with sham TENS. In 2 of the 3 class II studies, no significant differences were found between TENS and sham TENS. In the third class II study, the benefit was found in 1 of 11 patients treated with conventional TENS, 4 of 11 treated with burst-pattern TENS and 8 of 11 treated with frequency-modulated TENS. Overall, evidence was conflicting. Because class I studies provide stronger evidence, AAN considered the evidence sufficient to conclude that TENS is ineffective for the treatment of chronic low back pain.

Cochrane reviews by Khadilkar et al. (2005; 2008), concluded that there is limited and inconsistent evidence for the use of TENS as an isolated treatment for low back pain. (19, 20)

Randomized Controlled Trials

Jalalvandi et al. (2022) compared the effects of TENS (n=22) to back exercises (including strengthening and stretching; n=22) in operating room nurses with chronic low back pain. (35) After 6 weeks, average pain and disability scores significantly decreased in both treatment groups as compared to the baseline. After adjusting for the baseline values, the TENS group had a significantly higher pain score reduction (mean difference [MD]: 4.23; p=.030) and a significantly greater decrease in the disability scores (MD: -3.99; p=.021) when compared to the back exercises group.

Leemans et al. (2020) evaluated the effects of heat and TENS in 50 patients with chronic low back pain. (36) Patients were randomized to heat plus TENS or no treatment. At 24 hours after the procedure, there was no significant difference between the groups for average pain in the last 24 hours or maximum pain experienced in the last 24 hours. Measurements were repeated at 4 weeks and no significant differences in pain scores were found between groups at that time point either.

Keskin et al. (2012) reported on an RCT of TENS for pregnancy-related low back pain. (37) Seventy-nine patients were randomized to 6 TENS sessions over 3 weeks, a home exercise program, acetaminophen, or a no-treatment control. In the control group, pain intensity increased in 57% of participants. Pain decreased in 95% of participants in the exercise group and in all participants in the acetaminophen and TENS groups. The VAS score improved by a median of 4 points in the TENS group and by 1 point in the exercise and acetaminophen groups. In the control group, the VAS score worsened by 1 point. Roland-Morris Disability Questionnaire scores indicated significantly greater improvement in function in the TENS group (-8.5) compared with the control (+1), exercise (-3), and acetaminophen (-3) groups. This trial lacked a sham TENS control. In a subsequent RCT by Jamison et al. (2019), that also lacked a sham control group and had fewer patients (n=33), compared to treatment-as-usual, use of high-frequency TENS along with a smartphone tracking app resulted in greater reductions in pain intensity. (38)

<u>Diabetic Peripheral Neuropathy</u>

Systematic Reviews

The AAN’s 2010 evidence-based review also identified 2 class II studies comparing TENS with sham TENS and 1 class III study comparing TENS with high-frequency muscle stimulation for patients with mild diabetic peripheral neuropathy. (33) The studies found a modest reduction in VAS scores for TENS compared with sham, and a larger proportion of patients experiencing benefit with high-frequency muscle stimulation than with TENS. Reviewers concluded that, on the basis of these 2 class II studies, TENS was likely effective in reducing pain from diabetic peripheral neuropathy; however, no studies compared TENS with other treatment options.

Randomized Controlled Trials

A small RCT by Gossrau et al. (2011) found no difference between microcurrent TENS (micro-TENS) compared with sham in 41 patients with diabetic peripheral neuropathy. (39) In this trial, current was applied at an intensity of 30 to 40 microamps rather than the usual intensity of several milliamps, and patients were treated for 30 minutes, 3 times per week. After 4 weeks of treatment, 29% of the micro-TENS group and 53% of the sham group showed a response to therapy, defined as a minimum 30% reduction in neuropathic pain score. Median Pain Disability Index was reduced to a similar extent in the TENS group (23%) and the sham groups (25%).

Cancer Pain

For a Cochrane review by Robb et al. (2008), which evaluated TENS for cancer pain, only 2 RCTs (N=64 participants) met the selection criteria. (29) There were no significant differences between TENS and placebo in the included studies. One RCT found no differences between TENS and placebo for pain secondary to breast cancer treatment. The other RCT examined acupuncture-type TENS in palliative care patients but was underpowered. The results of the review were considered inconclusive due to a lack of suitable RCTs. A 2012 update of the Cochrane review identified an additional RCT (a feasibility study of 24 patients with cancer bone pain) that met selection criteria. (18) The small sample sizes and differences in patient study populations across the 3 RCTs precluded meta-analysis. Results on TENS for cancer pain remain inconclusive.

Fibromyalgia

Systematic Review

Amer-Cuenca et al. (2023) conducted a systematic review and meta-analysis of TENS for analgesia in patients with fibromyalgia. (40) When the 11 included RCTs were analyzed with a random-effects model, there was no effect of TENS on pain ($p>.05$). In contrast, a mixed-effects model that considered the TENS dosage found significant effect sizes with the number of TENS sessions ($p=.005$), TENS frequency ($p=.014$), and TENS intensity ($p=.047$). The authors concluded that TENS can reduce fibromyalgia pain when used at high frequency, high intensity, or for more than 10 sessions. A limitation of the review is that about half of the included studies had a high risk of bias.

Randomized Controlled Trials

A placebo-controlled crossover RCT by Dailey et al. (2013) investigated the effect of a single treatment of TENS in 41 patients with fibromyalgia. (41) Patients were blindly allocated to no treatment, active TENS treatment, or placebo treatment. Each treatment arm had therapy once weekly for a 3-week period. Patients rated the average pain intensity before and after treatment on a 0-to-10 scale and found less pain with movement was less during active TENS compared with placebo or no TENS ($p<0.05$). Patients also rated fatigue with movement and found that fatigue decreased with active TENS compared with placebo or no TENS ($p<0.05$ and $p<0.01$, respectively). Pressure pain threshold improvement was significantly greater with active TENS (30%, $p<0.05$) than with placebo (11%) or no TENS (14%).

Another RCT by Lauretti et al. (2013) investigated TENS in fibromyalgia. (42) However, there was no comparison between active treatment and placebo reported; only change from baseline within each group was reported. TENS was administered for 20 minutes at 12-hour intervals for 7 consecutive days. In the dual placebo group, VAS pain scores did not improve compared with baseline. Patients who had a single site of active TENS reported a reduction in pain of 2.5 cm ($p<0.05$ vs baseline), and patients in the dual TENS group experienced the greatest reduction in pain of 4.2 cm ($p<0.02$ vs baseline). Consumption of medication for pain was also decreased significantly from baseline in the single TENS ($p<0.05$) and dual TENS groups ($p<0.02$). Sleep improvements were reported by 10 patients in the dual TENS group, eight in the single TENS group, and four in the placebo group. Fatigue increased for 3 patients in the placebo group but decreased in 7 patients in the dual TENS group; moreover, fatigue decreased for 5 patients in the single TENS group. No adverse events were reported.

Jamison et al. (2021) evaluated the efficacy and safety of a wearable TENS device in adults with fibromyalgia (43) In this single-center, parallel-group study, 119 patients were randomly assigned to a wearable TENS device (Quell®; n=62) or a sham device (n=57) for 3 months. The primary outcome measure was the Patient Global Improvement of Change (PGIC), which represents the patient's overall belief about the efficacy of treatment on a 7-point categorical verbal rating scale. Selection of 1 means "no change or condition has gotten worse" to 7 meaning "a great deal better and a considerable improvement that has made all the difference." Overall, no differences were found between active and sham treatment on PGIC scores at 3 months (mean difference: 0.34; 95% CI, -0.37 to 1.04; p=.351) in the intention-to-treat population. In the higher pain sensitivity subgroup, the mean PGIC score at 3 months was 4.05 for active treatment versus 2.86 for sham treatment (mean difference: 1.19; 95% CI, 0.24 to 2.13; p=.014). After 3 months of active treatment, all secondary efficacy measures (e.g., disease impact and health-related QOL) exhibited significant within-group improvement compared to pre-treatment baseline. A total of 12 (5 active, 7 sham) adverse events were reported. Nine of the events were definitely or possibly related to TENS use but were minor and self-limited. The authors concluded that the study demonstrated modest treatment effects of reduced disease impact, pain, and functional impairment from wearable TENS in patients with fibromyalgia.

Refractory Chronic Pelvic Pain

Observational Data

There is limited literature on the use of TENS for chronic pelvic pain. No RCTs were identified. An observational study by Schneider et al. (2013) assessed 60 men consecutively treated with TENS for refractory chronic pelvic pain syndrome. (44) TENS was performed at home for 12 weeks with participants keeping a pain diary to calculation VAS score. A successful treatment response was defined as a 50% or greater reduction in VAS and absolute VAS of less than 3 at the end of treatment. TENS was successful in 29 (48%) of patients, and treatment response was sustained at a mean follow-up of 44 months (95% CI, 33 to 56 months). After 12 weeks of treatment, VAS scores decreased significantly (p<0.001) from 6.6 to 3.9. QOL assessed by the National Institutes of Health Chronic Prostatitis Symptom Index, improved significantly after 12 weeks of TENS treatment (p<0.001). No adverse events were reported.

Osteoarthritis of the Knee

Systematic Reviews

A Cochrane review by Rutjes et al. (2009) found that the evidence on TENS for pain relief in patients with osteoarthritis of the knee was inconclusive. (30) Included in the review were 18 small trials assessing 813 patients; 11 trials used TENS, four used interferential current stimulation, one used both TENS and interferential current stimulation, and two used pulsed electrostimulation. Methodologic quality and quality of reporting were rated poor. Additionally, there was a high degree of heterogeneity among the trials, and the funnel plot for pain was asymmetrical, suggesting both publication bias and bias from small studies.

Randomized Controlled Trials
Additional randomized trials were published after the Rutjes et al. (2009) systematic review.

Reichenbach et al. (2022) compared treatment with TENS (n=108) to sham TENS (n=112) in patients with knee osteoarthritis in 6 outpatient clinics in Switzerland. (45) The primary outcome of mean Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain subscale score at 3 weeks did not significantly differ between the TENS (2.20) and sham TENS group (2.34; MD: -0.06; 95% CI, -0.41 to 0.29; p=.74); there was also no significant between-group difference at 15 weeks (2.53 vs. 2.60, respectively; MD: 0.01; 95% CI, -0.37 to 0.39; p=.98).

Cherian et al. (2016) compared TENS with standard of care in the treatment for 70 patients who had knee osteoarthritis; all patients had previously taken part in a prospective 3-month trial of TENS, allowing researchers to collect data on the long-term efficacy of TENS (mean follow-up time, 19 months). (46) The follow-up study evaluated pain (using a VAS) and function (measured by new Knee Society Scale and Lower-Extremity Functional Scale scores) and a number of secondary outcomes, including medication usage, QOL, device use, and conversion to total knee arthroplasty. For all outcomes, reviewers reported a general trend of improvement for the TENS group compared with the standard of care group; however, no statistical analyses were provided for secondary outcomes, and several differences were not significant among primary outcomes. When measured from pretreatment to final follow-up, Knee Society Scale (p=0.002) and Lower-Extremity Functional Scale (p<0.001) scores were significantly increased for the TENS group. The trial's limitations included its small sample size and possible variance in the amount of medication taken by each patient; also, the interviews were not conducted in person, meaning that some conclusions about functional improvement were not confirmed by a physical examination.

An RCT by Palmer et al. (2014) evaluated 224 participants with osteoarthritis of the knee that assigned patients to 1 of 3 interventions: TENS combined with education and exercise (n=73), sham TENS combined with education and exercise (n=74), or education and exercise alone (n=77). (47) Investigators and participants were blinded to treatment. Participants were treated for 6 weeks and directed to use the TENS device as needed for pain relief. WOMAC pain, function, and total scores improved significantly over time from baseline to 24 weeks but did not vary between groups (p>0.05). TENS as an adjunct to exercise did not elicit additional benefits.

In another RCT, Vance et al. (2012) assessed 75 patients given a single session of high-frequency TENS, low-frequency TENS, or placebo TENS. (48) All 3 groups reported a reduction in pain at rest and during the Timed Up & Go test, and there were no differences in pain scores between groups.

