

Cigna Medical Coverage Policy- Therapy Services Electric Stimulation for Pain, Swelling and Function in a Clinic Setting

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Medically Necessary

Use of electric stimulation (e.g. TENS, EMS) is considered medically necessary in a clinic setting and under the direct supervision of a physical therapist or similar professional when prescribed as part of a comprehensive treatment program for pain and swelling, and only used short term up to 2 weeks.

Note: The medical records must document a response to the use of electrical stimulation, including specific parameters related to the type of electric stimulation (e.g. low or high frequency TENS, electrode placement).

Electric Stimulation for Pain, Swelling and Function in a Clinical Setting (CPG 272)

Neuromuscular Electrical Stimulation (NMES) is considered medically necessary for disuse atrophy where the nerve to the muscle is intact and the individual has any of the following non-neurological reasons for the disuse atrophy and only in conjunction with active exercise:

- Major hip or knee surgery where there is failure to respond to basic therapeutic exercises as initiated in physical therapy/rehabilitation; or
- Previous immobilization (e.g. casting or splinting) of an extremity (arm or leg)

Experimental, Investigational, Unproven

Each of the following electrical stimulation devices, therapies, and treatments is considered experimental, investigational, or unproven for the treatment of any condition:

- Cranial electrotherapy stimulation
- Deep Pharyngeal Neuromuscular Stimulation (DPNS)
- Hako-Med treatments
- H-WAVE® stimulation
- Microcurrent electrical nerve stimulation (MENS) therapy
- Microcurrent point stimulation
- Neufit Neubie device
- NMES/Electrical Stimulation (e.g. Guardian dysphagia dual chamber unit, VitalStim Therapy device)
- Pelvic floor stimulation (electric and magnetic stimulation)
- Percutaneous Electrical Nerve Stimulation (PENS) and Percutaneous Neuromodulation Therapy (PNT)
- RST-SANEXAS neoGEN® Electric cell-Signaling Treatments (EcST)
- Transcutaneous electrical modulation pain reprocessing (TEMPR) (e.g., Scrambler therapy, Calmare®)
- Threshold Electrical Stimulation

Electrical stimulation (except NMES) is contraindicated in areas of sensory deficits. A patient's sensory deficits (decrease or loss) do not allow them to provide the correct feedback necessary for the safe and effective application to the affected area. Electrical stimulation in other related areas without sensory deficits may be appropriate.

Note: For information on home electrical stimulation devices (electrical stimulators) please refer to Cigna Coverage Policy Electrical Stimulation Therapy and Home Devices.

DESCRIPTION

Electrical stimulation (ES) therapy involves the application of electrodes to the affected area of the body for the purpose of delivering electrical current. There are several forms of electrical current used in rehabilitation settings. Electrical stimulation is used for muscle re-education (disuse atrophy), pain relief, reduction of swelling, and healing enhancement. This CPG will focus on the use of electric stimulation for pain, swelling and function (muscle re-education/disuse atrophy) when used in the outpatient clinic setting.

GENERAL BACKGROUND

A TENS unit must be distinguished from other electrical stimulators (e.g., neuromuscular stimulators) which are used to directly stimulate muscles and/or motor nerves. Transcutaneous electrical nerve stimulation (TENS) is characterized by biphasic current and selectable parameters such as pulse rate and pulse width. TENS uses a battery-operated device that applies electrical stimulation via transmission of pulses of various configurations at the site of pain by wired electrodes that are taped to the surface of the skin. For example, conventional TENS or

high frequency TENS delivers 40–150 hertz (Hz) compared to acupuncture-like TENS that delivers a low frequency at 1–10 Hz. Pulsed TENS uses low-intensity firing in high-frequency bursts at 100 HZ. Units often have preset programs with variations and modulations of frequencies and durations of pulses. TENS has been used for a number of applications. In theory, TENS stimulates sensory nerves to block pain signals; it also stimulates endorphin production to help normalize sympathetic function. TENS has been used to relieve acute or chronic pain related to musculoskeletal conditions, pain associated with active or post-trauma injury, obstetrical pain, or postoperative pain. TENS for pain control occurs via the gate theory or the endogenous opiate theory. Conventional transcutaneous electrical stimulation (TENS) is an example of the use of the gate theory to control or block pain. Low rate TENS is an example of the use of the endogenous opiate theory of pain control. TENS can also be delivered through the use of a form-fitting conductive garment (for example, a garment with conductive fibers that are separated from the individual's skin by layers of fabric). This garment is applied when a condition exists that precludes conventional TENS electrode placement.