A small RCT by Chen et al. (2013) compared intra-articular hyaluronic acid injections with TENS for the management of knee osteoarthritis in 50 participants. (49) Twenty-seven patients were randomized to hyaluronic acid and received 1 intra-articular injection weekly for 5 weeks. Twenty-three patients in the TENS group received 20-minute sessions of TENS 3 times weekly for 4 weeks. The TENS group exhibited a modest but significantly greater improvement (p=0.03) than the hyaluronic acid group on VAS pain score (mean final score, 4.17 vs 5.31, respectively) at 2 weeks, but there was no difference between groups at 2 or 3 months post-treatment. The TENS group also had a greater improvement on the Lequesne Index at 2-week follow-up compared with the hyaluronic acid group (mean final score, 7.78 vs 9.85, respectively; p=0.01) and at 3-month follow-up (mean final score, 7.07 vs 9.2, respectively; p=0.03). Both treatment groups reported significant improvements from baseline to 3 months on scores in walking time, patient global assessment, and disability in activities of daily life.

Rheumatoid Arthritis

Two Cochrane reviews (2002, 2003) concluded that outcomes for patients with rheumatoid arthritis treated with TENS were conflicting. (13, 14)

Multiple Sclerosis

Systematic Reviews

Sawant et al. (2015) reported a systematic review of 4 RCTs of TENS for the management of central pain in multiple sclerosis. (50) Sample sizes ranged from 10 to 60 patients. One study examined the effect of TENS on upper-extremity pain, and the other three studied the effect of TENS on low back pain. The exact electrode placement could not be identified. Effect sizes, extracted from the 4 studies, showed a medium sized effect of TENS (Hedges' g=0.35, p=0.009). The overall level of evidence was considered to be GRADE 2. Similar findings were reported in a subsequent review by Amatya et al. (2018). (51)

Phantom Limb Pain

Systematic Reviews

A Cochrane review by Johnson et al. (2015) found no RCTs on TENS for phantom limb or stump pain after amputation. (52) Reviewers concluded that the published literature on TENS for phantom limb pain in adults lacked the methodologic rigor and robust reporting needed to assess its effectiveness confidently and that RCT evidence is required.

Neck Pain

Systematic Reviews

A Cochrane review reported by Martimbianco et al. (2019) assessed the evidence of TENS for the treatment of chronic neck pain. (22) Seven RCTs (N=651) comparing TENS alone or in combination with other treatments versus active or inactive treatments were included. Due to heterogeneity in interventions and outcomes, the results were not pooled for a meta-analysis. There was very low-certainty evidence from 2 trials about the effects of conventional TENS versus sham TENS at short-term (up to 3 months after treatment) follow-up. There was no statistically significant difference in outcomes between groups for pain, as assessed by the VAS, (MD, -0.10; 95% CI, -0.97 to 0.77) and the percentage of participants presenting improvement of pain (relative risk [RR], 1.57; 95% CI, 0.84 to 2.92). The authors concluded that there is insufficient evidence regarding the use of TENS in patients with chronic neck pain.

Randomized Controlled Trials
Martins-de-Sousa et al. (2023) conducted an RCT of TENS combined with a therapeutic exercise program in patients with chronic neck pain. (53) Patients were randomized to 8 sessions of placebo TENS (n=20), high frequency TENS (n=20), or low frequency TENS (n=20). The primary outcome, disability after 8 treatment sessions, was similar between groups (p>.05). Other outcomes including pain intensity at the end of treatment and 4 weeks after the end of treatment were also similar between groups. The small sample size may have limited the power to detect a difference between groups.

Diaz-Pulido et al. (2021) compared the effects of manual therapy versus TENS on cervical active mobility and muscle endurance in 90 adults diagnosed with subacute and chronic mechanical neck disorders. (54) TENS (n=43) and manual therapy (n=47) interventions each consisted of 10 sessions, provided by primary care physical therapists for 30 minutes on alternate days. Outcome measures included active range of motion and endurance of the neck muscles; evaluated pre- and post-intervention and at 6-month follow-up. Of the 90 participants, 72 completed all interventions. Results revealed that manual therapy yielded a significant improvement in active mobility and endurance at post-intervention. At 6-month follow-up, the differences were only significant in endurance and in sagittal plane active mobility. No significant improvement was noted in the TENS group.

<u>Pain After Stroke</u>
Systematic Reviews
Evidence on the efficacy of TENS for shoulder pain after stroke was considered inconclusive in a Cochrane review by Price et al. (2000). (27)

<u>Pain After Spinal Cord Injury</u>
Systematic Reviews
A Cochrane review by Boldt et al. (2014) evaluated non-pharmacologic interventions for chronic pain in individuals with spinal cord injury identified an RCT on TENS. (55) This trial had a high risk of bias, and no conclusion could be drawn on the effectiveness of TENS compared with sham for reducing chronic pain in this population.

<u>Facial Myalgia</u>
Randomized Controlled Trials
A RCT by De Giorgi et al. (2017) evaluated the efficacy of TENS in treating subjective and objective pain in 49 women diagnosed with chronic facial myalgia; 34 patients received TENS treatment daily for 10 weeks and were evaluated for pain up to 25 weeks, and 15 patients received no treatment and were evaluated for pain up to 10 weeks. (56) TENS treatment consisted of daily 60-minute sessions at 50 Hz, and VAS scores were taken for average and maximum pain intensity in the previous 30 days, as well as the level of pain at examination. The other primary outcome was the assessment of pain at muscular palpation sites, measured by the Pericranial Muscle Tenderness Score and Cervical Muscle Tenderness Score. For this outcome and that of VAS (mean and maximum measurements), patients in the TENS group had

significantly lower pain levels than those for the control group at 10 weeks ($p<0.05$). Within the TENS group, the trialists found that VAS scores tended to decrease during the trial, as did Pericranial Muscle Tenderness and Cervical Muscle Tenderness scores ($p<0.05$). These differences were significant except for the period between 15 weeks and 25 weeks. Secondary outcomes included mandibular movement and range of motion, and the TENS group showed no significant improvement over the control group for either outcome. Although a limitation of the trial was that observation of control patients ended at 10 weeks, these results confirmed results of several similar studies of TENS in treating musculoskeletal pain. The trialists concluded that TENS is an effective treatment for chronic facial myalgia, although studies with more participants are needed.

Temporomandibular Disorder

Systematic Reviews

de Castro-Carletti et al. (2023) conducted a systematic review and meta-analysis of controlled trials with electrotherapy for orofacial pain. (57) The systematic review yielded 43 studies (N=1939) for temporomandibular disorder and none for other types of orofacial pain. The quality of evidence was low, but meta-analysis was performed with 20 studies. Regardless of the type of temporomandibular disorder, TENS did not demonstrate a significant benefit compared to placebo or other forms of electrotherapy for pain intensity, maximal mouth opening, or tenderness. A limitation of the analysis is that almost all studies (n=41) had a high risk of bias.

Serrano-Munoz et al. (2023) conducted a systematic review and meta-analysis of electrical stimulation modalities for temporomandibular disorders. (58) Seven RCTs were included, 4 of which evaluated TENS. Overall, TENS reduced pain intensity (MD, -1.09; 95% CI, -0.71 to -1.47; I^2=72%). TENS did not have a significant effect on range of movement or muscle activity.

Randomized Controlled Trials

A randomized placebo-controlled trial by Ferreira et al. (2017) evaluated TENS in the treatment of individuals with temporomandibular disorder; 40 patients (30 female, 10 male) were randomized into 2 groups (placebo or active TENS). (59) The trial used both high- and low-frequency TENS, allotting to the active TENS patients 25 minutes of 4 Hz followed by 25 minutes of 100 Hz; measuring pain intensity and pressure pain threshold immediately after treatment and again 48 hours later. When compared with baseline values, pain intensity was reduced for patients in the active TENS group, and pressure pain threshold was significantly increased ($p<0.05$). For those in the placebo group, there were no significant improvements for either primary outcome. Limitations of the trial included the short duration of the assessment, and the absence of control groups either receiving no treatment or evaluating the same treatment in patients without temporomandibular disorder.

Myofascial Trigger Points

Systematic Reviews

A systematic review by Ahmed et al. (2019) evaluated the effects of various electric stimulation techniques in individuals with myofascial trigger points, including 13 RCTs of TENS compared with sham TENS. High-frequency TENS (>50 Hz) was used in the majority of RCTs. Unclear allocation concealment and blinding were the most common study limitations. Meta-analysis of post-treatment pain intensity scores found that TENs did not significantly reduce pain (SMD, -0.16: 95% CI, 0.39 to 0.07). (60)

Randomized Controlled Trials
Effects of TENS combined with ultrasound were more positive in an RCT by Takla et al. (2019) of 70 participants with acute mechanical neck pain and at least 2 active myofascial trigger points. Participants were randomized to three sessions per week for four consecutive weeks of low-frequency, high-intensity burst TENS combined with ultrasound, medium-frequency, low-intensity amplitude modulated frequency TENS combined with ultrasound or sham combined therapy. Pressure pain threshold and active cervical lateral flexion range of motion were improved in both combined therapy groups - more so in the high-intensity burst TENS combined with ultrasound - but not in the sham group. (61)

<u>Mixed Chronic Pain Conditions</u>
Systematic Reviews
A systematic review and meta-analysis by Johnson et al. (2022) investigated TENS for relief of various acute and chronic pain conditions in adults. (62) In total, the review included 381 RCTs (N=24,543), with 164 RCTs having sufficient data for meta-analyses. In the subgroup of patients with chronic pain (31 RCTs; n=1417), TENS reduced pain intensity when compared to placebo (SMD: -0.87; 95% CI, -1.19 to -0.55). The authors concluded that for the overall population of patients with acute and chronic pain, there was moderate-certainty evidence that pain intensity is lower during or immediately after TENS compared with placebo. However, levels of evidence were downgraded because of small-sized trials contributing to imprecision in magnitude estimates.

An overview of Cochrane review by Gibson et al. (2019) evaluated the evidence from 8 Cochrane reviews that consisted of 51 RCTs which compared TENS vs sham or usual care/no treatment/waiting list control in 2895 participants with various chronic pain conditions. As with previous reviews, due to the serious methodological limitations described below, authors were unable to draw conclusions about the effects of TENS on pain control, disability, health related QOL, use of pain-relieving medications, global impression of change, or harms. (63)

<u>Section Summary: Transcutaneous Electrical Nerve Stimulation for Chronic Pain</u>
For individuals who have chronic pain (e.g., musculoskeletal, neuropathic, and mixed pain conditions) who receive TENS, the evidence includes numerous RCTs and systematic reviews. The overall strength of the evidence is weak. The best evidence exists for the treatment of chronic, intractable pain. Systematic reviews have found potential pain relief benefits with TENS for diabetic peripheral neuropathy and fibromyalgia. For low back pain and myofascial trigger points, available evidence suggests that TENS is ineffective. Available evidence from systematic reviews are inconclusive for cancer pain, osteoarthritis of the knee, rheumatoid arthritis, phantom knee pain, chronic neck pain, temporomandibular disorder, pain after stroke, and pain after spinal cord injury.

TENS For Acute Pain

Clinical Context and Therapy Purpose

The purpose of TENS is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with acute pain (e.g., surgical, musculoskeletal, labor, and mixed pain conditions).

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest is individuals who suffer from acute pain conditions (e.g., surgical, musculoskeletal, labor, and mixed pain conditions).

Interventions

The therapy being considered is TENS.

Comparators

The following therapy is currently being used to treat acute pain: pharmacotherapy.

Outcomes

The general outcomes of interest are symptoms, functional outcomes, QOL, and medication use. Given the different types of pain conditions, follow-up at 2, 4, and 6 weeks is of interest to monitor outcomes.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Injury

Systematic Review

Davison et al. (2022) conducted a systematic review of 4 studies that evaluated the effect of electrical stimulation after hip fracture. (64) Based on the results of one study, TENS decreased pain as assessed by VAS scores (MD, 3.3 points; p<.001), increased range of motion at 10 days (MD, 25.7 degrees; p<.001), and improved functional recovery (p<.001). Results were conflicting regarding the effects of TENS on muscle strength and mobility. The authors concluded that additional high quality trials were needed.

Randomized Controlled Trials

One double-blind, randomized, sham-controlled trial reported by Lang et al. (2007) found that during emergency transport of 101 patients, TENS reduced posttraumatic hip pain (change in VAS score, 89 to 59), whereas the sham-stimulated group remained relatively unchanged (change in VAS score, 86 to 79). (65)

Surgical Pain

Systematic Reviews

Zimpel et al. (2020) conducted a systematic review with meta-analysis to investigate the efficacy of various complementary alternative therapies, including TENS, for post-caesarean pain. (32) Ten studies were included that evaluated TENS, with or without analgesia, for pain relief. One study (N=40) evaluated TENS with no treatment and found that it may reduce pain at 1 hour (MD: -2.26; 95% CI, -3.35 to -1.17). TENS plus analgesia, as compared to placebo plus analgesia, may reduce pain at 1 hour (SMD -1.10, 95% CI, -1.37 to -0.82 based on 3 studies with 238 women). Both findings were rated as low-certainty evidence by the Cochrane review.

Zhu et al. (2017) conducted a systematic review with meta-analysis to investigate the efficacy of TENS on patients experiencing pain after a total knee arthroplasty. (66) Two independent investigators searched PubMed, Embase, Web of Sciences, EBSCO, and Cochrane Library databases and identified 6 RCTs that assessed the effect TENS had on VAS scores of 529 patients who had a total knee arthroplasty. A meta-analysis indicated that, compared with control intervention, TENS significantly reduced VAS scores over a 24-hour period (SMD, -0.47; 95% CI, -0.87 to -0.08; p=0.02). The study was limited by the number of RCTs and sample sizes (4 of 6 selected RCTs had <100 patients), as well as differences in TENS intensities, differences in follow-up times, ethnic diversity of patients, and possible unpublished or missing data.

Randomized Controlled Trials

Hatefi et al. (2023) conducted a double-blind RCT of TENS for pain associated with chest tube removal in 120 patients who underwent coronary artery bypass grafting. (67) The 4 treatment groups were TENS, cold compress, TENS plus cold compress, and placebo (room temperature compress plus sham TENS), all administered for 15 minutes before chest tube removal. Mean pain intensity scores were lowest in the combined TENS plus cold compress group compared to the other groups at all time points (during chest tube removal, immediately after removal, and 15 minutes after removal [p<.001]). Safety of the intervention was not addressed.

Ramanathan et al. (2017) published a prospective RCT of 66 patients having undergone total knee arthroplasty who were assigned to active or placebo TENS. Patients used the device as needed for 2 hours and had follow-up visits 2, 4, and 6 weeks after surgery. (68) For the primary outcome (reduction of opioid intake), no significant difference was observed between active and placebo TENS groups (p=0.60). This was also the case for secondary outcomes, which included assessment of pain, function, and clinical outcomes. The trial was limited by a high withdrawal rate (only 66 of 116 patients enrolled completed the trial) and a lack of uniformity in the device settings chosen by patients. The investigators found no significant benefit of TENS treatment following total knee arthroplasty.

Parseliunas et al. (2020) evaluated TENS use as a component of multimodal pain control after open inguinal hernia surgery in a randomized, double-blind, placebo-controlled trial. (69) Eighty male patients with unilateral inguinal hernia treated by elective surgery were enrolled and randomly allocated to TENS (n=40) or placebo-TENS (n=40) on the first postoperative day. The primary outcome measure was the change in pain intensity after each TENS application, using VAS and an algometer. Results revealed a significant reduction in VAS pain scores in the TENS group following the procedure (p<.001). Absolute and relative pain relief were significantly improved in the TENS group for pain at rest (p<.01), when walking (p<.01), and when standing up from the bed (p<.01). Administration of additional nonopioid analgesics was reduced in the TENS group on the first and second postoperative days (p<.001). No postoperative surgical complications or TENS-related adverse effects were seen.

Smaller studies with higher risk of bias – often due to lack of a sham TENS group - have tended to support the use of TENS. In an RCT of 48 patients who had undergone abdominal surgery, compared to a control group that did not receive any electrical stimulation, Oztas et al. (2019) found significantly lower pain scores and analgesic consumption in patients who underwent TENS. (70) In an assessor-blinded study of TENS in 74 living kidney donors, Galli et al. (2015) found a modest reduction in pain at rest and during the measurement of pulmonary function 1 day postoperatively. (71) A patient-blinded study post abdominal surgery (N=55) by Tokuda et al. (2014) found that application of TENS for 1 hour per day resulted in a significant reduction in pain, particularly at rest, measured both during and immediately after treatment compared with sham TENS. (72) Pulmonary function (vital capacity, cough peak flow) was also significantly better in the active TENS arm. In a single-blinded randomized trial with 42 patients, Silva et al. (2012) assessed the analgesic effect of TENS after laparoscopic cholecystectomy. (73) Pain improved by a median of 2.4 points of 10 after TENS compared with 0.4 points after placebo treatment. The relative risk of nausea and/or emesis was 2.2 times greater for patients in the placebo group. In a double-blind RCT of 40 patients undergoing inguinal herniorrhaphy, DeSantana et al. (2008) reported on two 30-minute sessions of TENS at 2 and 4 hours after surgery (vs sham) reduced both analgesic use and pain scores when measured up to 24 hours post-surgery. (74) Pulmonary function (vital capacity, cough peak flow) was also significantly better in the active TENS arm. One exception comes from a single-blind RCT by Forogh et al. (2017) of 70 male athletes, which found that adding 20 sessions of high-frequency TENS for 35 minutes a day to semi-supervised exercise did not significantly improve VAS scores. (75)

<u>Bone Marrow Sampling</u>

Randomized Controlled Trials

Tucker et al. (2015) reported on a double-blind RCT of TENS administered during bone marrow sampling in 70 patients. (76) There was no significant difference in a numeric pain score between patients who received strong TENS impulses and the control group that received TENS just above the sensory threshold as reported immediately after the procedure (5.6 vs 5.7, respectively). Over 94% of patients in both groups felt they benefited from TENS.

<u>Low Back Pain</u>

Systemic Reviews

A systematic review by Binny et al. (2019) included 3 placebo-controlled studies with 192 women with acute low back pain. Although a low-quality RCT found that TENS in an emergency-care setting provided clinically worthwhile pain relief for moderate to severe acute low back pain, evidence was inconclusive in the other two RCTs. Review authors concluded that, overall, the evidence is insufficient to support or refute the use of TENS for acute low back pain. (77)

Koukoulithras et al. (2021) reported a systematic review that included 13 RCTs evaluating the effectiveness of non-pharmaceutical interventions upon pregnancy-related low back pain in 2213 patients. (78) TENS and muscle relaxation exercises accompanied by music were found to be the most effective interventions, having a statistically significant impact on lumbar pain. There was high heterogeneity among the studies including sample sizes.

Dysmenorrhea

Systematic Reviews

Arik et al. (2020) conducted a meta-analysis evaluating the effectiveness of TENS for primary dysmenorrhea. (79) Four RCTs (N=260) that compared TENS to a sham device were included in the analysis. Pain, as measured by VAS scores, was statistically reduced in the TENS group compared to the sham group (SMD, 1.384; 95% CI, 0.505 to 2.262).

Randomized Controlled Trials

Guy et al. (2022) reported on a crossover RCT that took place in France and compared TENS (n=20) to sham TENS (n=20) for primary dysmenorrhea. (80) The change in pain intensity (measured using VAS) after the first 2 applications (the primary outcome) was significantly greater with TENS (-36.6) vs sham TENS (-2.6; between-group difference: -34.1; p<.0001).

Hysteroscopy

Randomized Controlled Trials

Platon et al. (2020) reported the pain relief effects in 74 patients who were randomized to TENS or morphine 5 mg in the post-anesthesia care unit (PACU) after hysteroscopy. (81) At PACU discharge, both groups reported a significant reduction in pain, with a decrease of VAS scores from 5.6 to 1.4 in the TENS group and 5.1 to 1.3 in the opioid group. There were no significant differences between groups. Sixteen patients in each group reported a VAS ≥3 after initial treatment and were crossed over to receive the other treatment during the study as defined by the protocol.

Lison et al. (2017) published an RCT assessing the effect of TENS on pain in women undergoing hysterectomy without sedation; the study included 138 women receiving active TENS, placebo TENS, or neither treatment during the procedure. (82) Women in the active TENS group reported significantly lower VAS scores than women in the control or placebo TENS groups reported. This was the case at each stage measured (entry, contact, biopsy [when necessary], and residual). To validate these measurements, the investigators included a second pain scale (Likert scale) and found a significant correlation with the VAS results (p<.001). For secondary endpoints (e.g., procedure duration, vital parameters, vasovagal symptoms), the trialists reported that differences between the groups were not statistically significant. However, patient satisfaction was significantly higher in the active TENS group than in either placebo TENS or control groups ($p<.001$ and $p=.001$, respectively). Trial limitations included the failure to account for the use of a flexible hysteroscope, instead of using a rigid hysteroscope; this might have limited the generalizability of the results.

Labor and Delivery

Systematic Reviews

A Cochrane review by Deussen et al. (2020) included 28 studies involving 2749 women experiencing uterine cramping after vaginal delivery. (83) There was a very low-certainty that TENS is better than no TENS for adequate pain relief as reported by 32 women in 1 applicable RCT.

A systematic review and meta-analysis by Thuvarakan et al. (2020) evaluating the efficacy of TENS for labor pain included 26 studies with 3348 patients. (84) TENS showed a statistically significant effect in the reduction of pain intensity (pooled RR, 1.52; 95% CI, 1.35 to 1.70). The authors noted that there was high study heterogeneity ($I^2=89\%$) and the majority of included studies were judged to be low quality.

A Cochrane review by Dowswell et al. (2009) included 19 studies with 1671 women in labor. (17) Overall, there was little difference in pain ratings between TENS and control groups, although women receiving TENS to acupuncture points were less likely to report severe pain (RR, 0.41). Reviewers found limited evidence that TENS reduced pain in labor or had any impact (either positive or negative) on other outcomes for mothers or babies.

Randomized Controlled Trials

Kurata et al. (2022) published the results of a RCT comparing TENS (n=60), sham TENS (n=60), and no TENS (n=60) after cesarean birth. (85) The primary outcome of median opioid consumption within 60 hours of cesarean delivery was 7.5 morphine milligram equivalents (MME) with TENS vs 0 MME with sham TENS ($p=.31$). In the no TENS group, the median opioid consumption within 60 hours of cesarean delivery was 7.5 MME ($p=.57$ vs sham TENS).

A placebo-controlled, randomized trial by Kayman-Kose et al. (2014) assessed 200 women who gave birth between January and July 2010. (86) One hundred women who gave birth vaginally were allocated to active TENS or sham TENS in a 1:1 ratio; this same assignment was performed for 100 women who gave birth by cesarean delivery. TENS was performed once for 30 minutes after childbirth was completed. After vaginal delivery or cesarean delivery, but before the administration of TENS, the placebo and active groups did not significantly differ in VAS scores or verbal numeric scale (VNS) scores. However, after active TENS in the cesarean group, there was a significant reduction in VAS ($p<0.001$) and VNS score ($p<0.001$) compared with the placebo group. A similar benefit was observed in the vaginal delivery group with the active treatment showing a significant reduction in VAS ($p=0.022$) and VNS ($p=0.005$) scores.
The investigators also assessed whether TENS reduced the need for additional analgesia. There was no difference between the active TENS and the placebo groups for vaginal delivery ($p=0.83$), but, in the cesarean arm, the active treatment group had a significant reduction in

analgesic need (p=0.006). Results were consistent in a much smaller RCT by Baez Suarez et al. (2019) of 10 women in labor with a breech vaginal delivery. In this RCT, only women who received active TENS experienced a clinically significant improvement in VAS scores. (87)

Njogu et al. (2021) assessed the effects of TENS during the first stage of labor in a single-blind RCT involving 326 adult pregnant women anticipating spontaneous vaginal delivery. (88) Enrolled patients were randomly assigned to TENS (n=161) or routine obstetric care (n=165) at the beginning of active labor until the second labor stage. The primary outcome was labor pain intensity as assessed by VAS immediately after randomization, at 30, 60, and 120 minutes after TENS therapy, and 2 to 24 hours post-delivery. Prior to the TENS intervention, there was no statistically significant difference in mean VAS scores between the groups (p>.05). The TENS group had significantly lower mean VAS scores as compared to control at all time points post-intervention and at 2 to 24 hours post-delivery (all p<.0001). The TENS group had a significantly shorter duration of the active labor phase as compared to controls (p<.001) and the time of the second and third stages of labor were similar between the groups (p>.05). The authors concluded that TENS can be used as a non-pharmacologic therapy to reduce labor pain and shorten the active labor phase duration. Limitations cited were lack of a double-blind, sample size, single-center analysis, and inclusion of only a low-risk pregnancy population.