Microcurrent Electrical Nerve Stimulation (MENS) involves the use of a device that delivers small amounts of electrical current (millionths of an amp) to help relieve pain and heal soft tissues of the body. The application of microcurrent stimulation to an injured area is proposed to realign the body's electrical current and increase the production of adenosine triphosphate, resulting in increased healing and recovery and blocking of perceived pain. The electrical current is subsensory and usually not felt. MENS differs from TENS in that it uses a significantly reduced electrical stimulation (i.e., 1,000 times less current than TENS). The goal of TENS is to block pain, while MENS acts on naturally-occurring electrical impulses to decrease pain by stimulating the healing process (Frequency Specific Microcurrent, 2014). Frequency specific microcurrent (FSM) is a type of microcurrent therapy. The microcurrent device has two separate channels that allow both the frequency and current to be set independently for each channel. FSM is proposed as a treatment option for nerve and muscle pain, shingles, and herpes (Frequency Specific Microcurrent, 2011).

The H-WAVE[®] electrical stimulation device generates a biphasic, exponentially decaying waveform with pulse-wide widths. Its waveform distinguishes it from TENS and other forms of electrical stimulators. H-WAVE[®] is classified as a powered muscle stimulator. The hypothesis that the H-WAVE[®] device (Electronic Waveform Lab, Inc., Huntington Beach, CA), a small-diameter fiber stimulator, is a paradigm shift of electrotherapeutic treatment of pain associated with human neuropathies and sports injuries is based on a number of its properties. The primary effect of H-WAVE[®] device stimulation (HWDS) is the stimulation of "red-slow-twitch" skeletal muscle fibers. The authors propose, based on the unique waveform, that the H-WAVE[®] device specifically and directly stimulates the small smooth muscle fibers within the lymphatic vessels ultimately leading to fluid shifts and reduced edema. The H-WAVE[®] device was designed to stimulate an ultra-low frequency (1-2 Hz), low tension, non-tetanic, and non-fatiguing contraction, which closely mimics voluntary or natural muscle contractions. The H-WAVE[®] device can stimulate small fibers due in part to its exponentially decaying waveform and constant current generator activity. The main advantage of these technologies over currently applied electrical stimulators (e.g., TENS, interferential, NMES high-volt galvanic, etc.) is that H-WAVE[®] small fiber contraction does not trigger an activation of the motor nerves of the large white muscle fibers or the sensory delta and C pain nerve fibers, thus eliminating the negative and painful effects of tetanic fatigue, which reduces transcapillary fluid shifts. Another proposed function of the H-WAVE[®] device is an anesthetic effect on pain conditions, unlike a TENS unit which in the short term activates a hypersensory overload effect (gate theory) to stop pain signals from reaching the thalamic region of the brain. When the H-WAVE[®] device is used at high frequency (60 Hz), it supposedly acts intrinsically on the nerve to deactivate the sodium pump within the nerve fiber, leading to a long-lasting anesthetic/analgesic effect due to an accumulative postsynaptic depression. The large pulse width theoretically enables contraction in the muscle for extended periods of time at a low fatigue rate and increases circulation, muscle relaxation, pain relief and wound healing. H-WAVE[®] stimulation has been used in the treatment of pain related to a variety of etiologies, such as diabetic neuropathy, muscle sprains, temporomandibular joint dysfunctions, or reflex sympathetic dystrophy. H-WAVE[®] electrical stimulation must be distinguished from the H-waves that are a component of electromyography.

Other waveforms are used for pain modulation as well, including interferential current (IFC), which is produced by two interfering alternating currents. Interferential stimulation (IFS) is characterized by 2 alternating-current sine waves of differing medium frequencies that combine together to produce an interferential current that is also known as a beat pulse or alternating modulation frequency. One of the 2 currents is held at 4,000 Hz, and the other can be held constant or varied over a range of 4,001 to 4,100 Hz. Interferential therapy (IFT) delivers a crisscross current at 4000–4150 pulses per second, resulting in deeper muscle penetration. It is theorized that

IFT prompts the body to secrete endorphins and other natural painkillers and stimulates parasympathetic nerve fibers to increase blood flow and reduce edema. Interferential currents reportedly can stimulate sensory, motor, and pain fibers. Because of the frequency, the interferential wave meets low impedance when crossing the skin to enter the underlying tissue. This deep tissue penetration can be adjusted to stimulate parasympathetic nerve fibers for increased blood flow. According to proponents, interferential stimulation differs from TENS because it allows a deeper penetration of the tissue with more comfort (compliance) and increased circulation.

High Voltage Galvanic Stimulation (HVGS) or high volt pulsed current (HVPC) is characterized by high voltage pulsed stimulation and is proposed primarily for local edema reduction through muscle pumping and polarity effect. High volt pulsed current (HVPC) is used for tissue healing and edema control based on polarity principles. Edema is comprised of negatively charged plasma proteins, which leak into the interstitial space. The theory of HVPC is that the high voltage stimulus applies an electrical potential which disperses the negatively charged proteins away from the edematous site, thereby helping to reduce edema (Cameron, 2017).

Neuromuscular electric stimulation (NMES) is the application of electrical current through electrodes on the skin to targeted muscles to elicit muscle contraction. NMES is proposed to promote neuromuscular re-education, improve motor unit recruitment, and thus to prevent or diminish muscle atrophy and is an established treatment modality for disuse atrophy when the nerve supply to the muscle is intact. NMES is typically used as a component of a comprehensive rehabilitation program. Compared to TENS, NMES delivers a stronger current with a wider pulse width. Neuromuscular electrical stimulation can be grouped into 2 categories: (i) stimulation of muscles to treat muscle atrophy due to disuse (e.g. post-surgical, immobilization), and (ii) enhancement of functional activity in neurologically impaired individuals. These devices within the second category use electrical impulses to activate paralyzed or weak muscles in precise sequence and have been utilized to provide SCI patients with the ability to walk (e.g., The Parastep I System). Neuromuscular electrical stimulation used in this manner is commonly known as functional electrical stimulation (FES).

Electric stimulated muscle contraction/neuromuscular electric stimulation (NMES) has been found to enhance muscle function gains post-surgically. Patients who have received an anterior cruciate ligament (ACL) reconstruction have demonstrated accelerated recovery and greater muscle function when NMES is used in combination with exercise; however the impact on functional outcomes is inconsistent (Cameron, 2017). Similar results were noted with knee OA patients and for other inflammatory conditions of the knee. Most research studied the use of NMES on the quadriceps muscle, however clinically NMES may be used for other joints and muscle groups (Cameron, 2017). Functional electric stimulation (FES) is proposed for use in certain neurologic populations. As an example, FES can be applied to the anterior tibialis muscle to assist in dorsiflexion during gait for patients with foot drop. Several studies support the integration of FES for patients with spinal cord injury or who have sustained a stroke for various activities. As long as the peripheral nervous system is intact, any patients with central nervous system dysfunction may benefit from FES use. In these situations, effectiveness of FES is thought to be most likely due to the direct effect of muscle strengthening in addition to increased excitability of the motor neuron pool produced by the motor level electrical stimulation (Cameron, 2017).