Medical Abortion

Randomized Controlled Trials

Goldman et al. (2021) evaluated whether the use of TENS reduced pain with medical abortion in a randomized, placebo-controlled trial involving 40 patients. (89) Enrolled women underwent a medical abortion with mifepristone and misoprostol and were randomly assigned to high-frequency TENS (80 Hz; n=20) or a sham device (n=20) to use at home. The primary outcome was a comparison of maximum pain scores within the first 8 hours after misoprostol administration using an 11-point numeric rating scale. Thirty-seven patients had data evaluable for the primary outcome. Median maximum pain scores within 8 hours after misoprostol were 7 and 10 for the high-frequency TENS and sham device, respectively. Patients administered high-frequency TENS experienced a significant reduction in post-treatment pain score as compared to those who were administered the sham device (-2.0 vs. 0; p=.008). No significant differences between the devices were found with regard to additional analgesia use, distribution of maximum pain scores at 24 hours, adverse effects, or measures of acceptability.

Mixed Acute Pain Conditions

Systematic Reviews

A systematic review by Johnson et al. (2022) was previously introduced. (62) In the subgroup of patients with acute pain (57 RCTs; n=3348), TENS significantly reduced pain intensity compared to placebo (SMD, -1.02; 95% CI, -1.24 to -0.79). The authors concluded that for the overall population of patients with acute and chronic pain, there was moderate-certainty evidence that pain intensity is lower during or immediately after TENS compared with placebo. However, levels of evidence were downgraded because of small-sized trials contributing to imprecision in magnitude estimates.

Randomized Controlled Trials
Butera et al. (2018) conducted a trial to determine the efficacy of using TENS to reduce musculoskeletal pain and improve function after exercise-induced muscle pain. (90) In this RCT, 36 patients were divided into 3 groups and received TENS, placebo TENS, or no treatment as a control. Treatment was administered for 90 minutes at 24, 48, and 72 hours after the onset of muscle soreness. Analysis indicated that active TENS and placebo TENS had no significant effect on pain. Limitations included a small sample size of young, relatively healthy individuals.

Tennis Elbow
Randomized Controlled Trials
A multicenter RCT of TENS as an adjunct to primary care management for tennis elbow was reported by Chesterton et al. (2013). (91) Thirty-eight general practices in the United Kingdom recruited 241 adults who had a new or first diagnosis of tennis elbow. Participants were randomized to TENS once a day for 45 minutes over 6 weeks or until resolution of pain plus primary care management (consultation with a general practitioner followed by information and advice on exercise) versus primary care management alone. Both groups saw large (>25%) within-group improvements in pain intensity, with the greatest improvement during the first 6 weeks of treatment. Intention-to-treat analysis revealed no difference in improvement of pain (-0.33; 95% CI, - 0.96 to 0.31; p=0.31) between the 2 groups at 6 weeks, 6 months (-0.20; 95% CI, -0.81 to 0.42; p=0.526), or 12 months (0.45; 95% CI, -0.15 to 1.06; p=0.139). However, adherence to exercise and TENS was very poor, with only 42 (35%) meeting prior adherence criteria. Per-protocol analyses only showed a statistically significant difference in favor of TENS at 12 months (p=0.030).

Section Summary: Transcutaneous Electrical Nerve Stimulation (TENS) for Acute Pain
The evidence for the use of TENS from high-quality trials remains inconclusive for most indications of acute pain. A systematic review of TENS for acute and chronic pain found some evidence that TENS reduces pain intensity over and above that seen with placebo and other control groups in patients with acute pain, but small-sized trials contributed to imprecision in magnitude estimates. Systematic reviews have found that TENS may help reduce pain in patients with post-operative pain (post-caesarean and total knee arthroplasty), dysmenorrhea, and pain associated with labor and delivery. For low back pain, systematic reviews have found insufficient evidence to support or refute the use of TENS. Randomized controlled trials have reported mixed results in the efficacy of TENS across various acute pain conditions.

Essential Tremor
Clinical Context and Therapy Purpose
The purpose of TENS is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with essential tremor.

The following PICO was used to select literature to inform this policy.

Populations
The relevant population of interest is individuals who suffer from essential tremor.

Interventions
The therapy being considered is TENS of the median nerve. Stimulation of the median nerve has been shown to spike activity in the thalamus.

Comparators
The following therapies are currently being used to treat essential tremor: pharmacotherapy.

Outcomes
The general outcomes of interest are reductions in symptoms and medication use, and improvements in functional outcomes and QOL.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence
Systematic Review
In a comprehensive review, Pascual-Valdunciel et al. (2021) analyzed 27 studies that reported the use of peripheral electrical stimulation to reduce tremor and discussed various considerations regarding peripheral electrical stimulation: the stimulation strategies and parameters, electrodes, experimental designs, results, and mechanisms hypothesized to reduce tremor. (92) While studies demonstrated the potential and usability of peripheral electrical stimulation as an intervention to reduce tremor, results were highly variable across studies and patients, which points out the need for consensus and standardized procedures to allow more reproducibility and cross-comparisons.

Nonrandomized Studies
Yu et al. (2020) investigated a recently developed therapy called transcutaneous afferent patterned stimulation (TAPS) and whether it may provide symptomatic tremor relief in essential tremor patients and improve patients' ability to perform functional tasks. (93) In a single-arm, open-label study, 15 essential tremor patients performed four hand tremor-specific tasks (postural hold, spiral drawing, finger-to-nose reach, and pouring) from the Fahn-Tolosa-Marin Clinical Rating Scale (FTM-CRS) prior to, during, and 0-, 30-, and 60-min following TAPS. At each time point, tremor severity was visually rated according to the FTM-CRS and simultaneously measured by wrist-worn accelerometers. The duration of tremor reduction was assessed using 1) improvement in the mean FTM-CRS score across all four tasks relative to baseline, and 2) reduction in accelerometer-measured tremor power relative to baseline for each task. Patients

were labeled as having at least 60 min of therapeutic benefit from TAPS with respect to each specified metric if all three (i.e., 0-, 30-, and 60-min) post-therapy measurements were better than that metric's baseline value. The mean FTM-CRS scores improved for at least 60 min beyond the end of TAPS for 80% (12 of 15, *p* = 4.6e–9) of patients. Similarly, for each assessed task, tremor power improved for at least 60 min beyond the end of TAPS for over 70% of patients. The postural hold task had the largest reduction in tremor power (median 5.9-fold peak reduction in tremor power) and had at least 60 min of improvement relative to baseline beyond the end of TAPS therapy for 73% (11 of 15, *p* = 9.8e–8) of patients. Clinical ratings of tremor severity were correlated to simultaneously recorded accelerometer-measured tremor power (*r* = 0.33–0.76 across the four tasks), suggesting tremor power is a valid, objective tremor assessment metric that can be used to track tremor symptoms outside the clinic. These results suggest TAPS can provide reductions in upper limb tremor symptoms for at least 1 h post-therapy in some patients, which may improve patients' ability to perform tasks of daily living.

Isaacson et al. (2020) evaluated the repeated home use of an FDA-cleared wrist-worn neuromodulation device in the Prospective Study for Symptomatic Relief of Essential Tremor with Cala Therapy (PROSPECT) trial. (94) For each active treatment session, the device electrically stimulated the median and radial nerves for 40 minutes with an alternating burst pattern tuned to the frequency of each patient's tremor. The pre-specified co-primary endpoints were improvements on the clinician-rated Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS) and patient-rated Bain & Findley Activities of Daily Living (BF-ADL) dominant hand scores. Of the 263 enrolled patients, 205 completed the visit 3 follow-up and were included in the primary analysis. Results revealed a significant improvement in TETRAS and BF-ADL from pre- to post-stimulation at each clinic visit (p<.0001 for all comparisons). Pre-stimulation tremor levels were improved from Visit 1 to 3 on both TETRAS and BF-ADL (p<.0001 for both). Patients rated as "severe" or moderate" improved with both TETRAS (49.3% at baseline to 21% at study exit) and BF-ADL (64.8% at baseline to 23% at study exit) scoring. Tremor power is a calculation of amplitude and frequency. Tremor power decreases with lower amplitude motions and lower frequency motions. Tremor power was also noted to significantly improve with therapy from pre- to post-stimulation (p<.0001). No device-related serious adverse events were reported. Non-serious device-related adverse events occurred in 18% of patients (e.g., persistent skin irritation, sore/lesion, discomfort, electrical burns, and minor skin irritation). Conclusions were that the repeated in-home use of this neuromodulation device over 3 months was effective and safe for patients with essential tremor. Limitations identified were the open-label, single-arm design, the lack of consensus for the definition of clinically meaningful improvement in TETRAS or BF-ADL, as well as the exclusion of 58 patients who exited the study early from the pre-specified primary and secondary endpoint analyses.

Brillman et al. (2022) offered a retrospective postmarket surveillance study evaluating the real-world effectiveness of TAPS from patients using therapy on-demand for at least 90 days between August 2019 through June 2021. (95) A total of 321 patients (average age 71 years, 32% female) met the criteria for this analysis, 216 of whom had tremor measurements available for analysis and 69 of whom completed the survey. Total usage period ranged from 90 to 663 days, with 28% of patients using the device for over one year. Patients used therapy 5.4 ± 4.5 (mean ± 1 standard deviation) times per week. TAPS reduced tremor power by 71% (geometric mean) across all sessions, with 59% of patients experiencing >50% tremor reduction after their sessions. Eighty-four percent (84%) of patients who returned the voluntary survey reported improvement in at least one of eating, drinking, or writing, and 65% of patients reported improvement in QOL. Self-reported device-related safety complaints were consistent with adverse events in prior clinical trials.

Randomized Controlled Trials
Lin et al. (2018) reported on a sham-controlled pilot trial that evaluated the efficacy of median and radial nerve stimulation as a noninvasive, nonpharmacological treatment to aid in the symptomatic relief of hand tremor in individuals with essential tremor. (96) Twenty-three blinded subjects were examined at a single site under an institutional review board-approved protocol. Subjects were randomized to treatment or sham groups. For stimulation, hydrogel electrodes were positioned on the wrist over the median and radial nerves. Efficacy was measured as the change in the TETRAS Archimedes spiral drawing task following stimulation compared with prestimulation. The response in the treatment group was significant compared with both baseline and sham. In the treatment group, blinded rater scores significantly improved following stimulation (1.77 ± 0.21) compared with prestimulation (2.77 ± 0.22; *P* = 0.01). In the sham group, scores did not change significantly following stimulation (2.37 ± 0.22) compared with prestimulation (2.62 ± 0.14; *P* = 0.37). The response to treatment corresponded to an estimated hand tremor amplitude reduction of 60% ± 8.4% and was significantly greater in the treatment than in the sham group (*P* = 0.02). Three subjects experienced transient redness and/or itchiness under the hydrogel electrodes that resolved without intervention. No unanticipated device effects occurred during the study. Authors acknowledged that this was only a pilot study with too few subjects for subanalyses of the effects of age, medication status, or medical history, and that future studies should expand the subject count, investigate the response rate, repeatability, durability, and effects of chronic use, and add assessments of QOL.