PENS and PNT combine the theories of electroacupuncture and TENS and the terms are often used interchangeably. PENS involves the delivery of an electrical current through the insertion of a needle below the skin at the site of pain compared to acupuncture that places needles based on energy flow. It is not the same as acupuncture. PENS is similar to TENS except that the needles are inserted one to four centimeters around or adjacent to the applicable nerve. Up to ten needs with five electrical channels may be used. PENS is generally reserved for patients who fail to obtain pain relief from TENS. PENS may also involve the application of electric stimulation to needles placed at the dermatomal levels corresponding to the painful area. PNT is a variation of PENS which was developed as a treatment for neck and back pain. This treatment involves insertion of very fine needle-like electrodes into the skin of the neck or back to stimulate nerve fibers in the deep tissues. The treatment regimen suggested by manufacturers typically consists of two to three, 30-minute sessions per week, for two to six weeks.

VitalStim[®] Therapy is a type of NMES that uses a mild electrical current that is intended to treat dysphagia by re-educating the muscles and improving swallowing. Guardian dysphagia dual chamber unit is proposed for use for muscle re-education by application of external stimulation for pharyngeal contraction. VitalStim[®] therapy was approved by the US Food and Drug Administration in 2001 for the treatment of dysphagia through the application of neuromuscular electrical stimulation to cervical swallowing muscles. To date, however, aside from

the developer's own studies, there are no peer-reviewed publications supporting these claims. Deep pharyngeal neuromuscular stimulation (DPNS) is an electrical stimulation therapy for people with dysphagia. DPNS stimulates the cranial nerves by directly touching specific areas within the mouth and throat. This causes the pharyngeal and lingual muscles to contract. Over time, this is postulated to strengthen the patient's gag reflex and help to improve long-term swallowing functionality.

Transcutaneous electrical modulation pain reprocessing (TEMPR), also called Scrambler therapy or Calmare® pain therapy, delivers electrical stimulation via the nerve fibers to convey a message of normality to the central nervous system (CNS) by a procedure defined as “scrambling” or “tricking” of information. The device is proposed to send a very low current of electrical stimulation through the nerve fibers, which carries a “no pain” signal to the brain that overrides the previous pain signal. Unlike conventional TENS, the procedure is administered in an outpatient setting and is not intended for home use. Up to five pairs of electrodes are placed on the patient's skin in the dermatome areas of pain above and below the dermatome. Amperage ranges from 3.5 to 5.0 milliamperes with a voltage range of 6.5 to 12.5 volts. Electrical stimulation is increased to the maximum tolerated intensity until pain is relieved. The device is proposed to simultaneously stimulate multiple pain areas in a patient. TEMPR has been proposed for the treatment of chemotherapy-induced peripheral neuropathy, intractable cancer pain, failed back surgery syndrome, phantom limb pain, sciatica, post-surgical pain, neuropathic pain, brachial plexus pain, low back pain, neck pain, reflex sympathetic dystrophy and post-herpetic neuralgia (PHN). Recommended treatment regimen for neuropathic pain is 10–12 daily sessions (30–45 minute) and 10–12 treatments for oncologic patients based on the patient's pain control needs (Competitive Technologies, 2020; Marineo, et al., 2012).

LITERATURE REVIEW

TENS

There are many published reports regarding the use of TENS for various types of conditions such as low back pain (LBP), myofascial and arthritic pain, sympathetically mediated pain, neurogenic pain, visceral pain, diabetic neuropathy and postsurgical pain. While randomized controlled trials (RCTs) have focused on both high and low frequency TENS, all of the currently available studies have methodological flaws that limit interpretation, including inadequate blinding, lack of reporting of drop outs, lack of reporting of stimulation variables, and lack of proper outcome measures (Johnson et al., 2015). However, it is recognized that TENS is widely accepted in the physician and therapy community as a treatment of a variety of etiologies of pain in combination with comprehensive treatment program.