Pahwa et al. (2018) conducted a randomized controlled study of 77 essential tremor patients evaluating the safety and effectiveness of a wrist-worm peripheral nerve stimulation device in patients with essential tremor in a single in-office session. (97) Patients received either treatment stimulation (N = 40) or sham stimulation (N = 37) on the wrist of the hand with more severe tremor. Tremor was evaluated before and immediately after the end of a single 40-minute stimulation session. The primary endpoint compared spiral drawing in the stimulated hand using the TETRAS Archimedes spiral scores in treatment and sham groups. Additional endpoints included TETRAS upper limb tremor scores, subject-rated tasks from the Bain and Findley activities of daily living (ADL) scale before and after stimulation as well as clinical global impression-improvement (CGI-I) rating after stimulation. Subjects who received peripheral nerve stimulation did not show significantly larger improvement in the Archimedes spiral task compared to sham but did show significantly greater improvement in upper limb TETRAS tremor scores (p = 0.017) compared to sham. Subject-rated improvements in ADLs were significantly greater with treatment (49% reduction) than with sham (27% reduction; p = 0.001).

A greater percentage of ET patients (88%) reported improvement in the stimulation group as compared to the sham group (62%) according to CGI-I ratings ($p = 0.019$). No significant adverse events were reported; 3% of subjects experienced mild adverse events. Researchers concluded that peripheral nerve stimulation in essential tremor may provide a safe, well-tolerated, and effective treatment for transient relief of hand tremor symptoms, but that future studies are needed to confirm the effectiveness of this noninvasive therapy over time.

ECRI
In a February 2024 Clinical Evidence Assessment, ECRI deemed the evidence on Cala Transcutaneous Afferent Patterned Stimulation Therapy (TAPS)for treating essential tremor to be “favorable”. (98) They concluded that Cala TAPS is safe, reduces ET severity and improves activities of daily living (ADLs) for approximately one hour after treatment in most patients with ET at up to three-month follow-up, based on evidence from three randomized controlled trials (RCTs) and three before-and-after studies. One RCT indicates Cala TAPS improves ADL over best available care. Studies with follow-up durations longer than three months that report on patient-oriented outcomes are needed to validate findings and determine whether Cala TAPS therapy’s benefits are sustained beyond three months.

UpToDate
In an April 2024 article on the treatment and prognosis of essential tremor, UpToDate listed “neuromodulation” as one of several different devices being developed to noninvasively modulate and/or compensate for tremor severity. (99) Patients with disabling tremor who are either not candidates for other treatment modalities or have suboptimal tremor control were identified as being the best candidates for these adaptive devices.

Section Summary: Transcutaneous Electrical Nerve Stimulation for Essential Tremor
The evidence for the use of TENS for essential tremor includes results from a comprehensive review, two small randomized controlled trials, and several nonrandomized studies. Although results suggest that repeated in home non-invasive neuromodulation therapy may be effective and safe for patients with essential tremor, a number of evidence limitations have been identified, including but not limited to, poor study design, small study size, high risk of bias, and short follow-up duration. Larger long-term, multicenter studies controlling for tremor severity and medication use and comparing TENS with pharmacologic therapy alone and with deep brain stimulation are needed.

Attention Deficit Hyperactivity Disorder
Clinical Context and Therapy Purpose
The purpose of TENS is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with attention deficit hyperactivity disorder (ADHD).

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest is individuals who suffer from ADHD (7 to 12 years of age) who are not currently taking prescription ADHD medication.

Interventions
The therapy being considered is TENS. Monarch® external Trigeminal Nerve Stimulation (eTNS) System is based on a purported mechanism of action that the trigeminal nerve stimulates brain areas thought to be involved in ADHD. While the exact mechanism of action is not yet known, neuroimaging studies have shown that eTNS increases activity in the brain regions that are known to be important in regulating attention, emotion, and behavior.

Comparators
The following therapies are currently being used to treat ADHD: pharmacotherapy.

Outcomes
The general outcomes of interest are reductions in symptoms and medication use, and improvements in functional outcomes and QOL.

<u>Study Selection Criteria</u>
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

<u>Review of Evidence</u>
Randomized Controlled Trials
McCough et al. (2019) assessed the efficacy and safety of TENS in a double-blind, sham-controlled pilot study of pediatric patients with ADHD. (100) Key characteristics of the trial are summarized in Table 1. The study was a 4-week trial followed by 1 blinded week without intervention. Clinical assessments included weekly clinician-administered ADHD-Rating and Clinical Global Impression (CGI) scales, and quantitative electroencephalography (EEG) at baseline and week 4. The primary outcome measure was the clinician completed ADHD-Rating Scale total score. Results revealed that ADHD-Rating Scale totals showed significant group-by-time interactions, demonstrating a differential treatment effect (F=8.12, df=1/228, p=.005). The CGI-Improvement scale also favored active treatment over sham (p=.003). Quantitative EEG readings were obtained in both groups but there were no participant specific correlations to other outcomes. No serious adverse events were observed in either group and no patient withdrew from the study due to adverse events. Significant increases in weight and pulse were seen with active TENS over the trial period; however, no differences between active and sham TENS with regard to blood pressure were seen. Conclusions were that TENS therapy is

efficacious and well-tolerated in pediatric patients with ADHD. Limitations cited were sample size and short duration of treatment and follow-up.

Table 1. Summary of Key RCT Characteristics

Study	**Countries**	**Sites**	**Dates**	**Participants**	**Interventions**	
					Active	*Comparator*
McGough et al. (2019) (100)	US	1	NR	62 patients (8 to 12 years) with ADHD based on the KSADS and clinical interview with a minimum total of 24 on the clinician-administered parent ADHD-IV Rating Scale, baseline CGI-S ≥4, and full-scale IQ ≥85. Children were medication free for at least 1 month prior to enrollment	TENS device (Monarch eTNS System) administered nightly for 4 weeks (n=32)	Sham TENS device administered nightly for 4 weeks (n=30)

ADHD: attention deficit hyperactivity disorder; CGI-S: Clinical Global Impression-Severity; IQ: intelligence quotient; KDADS: Kiddie Schedule for Affective Disorders and Schizophrenia; NR: not reported; RCT: randomized controlled trial; TENS: transcutaneous electrical nerve stimulation: US: United States.

Section Summary: Transcutaneous Electrical Nerve Stimulation for Attention Deficit Hyperactivity Disorder

The evidence for the use of TENS for ADHD includes a RCT. Results concluded that TENS is an effective and safe treatment option for pediatric patients with ADHD; however, the study included a small patient sample and was of relatively short duration.

Migraine

Clinical Context and Therapy Purpose

The purpose of TENS in individuals with migraine is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with migraine.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest is individuals with episodic or chronic migraine.

Migraine is categorized as episodic or chronic depending on the frequency of attacks. Generally, episodic migraine is characterized by 14 or fewer headache days per month and chronic migraine is characterized by 15 or more headache days per month. (101)

Specific International Classification of Headache Disorders (102), diagnostic criteria are as follows:

- Episodic migraine:
    A. Untreated or unsuccessfully treated headache lasting 4 to 72 hours
    B. Headache has at least 2 of the following characteristics:
        1. Unilateral location
        2. Pulsating quality
        3. Moderate or severe pain intensity
        4. Aggravation by or causing avoidance of routine physical activity
    C. At least 1 of the following during headache:
        1. Nausea and/or vomiting
        2. Photophobia or phonophobia.

- Chronic migraine:
    A. Migraine-like or tension-type headache on 15 or more days per month for more than 3 months
    B. At least 5 headache attacks without aura meet episodic migraine criteria 1 to 3, and/or at least 5 headache attacks with aura meet episodic migraine criteria 2 to 3
    C. On more than 8 days per month for more than 3 months, fulfilling any of the following criteria:
        1. For migraine without aura, episodic migraine criteria 2 and 3
        2. For migraine with aura, episodic migraine criteria 1 and 2
        3. Believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative.

Interventions

The therapy being considered is TENS. Several TENS devices are approved for both prevention and treatment of migraine.

Comparators

The following therapies are currently being used to treat acute migraine due to episodic or chronic migraine: Medical management or no treatment. A number of medications are used to treat acute migraine. First-line therapy for mild or moderate migraine includes oral non-steroidal anti-inflammatory drugs (NSAIDs) or acetaminophen. More severe migraine can be treated through the use of triptans or an NSAID-triptan combination through a variety of routes (e.g., oral, nasal [spray or powder], subcutaneous). Antiemetics can be added for migraine accompanied by nausea or vomiting. Other pharmacologic interventions used to treat acute migraine include calcitonin-gene related peptide antagonists, which can be used in patients with an insufficient response or contraindications to triptans, lasmiditan, and dihydroergotamine.

The following therapies are currently being used to prevent acute migraine in individuals with episodic or chronic migraine: medical management or no treatment. A number of medications are used as prevention for migraine. For most adults with episodic migraines who may benefit from preventive therapy, initial therapy with an antiepileptic drug (divalproex sodium, sodium valproate, topiramate) or beta-blockers (metoprolol, propranolol, timolol) is recommended. Frovatriptan may be beneficial as initial therapy for prevention of menstrually-associated migraine. Antidepressants (e.g., amitriptyline, venlafaxine), alternative beta-blockers (atenolol, nadolol), and additional triptans (naratriptan, zolmitriptan for menstrually-associated migraine prevention) may be considered if initial therapy is unsuccessful. For preventive treatment of pediatric migraine, many children and adolescents who received placebo in clinical trials improved and most preventive medications were not superior to placebo. Possibly effective preventive treatment options for children and adolescents may include amitriptyline, topiramate, or propranolol.

Outcomes
For treatment of acute migraine, specific important health outcomes include freedom from migraine pain and bothersome symptoms, restored function (e.g., return to normal activities), and patient-assessed global impression of treatment. Examples of relevant outcome measures appear in Table 2. Follow-up over several hours is needed to monitor for treatment effects.

For prevention of acute migraine in individuals with chronic or episodic migraine, specific important health outcomes include reduction of future attack frequency, severity, and duration, improved responsiveness to acute treatments, improved function and reduced disability, and prevention of progression of episodic migraine to chronic migraine. Follow-up over several days to months is needed to monitor for preventive treatment effects.

Table 2. Health Outcome Measures Relevant to Acute Migraine Attack (101, 103, 104)

Outcome	**Description**
Pain free	No pain at defined assessment time (e.g., 2 hours)
Pain relief	Improvement of pain from moderate to severe at baseline to mild or none or pain scale improved at least 50% from baseline at defined assessment time (e.g., 2 hours)
Sustained pain free	No pain at initial assessment (e.g., 2 hours) and remains at follow-up assessment (e.g., 1 day) with no use of rescue medication or relapse (recurrence) within that time frame
Sustained pain relief	Improvement of pain from moderate to severe at baseline to mild or none or pain scale improved at least 50% from baseline at defined assessment time (e.g., 2 hours) and remains improved at follow-up assessment (e.g., 1 day) with no use of rescue medication or relapse (recurrence) within that time frame
Symptom relief	Improvement of most bothersome symptom(s) from moderate to severe at baseline to mild or none at defined assessment time (e.g., 2 hours)

Function relief	Improvement of function from moderate to severe at baseline to mild or none at defined assessment time (e.g., 2 hours)
Restored function	No restriction to perform work or usual activities at a defined assessment time (e.g., 2 hours)
Global impact of treatment	Patient assessment of functional disability and health-related quality of life using a Likert or other validated scale at a defined assessment time (e.g., 2 hours)
Global evaluation of treatment	Patient assessment of overall treatment effect (pain, symptom relief, adverse events) using a Likert or other validated scale at a defined assessment time (e.g., 2 hours)

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Treatment of Acute Migraine

Randomized Controlled Trials

Three double-blind, sham-controlled RCTs evaluated TENS for acute migraine treatment (Tables 3 and 4). Two of the studies evaluated healthcare-provider administration of the device during a single episode in emergency departments, and 1 evaluated self-administration of the device at home during acute episodes over a 3-month period.

Chou et al. (2019) conducted an RCT of TENS to the trigeminal nerve with the Cefaly device in 106 individuals experiencing migraine headaches with or without aura. (105) Eligibility criteria specified that participants may have used any acute medications to treat the attack, but not within the 3 hours before enrollment; 29% had treated the current migraine with an acute medication prior to enrollment. Patients received 1 hour of TENS or sham treatment. The primary outcome, mean pain intensity at 1 hour compared to baseline (using a VAS score of 0 to 10), improved by 3.46 ± 2.32 points in the TENS group versus 1.78 ± 1.89 points in the sham group ($p<.0001$). Patients without aura had significant improvement in pain intensity at 1 hour compared to sham ($p=.0006$) but there was no difference between treatments among patients with aura ($p=.06$). Seven minor adverse effects were reported, and there were no serious adverse events.

Hokonek et al. (2021) conducted a single center RCT (N=78) to evaluate the use of TENS in individuals presenting to an emergency department with a migraine. (106) Participants had not received any medication prior to being admitted to the emergency department. Participants were randomized to TENS or a sham device, and their pain was assessed after 20 and 120 minutes. The change in VAS (0 to 100 mm) score from 0 to 20 min was -51.13 ± 2.94 for the TENS group, while the mean VAS score in the sham group was similar between baseline and 20 minutes (73 ± 3 vs. 72 ± 2). The change in VAS (0 to 100 mm) score from 0 to 120 min was -65 ± 25 for the TENS group and -9 ± 2 for the sham group (p<.001). Following randomization, 3 participants in the intervention group withdrew due to paresthesia caused by TENS administration and 2 in the control group withdrew due to severe pain; these individuals were not included in the analysis.

Domingues et al. (2021) evaluated the analgesic efficacy of a portable, disposable, and home self-applied TENS device during migraine attacks. (107) Participants (74 adults) who had been diagnosed with migraine by a specialist were randomized in this double-blind clinical trial to the active intervention (n=42) or a sham (n=32) with monthly follow-up for 3 months. The primary outcome measure was an evaluation of pain intensity following treatment. Subjects in both groups reported reduced pain scores; with significantly lower pain scores in the intervention group compared to the sham group (p=.004). Patients in the active intervention group also showed a significant improvement in functional disability scores. No adverse effects were reported.

Study limitations are summarized in Tables 5 and 6. Strengths of the RCTs included the use of a sham device and blinded outcome assessment using validated outcome measures. Although short-term pain relief was demonstrated at some time points, the quality of the overall body of evidence was downgraded due to inconsistency of results and heterogeneity in study settings. Supporting evidence from additional RCTs is needed.

Table 3. Summary of Key RCT Characteristics

Study; Trial	**Setting**	**Sites**	**Dates**	**Participants**	**Interventions**	
					Active	*Comparator*
Chou et al. (2019) (105)	Emergency Depts., United States	3	2016-2017	Adults (18 to 65 years of age) with IHS-defined acute migraine attack with or without aura for at least 3 hours before enrollment. Participants may have used any acute medications to treat the attack, but not within the 3 hours before	TENS (1 hour) with the Cefaly device (n=52)	Sham TENS (1 hour) using low-frequency pulses (n=54)

				enrollment. 29% had treated the current migraine with an acute medication prior to enrollment.		
Hokonek et al. (2021) (106)	Emergency Dept., Turkey	1	June-Oct 2019	Adults (ages 18 to 50 years) with IHS-defined migraine with or without aura, no preventive migraine treatment in the prior 30 days, presenting to the ED with an untreated acute migraine episode. Participants had not received any medication prior to being admitted to the ED.	TENS (20 minutes) (n=39)	Sham TENS using a device with an empty battery (20 minutes) (n=39)
Domingues et al. (2021) (107)	Home, Brazil	NR	Nov 2017-Jul 2018	Adults (18 to 65 years of age) with IHS-defined migraine with or without aura. Most participants were under pharmacological treatment for migraine but specifics of treatment for acute episodes during the study period were not reported.	TENS (20 minutes, self-applied at home) (n=42)	Sham TENS using a device with settings that did not meet those required for effective analgesic treatment by TENS devices (20 minutes, self applied at home) (n=32)

ED: emergency department; IHS: International Headache Society; RCT: randomized controlled trial; TENS: transcutaneous electrical nerve stimulation.

Table 4. Summary of Key RCT Results

Study	**Pain score**	**Rescue medication use**	**Adverse events**
Chou et al. (2019) (105)	N=106	N=106	--
TENS	Mean change After 1 hour: -3.46±2.32 After 2 hours: -2.87±2.24 After 24 hours: -3.46±2.65	After 2 hours: 6% After 24 hours: 40%	No serious adverse events. Inability to tolerate paresthesia sensation: 2 discontinued before first 5 mins elapsed 3 discontinued before the full hour
Sham TENS	Mean change After 1 hour: -1.78±1.89 After 2 hours: -1.85±1.96 After 24 hours: -2.38±2.27	After 2 hours: 4% After 24 hours: 41%	1 discontinued before first 5 mins elapsed 1 discontinued before the full hour
p for difference	1 hour: <.0001 .2 hours: 028 24 hours:.062	After 2 hours:.66 After 24 hours: 1.0	--
Hokonek et al. (2021) (106)	N=78	N=78	--
	Likert-type verbal scale (1=severe pain, 5=more than fine)	Additional analgesi medication required at 120 minutes	--
TENS	change in pain intensity 1 hour 4.5	1/39 (2.6%)	3/83 withdrew due to paresthesia caused by TENS administration
Sham TENS	mean at 1 hour 1.2	30/39 (76.9%)	2/83 withdrew due to severe pain
p for difference	<.001	74.3%; 95% CI, 59.9% to 87.6%)	--
Domingues et al. (2021) (107)	N=74	N=74	--

TENS	Median (IQR) Month 1: -3 (-10 to 0) Month 2: -2 (-10 to 0) Month 3: -2 (-10 to 0)	0 (0 to 3)	--
Sham TENS	Median (IQR) Month 1: 0 (-7 to 0) Month 2: -2 (-10 to 0) Month 3: -2 (-10 to 0)	1 (9 to 5)	No adverse events or intolerance to the electrical stimuli
p for difference	Month 1:.001 Month 2:<.001 Month 3:.129	.427	No adverse events or intolerance to the electrical stimuli

IQR: interquartile range; NR: not reported; RCT: randomized controlled trial; TENS: transcutaneous electrical nerve stimulation; VAS: visual analogue scale.

Table 5. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
Chou et al. (2019) (105)	1. Intended use population is unclear (e.g., treatment naive, those with contraindications to medication, or those who have failed pharmacologic treatment)				
Hokonek et al. (2021) (106)	1. Intended use population is unclear (e.g., treatment naive, those with contraindications to medication, or those who have failed pharmacologic treatment)			Pain measure described as "likert-type verbal scale," unclear if validated	
Domingues et al. (2021) (107)	1, 2. Intended use population is unclear (e.g., treatment naive, those with				Followup was for 3 months. There was no difference

	contraindications to medication, or those who have failed pharmacologic treatment); no details on timing or type of treatment of acute attacks during the study period.				between groups in pain score at the 3-month timepoint. Longer follow-up could provide more information about the effectiveness of the device over time.

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.

[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.

[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.

[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.

[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 6. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Chou et al. (2019) (105)						
Hokonek et al. (2021) (106)		1. Authors stated that TENS patients probably felt that the unit was active	1. No mention of registration	5/83 randomized not included in analysis (3 TENS, 2 sham); no ITT analysis		Confidence intervals NR for pain scale difference; post hoc analysis for scores at different timepoints. Table 1 does

						not provide a footnote to explain data points and no statistical comparison. Text provides means and p-value for pain scores but does not specify timepoint
Domingues et al. (2021) (107)						

TENS: transcutaneous electrical nerve stimulation.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.
[b] Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

Migraine Prevention

Randomized Controlled Trial

One RCT evaluated TENS for acute migraine prevention in individuals with chronic or episodic migraine (Tables 7 and 8). The Cefaly device for prevention of migraine was evaluated in the Prevention of Migraine using the STS Cefaly (PREMICE) trial (2013). (108) PREMICE was a double-blind, sham-controlled, randomized trial conducted at 5 tertiary care headache clinics in Belgium. Sixty-seven individuals with at least 2 migraine attacks per month were randomized to active (n=34) or sham (n=33) neurostimulation for 3 months, and 59 (88%) completed the trial on protocol. No serious adverse events occurred, although 1 patient discontinued the trial because of a reported device-caused headache. After a 1-month run-in period, patients were instructed to use the device daily for 3 months. Adherence was recorded by the TENS device. Ninety stimulation sessions were expected, but on average, 56 sessions were completed by the active group, and 49 were completed by the sham group. Primary outcome measures were changes in the number of migraine days and the percent of responders.

In the intention-to-treat analysis, the change in the number of migraine days (run-in vs. 3-month) was -2.06 (95% CI, -0.54 to -3.58) for the TENS group and 0.32 (95% CI, -0.63 to +1.27) for the sham group; this difference was not statistically significant (p=.054). The proportion of responders (≥50% reduction in the number of migraine days/month) was 38% (95% CI, 22% to 55%) in the TENS group and 12% (95% CI, 1% to 23%) in the sham group (p=.014). The number of migraine attacks from the run-in period to the 3-month evaluation was significantly lower for the active TENS group (decrease of 0.82 in the TENS group vs. 0.15 in the sham group; p=.044). The number of headache days was lower in the TENS group than in the sham group (decrease of 2.5 vs. 0.2; p=.041). Patients in the active TENS group reported a 36.6% reduction in the number of acute antimigraine drugs taken compared with a 0.5% reduction in the sham group (p=.008). The severity of migraine days did not differ significantly between groups. No adverse effects were reported among the study participants.

Table 7. Summary of Key RCT Characteristics

Study; Trial	**Countries**	**Sites**	**Dates**	**Participants**	**Interventions**	
					Active	*Comparator*
Schoenen et al. (2013); PREMICE (108)	Belgium	5	2009-2011	Adults (18 to 65 years of age) with IHS-defined migraine with or without aura and at least 2 migraine attacks per month	TENS (20 minutes daily) for 3 months (n=34)	Sham TENS (20 minutes daily) for 3 months (n=33)

RCT: randomized controlled trial; TENS: transcutaneous electrical nerve stimulation.

Table 8. Summary of Key RCT Results

Study	**Change in number of monthly migraine days at month 3**	**Responders at month 3**	**Change in antimigraine medication use at month 3**
Schoenen et al. (2013); PREMICE (108)	N=67	N=67	N=67
TENS	-2.06 (-0.54 to -3.58)	38.24%	-36.6%
Sham TENS	0.32 (-0.63 to 1.27)	12.12%	0.5%
p	.054	.023	.0072

RCT: randomized controlled trial; TENS: transcutaneous electrical nerve stimulation.

Table 9. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
Schoenen et al. (2013); PREMICE (108)					1. Follow-up limited to 3 months

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.

[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.

[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.

[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.

[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 10. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Schoenen et al. (2013); PREMICE (108)			1. No mention of registration		4. Power calculated for a different outcome than the outcome described as primary	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.

[b] Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.

[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.

[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.

[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.

[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

Section Summary: Transcutaneous Electrical Nerve Stimulation for Migraine

The evidence for the use of TENS for treatment of acute migraine includes 3 double-blind, sham-controlled RCTs. Two of the RCTs evaluated healthcare-provider administration of a TENS device during a single episode in emergency departments, and 1 evaluated self-administration of the device at home during acute episodes over a 3-month period. The studies conducted in emergency departments showed clinically and statistically significant reductions in pain intensity and medication use within 2 hours of use. The self-administration study had mixed results: The difference in median pain scores before and after treatment was significantly higher in the TENS group at months 1 and 2, but at month 3 the difference was not statistically significant. Function and analgesic medication use did not differ between groups at any time point. Strengths of the RCTs included the use of a sham device and blinded outcome assessment using validated outcome measures. Although short-term pain relief was demonstrated at some time points, the quality of the overall body of evidence was downgraded due to inconsistency of results and heterogeneity in study settings. It is not clear whether the pain intensity reductions demonstrated in emergency department settings would generalize to other settings over longer time periods. Supporting evidence from RCTs is needed. Additionally, based on the existing evidence, it is unclear how TENS would fit into the current migraine treatment pathway, although it could provide benefit for those who do not receive adequate benefit from pharmacologic first- or second-line therapies, or who may have a contraindication to pharmacologic therapies. The specific intended use must be specified in order to adequately evaluate net health benefit.