According to the Philadelphia Panel Evidence-Based Clinical Practice Guidelines on Selected Rehabilitation Interventions for Low Back Pain publication (2001), TENS demonstrated no effectiveness for improvements in pain or function in subjects with chronic low back pain (LBP). Evidence was stated as good (level I). The Panel recommends that there is poor evidence to include or exclude TENS alone as an intervention for chronic LBP. According to The Cochrane Collaboration systematic review on TENS for chronic LBP (Khadiikar et al., 2005) there is limited and inconsistent evidence to support the use of TENS as an isolated intervention for chronic LBP. In 2010, the Therapeutic and Technology Assessment Subcommittee of the American Academy of Neurology (AAN) published a report finding TENS ineffective for chronic low back pain (Dubinsky and Miyasaki, 2010). The results indicated that there are conflicting reports of TENS compared to sham TENS in the treatment of chronic low back pain, with two Class II studies showing benefit, but two Class I studies and another Class II study not showing benefit. Because the Class I studies are stronger evidence, TENS is established as ineffective for the treatment of chronic low back pain. Their recommendations were that TENS is not recommended for the treatment of chronic low back pain (Level A) and further research into the mechanism of action of TENS is needed, as well as more rigorous studies for determination of effectiveness. Per ACOEM guidelines, TENS for acute or sub-acute LBP or acute radicular pain syndromes is not recommended given insufficient evidence (ACOEM, 2007). In a review by Poitras and Brosseau (2008), it was determined that globally, high- and low-frequency TENS appears to have an immediate impact on pain levels in subjects with non-specific chronic LBP, with high-frequency TENS achieving better results. Studies included were of relatively poor quality and the lack of consistent parameters from study to study makes comparisons difficult. Based on this review, TENS appears to be of no benefit for long term pain or perceived disability (Poitras and Brosseau, 2008). Khadiikar et al. (2008) updated the 2005 Cochrane Review to determine whether TENS is more effective than placebo for the management of chronic LBP. Only randomized controlled clinical trials (RCTs) comparing TENS to placebo in patients with chronic LBP were included. Four high-quality RCTs (585 patients) met the selection criteria. Clinical heterogeneity prevented the use of meta-analysis. There was conflicting evidence

about whether TENS was beneficial in reducing back pain intensity and consistent evidence in two trials (410 patients) that it did not improve back-specific functional status. There was moderate evidence that work status and the use of medical services did not change with treatment. In general, patients treated with acupuncture-like TENS responded similarly to those treated with conventional TENS. However, in two of the trials, inadequate stimulation intensity was used for acupuncture-like TENS, given that muscle twitching was not induced. Adverse effects included minor skin irritation at the site of electrode placement. Authors concluded that the evidence from the small number of placebo-controlled trials does not support the use of TENS in the routine management of chronic LBP. Further research was encouraged.

The American Society of Anesthesiologists (ASA) and American Society of Regional Anesthesia and Pain Medicine (ASRA) support the use of TENS in their revised guideline recommending that "TENS should be used as a multimodal approach to pain management for patients with chronic back pain and may be used for other pain conditions (e.g. neck and phantom limb pain)" (ASA/ASRA, 2010). A Cochrane review that identified 25 eligible RCTs was not favorable in their analysis of the literature support of TENS for various chronic pain conditions, primarily due to the quality of the available literature (Nnoaham and Kumbang, 2008). These authors found positive results for pain relief in 13 out of 22 studies that compared TENS to a placebo or other inactive control group. In studies that compared different TENS modes, seven of nine studies found no difference in pain relief between high vs. low frequency TENS. Overall, the low methodological quality and low power of the available literature did not allow the authors to make firm conclusions regarding the effectiveness of TENS for chronic pain.