The evidence for the use of TENS for prevention of acute migraine in individuals with chronic or episodic migraine includes 1 RCT (N = 67) that reported a greater proportion of patients achieving at least a 50% reduction in migraines with TENS than with sham placebo. The RCT also reported modest reductions in the number of total headache and migraine days. This manufacturer-sponsored trial needs corroboration before conclusions can be made about the efficacy of TENS for preventing migraine headaches. Additionally, based on the existing evidence, it is unclear how TENS would fit into the current migraine prevention pathway, although it could provide benefit for those who do not receive adequate benefit from pharmacologic first- or second-line therapies, or who may have a contraindication to pharmacologic therapies.

Transcutaneous Electrical Modulation Pain Reprocessing (TEMPR)

In 2016, Majithia et al. conducted a review to investigate the preliminary data pertaining to the efficacy of Scrambler therapy. (110) All case studies and clinical trials were evaluated. Published articles reviewed included 20 reports of varying scientific quality prior to November 2015. The reviewers concluded that larger, randomized studies were required to further evaluate the efficacy of this approach.

Salahadin et al. (111) conducted a pilot case series of 10 patients with failed back syndrome. Patients received scrambler therapy treatment for 1 hour per day for 10 days. The study concluded that this therapy appears to reduce pain in patients with failed back surgery syndrome with no side effects, and further studies with more subjects are needed.

Ricci et al. (2019) conducted a prospective trial on 219 patients affected by chronic pain from April 2010 to March 2016 to evaluate the impact of Scrambler therapy. (112) The assumption, at the outset of the study was that chronic pain is often difficult to treat, especially for patients who are unresponsive to standard treatments for chronic pain, for which Scrambler Therapy (ST) is indicated. The study consisted of 2 consecutive weeks of treatment with ST (one 30-min daily session, 5 days a week) (T0, T1, T2) and a 2-week follow-up (T3, T4). Patients were asked to describe the pain using the Numeric Rating Scale (NRS) immediately prior to and after the treatment. Two hundred nineteen patients were treated for chronic pain of different nature with mean values of 6.44 (± 2.11) at T0, 3.22 (±2.20) at T2, and 3.19 (± 2.34) at T4. A reduction in the symptomatology from T0 to T2 was maintained throughout T4 (P value <.0001). Of the 219 patients treated with ST, 83 (37.9%) had cancer pain and 136 (62.1%) had non-cancer pain. No adverse events were reported. Researchers concluded that future research should focus on individual response, retreatment, and maintenance therapy.

Kashyap et al. (2017) conducted a prospective, observational study on 20 patients (10 men, 10 women) with chronic pain due to malignancy not responding to oral analgesics. (113) A total of 12 sessions, lasting 40 minutes, of scrambler therapy were planned, ten sessions on consecutive days and one session each on two follow-up visits after 1 week each. All patients had good pain relief; pain scores decreased significantly (P<0.01) after each session and at each follow-up and showed significant improvement in physical, psychological, social, and environmental health (P <0.01) after therapy. Results indicated scrambler therapy offers a promising role in pain management as an adjunct to pharmacological therapy for the treatment of chronic drug-resistant cancer pain. Authors concluded that larger prospective, randomized multicenter studies are needed to validate these findings.

Marineo et al. (114) conducted a pilot randomized, controlled study of 55 patients to determine if scrambler therapy relieved chronic neuropathic pain more effectively than guideline-based drug management over a 10-day cycle of sessions. The study concluded that scrambler therapy appeared to relieve chronic neuropathic pain better than guideline-based pharmacological treatment.

In a multi-center retrospective study, Compagnone et al. analyzed the efficacy and safety of scrambler therapy; 201 patients who were treated suffered from chronic pain. Causes of chronic pain included: post herpetic neuralgia 18.40%, chronic low back pain (LBP) 37.31%, polyneuropathy 10.94%, and peripheral neuropathy 14.42%. The remaining 18.93% included chronic pain due to other causes. The authors' results included the following: 7 patients stopped treatment due to lack of results, and 2 for personal reasons not ascribable to the treatment. The following conclusions were noted by the authors: Scrambler Therapy is an efficient and safe alternative for several different types of refractory chronic neuropathic pain, with a very rare possibility of adverse events. Only a few studies have tested the efficacy of Scrambler Therapy. Four of them have potential biases because they were done by the author of Scrambler Therapy and Scrambler Therapy is a partly operator dependent methodology. Treatment success is highly dependent on the ability of the operator to zero out pain during each single treatment without patient having discomfort. Failure to zero out pain during each treatment session leads to unsatisfactory results and is also the variable that could determine the highest study bias, creating the possibility of false nonresponsive patients. applied research, and owner of patents on technology application. Multiple operators can also influence the outcome due to placement, movement, and adjustments of the therapy. (115)

In a multi-center study to identify which factors are associated with treatment outcome for Calmare (Scrambler) therapy, Moon et al. analyzed data gathered from 3 medical centers on 147 patients with various pain conditions who underwent a minimum of either 3 Calmare therapies on consecutive days or 5 therapies overall. A successful outcome was predefined as ≥50% pain relief on a 0 to 10 numerical rating scale that persisted for longer than 1 month after the last treatment. Variables that were assessed for their association with outcome included: age, sex, study site, baseline pain score, etiology, type of pain, diagnosis, treatment compliance, coexisting psychopathology, opioid use, antidepressant use, and membrane stabilizer use. The authors noted the following results: Success rate was 38.1%. Variables found to be associated with a positive outcome in multivariate logistic regression included the presence of neuropathic or mixed pain. Factors that correlated with treatment failure were disease or traumatic/surgical etiologies and antidepressant use. Conclusions from the authors included the following: A neuropathic or mixed neuropathic-nociceptive pain condition was associated with a positive treatment outcome. Investigators should consider these findings when developing selection criteria in clinical trials designed to determine the efficacy of Calmare therapy. (116, 117)

Childs et al. (2021) conducted a clinical trial on Scrambler Therapy, a form of electroanalgesia to evaluate the efficacy when compared to transcutaneous electrical nerve stimulation (TENS) in treating chemotherapy-induced peripheral neuropathy (CIPN). (118) Fifty patients were accrued for the first half of this two-part, crossover trial consisting of a 2-week treatment period with either Scrambler or TENS, followed by an 8-week observation period, and then crossover treatment. Twenty-two patients proceeded to the crossover phase. The Scrambler treated patients were nearly twice as likely to have experienced a 50% reduction in their primary symptom score at 14 days, compared with the TENS treated patients. It is noteworthy that the same trend was observed during the crossover phase of this trial with 60% of the Scrambler-treated patients reaching that threshold compared with only 25% of the TENS-treated patients. It is not obvious why the Scrambler-treated patients experienced a more sustained/enduring improvement in their Global Impression of Change ratings for the 8-week follow-up period after crossover treatment, as opposed to the initial randomization period. Limitations include the obvious lack of blinding and small patient numbers. The standard treatment arm had more clinician interaction and was more inconvenient for patients than the TENS treatment that could be administered at home. Trends in the crossover data suggest that ST may be beneficial for alleviating CIPN symptoms. Evaluation of this modality in a larger, randomized control trial is warranted.

Transcutaneous Magnetic Stimulation (Axon Therapy)
Leung and colleagues (2014) stated peripheral nerve injury can result in the formation of neuroma/nerve entrapment, a persistent peripheral neuropathic pain state that is often refractory to invasive interventions or medications; thus, there is a need to develop innovative non-invasive therapy in treating post-traumatic peripheral neuropathic pain states. (119) A new intervention, transcutaneous magnetic stimulation (tMS), is derived from the use of transcranial magnetic stimulation in which a rapid discharge of electric current is converted into dynamic magnetic flux for modulating neuronal functions. In a case-series study, low-frequency (0.5 Hz) tMS was developed over the site of neuroma/nerve entrapment in 5 patients who have failed both steroid injection and conventional pain medications; 400 pulses of stimulation were delivered per treatment session. Each patient received 3 to 4 sessions of treatment over a period of 2 months. Pre- and post-intervention spontaneous pain levels were evaluated with Numeric Rating Scale (NRS); 5 patients with post-traumatic neuroma/nerve entrapment pain received the treatment. Average pre- and post-scores (± SD) on the NRS were 5.00 (± 1.41) and 0.80 (± 1.10), respectively, with an average pain reduction of 84 (± 21.91) % in the numerical rating pain scale (NRS) after 3 to 4 treatments within 2 months. This analgesic effect appeared to be sustainable with repeated treatment delivered at a 6- to 8-week duration. Pre-treatment tactile allodynia found in 3 patients resolved after the initial 2- month treatment sessions. The authors concluded that tMS offered a non-invasive therapeutic option for neuroma-related neuropathic pain conditions. Moreover, these researchers stated that RCTs are needed to validate the efficacy of this treatment modality; additional studies are also needed to examine the underlying electrophysiological mechanisms of the observed analgesic benefit.

Summary of Evidence
For individuals who have chronic pain (e.g., musculoskeletal, neuropathic, and mixed pain conditions) who receive transcutaneous electrical nerve stimulation (TENS), the evidence includes numerous randomized controlled trials (RCTs) and systematic reviews. Relevant outcomes are symptoms, functional outcomes, quality of life (QOL), and medication use. The overall strength of the evidence is weak. The best evidence exists for treatment of chronic, intractable pain. Available evidence indicates that TENS can improve chronic intractable pain in some patients, and there is support for its use in clinical guidelines by specialty societies. To best direct TENS toward patients who will benefit, a short-term trial of TENS is appropriate, with continuation only in patients who show an initial improvement. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have acute pain (e.g., surgical, musculoskeletal, labor, and mixed pain conditions) who receive TENS, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, QOL, and medication use. Overall, evidence for the use of TENS from high-quality trials remains inconclusive for most indications. A systematic review of TENS for acute and chronic pain found some evidence that TENS reduces pain intensity over and above that seen with placebo and other control groups in patients with acute pain, but small-sized trials contributed to imprecision in magnitude estimates. Systematic reviews have found that TENS may help reduce pain in patients with post-operative pain (post-caesarean and total knee arthroplasty), dysmenorrhea, and pain associated with labor and delivery. For low back pain, systematic reviews have found insufficient evidence to support or refute the use of TENS. Randomized controlled trials have reported mixed results in the efficacy of TENS across various acute pain conditions. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have essential tremor who receive TENS, the evidence a comprehensive review, two small randomized controlled trials, and several nonrandomized studies. The relevant outcomes are symptoms, functional outcomes, QOL, and medication use. Although results suggest that repeated in home non-invasive neuromodulation therapy may be effective and safe for patients with essential tremor, a number of evidence limitations have been identified, including but not limited to, poor study design, small study size, high risk of bias, and short follow-up duration. Further studies comparing TENS to standard of care therapy for essential tremor are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have attention deficit hyperactivity disorder (ADHD) who receive TENS, the evidence includes an RCT. Relevant outcomes are symptoms, functional outcomes, QOL, and medication use. Results of the RCT concluded that TENS is an effective and safe treatment option for pediatric patients with ADHD. However, the study included a small patient sample and was of short duration. Further studies comparing TENS to standard of care therapy for ADHD are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have chronic or episodic migraine who receive TENS for treatment of acute migraine, the evidence includes 3 double-blind, sham-controlled RCTs. Two of the RCTs evaluated healthcare-provider administration of a TENS device during a single episode in emergency departments, and 1 evaluated self-administration of the device at home during acute episodes over a 3-month period. The studies conducted in emergency departments showed clinically and statistically significant reductions in pain intensity and medication use within 2 hours of use. The self-administration study had mixed results: The difference in median pain scores before and after treatment was significantly higher in the TENS group at months 1 and 2, but at month 3 the difference was not statistically significant. Function and analgesic medication use did not differ between groups at any time point. Strengths of the RCTs included the use of a sham device and blinded outcome assessment using validated outcome measures. Although short-term pain relief was demonstrated at some time points, the quality of the overall body of evidence was downgraded due to inconsistency of results and heterogeneity in study settings. It is not clear whether the pain intensity reductions demonstrated in emergency department settings would generalize to other settings over longer time periods. Supporting evidence from RCTs is needed. Additionally, based on the existing evidence, it is unclear how TENS would fit into the current migraine treatment pathway, although it could provide benefit for those who do not receive adequate benefit from pharmacologic first- or second-line therapies, or who may have a contraindication to pharmacologic therapies. The specific intended use must be specified in order to adequately evaluate net health benefit. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have chronic or episodic migraine who receive TENS for migraine prevention, the evidence includes 1 RCT. Relevant outcomes are symptoms, functional outcomes, QOL, and medication use. The RCT (N=67) reported a greater proportion of participants achieving at least a 50% reduction in migraines with TENS than with sham placebo and modest reductions in the number of total headache and migraine days. In the intention-to-treat analysis, the reduction in the number of migraine days (run-in vs. 3-months) was not statistically significant. The proportion of responders (≥50% reduction in the number of migraine days/month) significantly higher in the TENS group. The number of migraine attacks from the run-in period to the 3-month evaluation, number of headache days, and antimigraine medication use were significantly lower for the active TENS group. The severity of migraine days did not differ significantly between groups. This manufacturer-sponsored trial needs corroboration before conclusions can be made with certainty about the efficacy of TENS for preventing migraine headaches. Additionally, based on the existing evidence, it is unclear how TENS would fit into the current migraine prevention pathway, although it could provide benefit for those who do not receive adequate benefit from pharmacologic first- or second-line therapies, or who may have a contraindication to pharmacologic therapies. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have pain (e.g., failed back surgery syndrome, neuropathic pain and mixed pain conditions) who receive transcutaneous electrical modulation pain reprocessing (e.g., scrambler therapy) therapy, the evidence includes a study of 219 patients with chronic pain, one observational study, one small randomized controlled trial (RCT), retrospective study analyses, case studies, one clinical trial, and a review of articles. The overall strength of evidence is weak. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

No studies were identified that evaluated devices using combination therapy (i.e., interferential, neuromuscular electrical stimulation, and transcutaneous electrical nerve stimulation modes). The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have persistent peripheral neuropathic pain who receive transcutaneous magnetic stimulation, the evidence includes a single case-series study of 5 patients who had failed both steroid injection and conventional pain medications. Although results were encouraging, RCTs are needed to validate the efficacy of this treatment modality and to examine the underlying electrophysiological mechanisms of the observed analgesic benefit. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements for TENS

American Academy of Neurology
In 2010, the American Academy of Neurology published an evidence-based review of the efficacy of TENS for the treatment of pain in neurologic disorders. (33) The Academy did not recommend TENS for the treatment of chronic low back pain due to lack of proven efficacy (level A, established evidence from 2 class I studies), but stated that TENS should be considered for the treatment of painful diabetic neuropathy (level B, probably effective, based on 2 class II studies).

American College of Physicians
In 2017, the American College of Physicians published guidelines on noninvasive therapies for acute and low back pain. (109) No recommendations for TENS were made; the College concluded that "evidence was insufficient to determine the effectiveness" of TENS and that there was no long-range data.

American Congress of Obstetricians and Gynecologists (ACOG)
In 2019 (reaffirmed in 2021), the ACOG guidelines on labor and delivery found that TENS may "help women cope with labor more than directly affect pain scores." (120)

American Society of Anesthesiologists, et al.
In 2010, the practice guidelines from the American Society of Anesthesiologists and American Society of Regional Anesthesia and Pain Medicine recommended that TENS be used as part of a multimodal approach to management for patients with chronic back pain and may be used for other pain conditions (e.g., neck and phantom limb pain). (121)

National Cancer Institute
The National Cancer Institute's Physician Data Query identifies TENS as a potential nonpharmacological modality for pain control for post-thoracotomy pain syndrome. (122)

National Comprehensive Cancer Network
National Comprehensive Cancer Network guidelines on adult cancer pain (v.2.2024) indicate that non-pharmacologic interventions, including TENS, may be considered in conjunction with pharmacologic interventions as needed (category 2A). (123)

National Institute for Health and Care Excellence
In 2016, The National Institute for Health and Care Excellence (NICE) guidance on low back pain indicated that, despite the long history of use of TENS for back pain, the quality of research studies is poor. (124) This guidance recommended against TENS as a treatment.

In 2014 (updated 2020), NICE guidance on osteoarthritis care and management in adults indicated that TENS be considered "as an adjunct to core treatments for pain relief." (125)

In 2017, NICE guidance on intrapartum care recommends:
- "TENS devices are not provided by the NHS, but if a woman wants to use TENS to manage her comfort during labour, support her choice

- there is very little evidence of its effectiveness in established labour, but no evidence of harm
- other forms of pain relief can be used alongside TENS if needed by the woman. [2007, amended 2023].” (126)

North American Spine Society

In 2020, the North American Spine Society clinical guidelines on the diagnosis and treatment of low back pain provided guidance on the effectiveness of different physical medicine and rehabilitation therapies. (127) The guideline noted that there is conflicting evidence that TENS results in improvement in pain or function at short- to medium-term follow-up. The work group further recommended that randomized clinical trials with long-term follow-up are needed to evaluate the benefits of TENS compared to exercise/physical therapy or as adjunctive use to usual care for low back pain.

In 2011, the North American Spine Society clinical guidelines on the diagnosis and treatment of cervical radiculopathy from degenerative disorders discussed the role of ancillary treatments such as bracing, traction, electrical stimulation, acupuncture, and TENS. (128) A consensus statement from the Society recommended that ozone injections, cervical halter traction, and combinations of medications, physical therapy, injections, and traction have been associated with improvements in patient-reported pain in uncontrolled case series. Such modalities may be considered, recognizing that no improvement relative to the natural history of cervical radiculopathy has been demonstrated. There were no specific statements about the role of TENS in this population.

Osteoarthritis Research Society International

In 2014, the guidelines from the Osteoarthritis Research Society International recommended that TENS was inappropriate for use in patients with multi-joint osteoarthritis; moreover, the guidelines suggested that TENS has an uncertain value for the treatment of knee-only osteoarthritis pain. (129) Updated guidance (2019) on the non-surgical management of knee, hip, and polyarticular osteoarthritis does not address TENS nor include it in their patient-focused treatment recommendations. (130)

Ongoing and Unpublished Clinical Trials for TENS

Some currently ongoing and unpublished trials that might influence this policy are listed in Table 11.

Table 11. Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT05939804	The Effect of Transcutaneous Electrical Nerve Stimulation (TENS) Application on Patients' Pain Level and Analgesic Use in Patients Undergoing Hip Replacement	60	Jul 2024 (not yet recruiting)

NCT05812885	Transcutaneous Electrical Nerve Stimulation (TENS) and Chronic Low-Back Pain: A Randomized Crossover Trial	34	Dec 2024
NCT04114149	Effective Postoperative Pain Relief After Laparoscopic Cholecystectomy With TENS Treatment for First Line of Treatment Compared to Conventional Treatment With Opioids	166	Mar 2024 (unknown status)
Unpublished			
NCT04092088	Effectiveness of Cerebral and Peripheral Electrical Stimulation on Pain and Functional Limitations Associated With Carpal Tunnel Syndrome: A Randomized, Double-blind, Multi-center, Factorial Clinical Trial	180	Oct 2020 (unknown status)
NCT04851938	Evaluation of the Effect of Transcutaneous Electrical Nerve Stimulation Applied in Different Frequencies on Hormone Levels, Birth Pain Perception and Anxiety During Delivery	112	Jun 2021 (unknown status)
NCT02642796	Comparison of the Efficacy of Two Different Transcutaneous Electrical Nerve Stimulation Application Sites in Reducing Postoperative Pain After Hip Fracture Surgery	120	Sep 2021
NCT05991921	The Effect of TENS Applied in the Early Postpartum Period on Incision Healing, Pain and Comfort	138	Aug 2023
NCT05320432	Transcutaneous Electrical Nerve Stimulation for Pain Control During First Trimester Abortion: a Blinded Randomized Controlled Trial	70	Jan 2024

NCT: national clinical trial.

Ongoing and Unpublished Clinical Trials For TEMPR
There are no ongoing and unpublished trials for TEMPR that might influence this policy.

Ongoing and Unpublished Clinical Trials For Devices Capable of Combination Therapies
There are no ongoing and unpublished trials for devices using combination therapy (i.e., interferential, neuromuscular electrical stimulation, and transcutaneous electrical nerve stimulation modes).

Ongoing and Unpublished Clinical Trials for Transcutaneous Magnetic Stimulation (Axon Therapy)
Some currently ongoing trials that might influence this policy are listed in Table 12.

Table 12. Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04795635	Axon Therapy for Post-Traumatic Peripheral Neuropathic Pain Compared to Conventional Medical Management	61	Aug 2024
Unpublished			
NCT05620225	Axon Therapy and Conventional Medical Management for Painful Diabetic Neuropathy Compared to Sham and Conventional Medical Management	93	Nov 2023

NCT: national clinical trial.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	97014, 97032, 0278T, 0766T, 0767T
HCPCS Codes	A4541, A4542, A4595, A4630, E0720, E0730, E0731, E0733, E0734, E1399, G0283, [Deleted 1/2024: K1016, K1017, K1018, K1019, K1023, 0768T, 0769T]

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been changed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
02/01/2025	Document updated with literature review. The following change was made to coverage: Added treatment of migraine headaches to the list of services that are Experimental, Investigational or Unproven for TENS. References 6, 40, 53, 57-58, 64, 67, 101-105, 118 and 131-133 added; others updated, and some removed.
07/01/2023	Document updated with literature review. Coverage unchanged. The following references were added/updated: 34, 43, 59, 75, 80, 89, 90, 92-96, 111, and 118.
06/15/2023	Document updated with literature review. The following change was made to Coverage: Added "Transcutaneous magnetic stimulation by focused low-frequency electromagnetic pulse (Axon Therapy) is considered experimental, investigational and/or unproven for all indications, including but not limited to chronic pain management." Added references 118, 119.
02/15/2023	Document updated with literature review. The following change was made to Coverage: Added migraine prevention, essential tremor, and management of attention deficit hyperactivity disorder to the experimental, investigational and/or unproven list. Distal transcutaneous electrical nerve stimulation (REN) coverage language removed from policy and now addressed on 701.046. References 16, 28, and 36 added.
10/01/2021	Document updated with literature review. The following change was made to Coverage: Added "Distal transcutaneous electrical nerve stimulation (also referred to as remote electrical neuromodulation [REN]) is considered experimental, investigational and/or unproven." Added references 103-105.
05/15/2021	Reviewed. No changes.
08/15/2020	Document updated with literature review. Coverage unchanged. References 27, 39, 41, 47-49, 60, 65, 67 and 70 added; others updated or deleted.
05/15/2019	Document updated with literature review. The following change was made to Coverage: Form-fitting conductive garments, (e.g., vest, gauntlet, etc.**),** may be considered medically necessary if specified criteria are met.

	References 25, 27, 28, 51, 63, 73, 85 and 86 added; others updated. Title changed from "Transcutaneous Electrical Stimulation (TENS) and Modulation (TEMPR)".
12/15/2018	Document updated with literature review. The following change was made to Coverage: Added "Devices capable of combination therapies (e.g., NexWave™) that provide several modalities (e.g., interferential, transcutaneous electrical nerve stimulation and neuromuscular electrical stimulation) are considered experimental, investigational and/or unproven." References added: 33, 39-40, 49, 55, 72, 74, 85-88.
07/15/2017	Reviewed. No changes.
05/01/2016	Document updated with literature review. Coverage unchanged.
08/15/2015	Reviewed. No changes.
06/01/2014	New medical document. Coverage is unchanged: TENS may be considered medically necessary when criteria are met. Also, headache, including migraine headache was added to the list of examples of indications that are considered experimental, investigational and/or unproven. This topic was previously addressed on MED201.026 Surface Electrical Stimulation.