In 2013, Pivec et al. studied the clinical and economic impact of TENS in patients with chronic LBP through analysis of a national database. This study evaluated patients who were given TENS compared with a matched group without TENS prior to intervention and at one-year follow-up. Patients who were treated with TENS had significantly fewer hospital and clinic visits, used less diagnostic imaging, had fewer physical therapy visits, and required less back surgery than patients receiving other treatment modalities. Jaurequi et al. (2016) conducted a systematic review and meta-analysis of the efficacy of TENS for the treatment of chronic, musculoskeletal low back pain. Thirteen studies, which included randomized controlled trials, cohort studies, and randomized crossover studies (n=267), met inclusion criteria. Follow-ups ranged from 2–24 weeks with a mean follow-up of seven weeks. The duration of treatment ranged from 2–24 weeks (mean 6 weeks). The overall standardized mean difference in pain from pre- to post-treatment with TENS showed a significant improvement of TENS on pain reduction. When subdivided into treatment duration, patients that were treated for less than five weeks (n=8 studies) had significant effects on pain, while those treated for more than five weeks did not. The heterogeneity among studies was substantially significant among the TENS groups. Limitations of the studies included: small patient populations; variations in treatment times, TENS frequency and length of follow-up; and conflicting outcomes. The authors noted that despite the positive results, large multi-center prospective randomized trials are needed to develop the appropriate treatment protocols for this patient population. According to the AHRQ Comparative Effectiveness publication on Non-Invasive Treatments for Low Back Pain (2016), additional evidence demonstrates that TENS is not effective versus sham TENS. Effectiveness of TENS was previously classified as insufficient and the strength of evidence remains low because of methodological limitations in the trials and imprecision. Evidence on harms associated with TENS was limited, but suggests an increased risk of skin site irritation without an increased risk of serious adverse events (AHRQ, 2016). According to the American College of Physician's Noninvasive Treatments for Acute, Subacute, and Chronic Low Back Pain clinical practice guideline (2017), evidence was insufficient to determine the effectiveness of transcutaneous electrical nerve stimulation (TENS).

Two practice guidelines support the use of TENS, one for rheumatoid arthritis based on positive results in one (1) RCT (Ottawa Panel Evidence-Based Clinical Practice Guidelines, 2004), and one for the treatment of knee osteoarthritis based on meta-analysis of five (5) RCTs included in the analysis (Philadelphia Panel Practice Guidelines, 2001). Johnson et al. (2015) assessed the analgesic effectiveness of TENS, as a sole treatment, for acute pain in adults. Only RCTs of adults with acute pain (< 12 weeks) were examined with TENS given as a sole treatment and assessed pain was with subjective pain scales. The types of acute pain included in this Cochrane Review were procedural pain, e.g. cervical laser treatment, venipuncture, screening flexible sigmoidoscopy and non-procedural pain, e.g. postpartum uterine contractions and rib fractures. There was a high risk of bias associated with inadequate sample sizes in treatment arms and unsuccessful blinding of treatment interventions. Seven trials reported minor adverse effects, such as mild erythema and itching underneath the electrodes and participants disliking TENS sensation. Authors concluded that this review offers

tentative evidence that TENS reduces pain intensity over and above that seen with placebo (no current) TENS when administered as a stand-alone treatment for acute pain in adults. The high risk of bias associated with inadequate sample sizes in treatment arms and unsuccessful blinding of treatment interventions makes definitive conclusions impossible.

Jin et al. (2010) conducted a systematic review to evaluate the effectiveness of TENS on diabetic peripheral neuropathy. Three randomized controlled trials (n=78) met inclusion criteria. TENS was reported more effective than placebo in the reduction of mean pain score at four and six weeks follow-up but not at 12 weeks. Pieber et al. (2010) conducted a systematic review of the literature to evaluate electrotherapy, including TENS, for the treatment of peripheral neuropathy in patients with diabetes. Three randomized controlled trials (n=76) and one retrospective review (n=54) evaluating TENS met inclusion criteria. The studies included short-term follow-ups and conflicting results. One study reported significant improvement in pain and another study reporting recurrence of pain after cessation of TENS. Due to the small patient populations, short-term treatment duration, short-term follow-up and poor study methodology, large multi-center randomized controlled trials are needed to further evaluate the long-term effect of TENS on diabetic neuropathy. Hurlow et al. (2012) conducted an update review of the 2009 review by Robb et al. One new study met inclusion criteria (n=24). There were significant differences in participants, treatments, procedures and symptom measurement tools used in the studies. The clinical utility of TENS for the treatment of cancer pain has not been established. Robb et al. (2009) conducted a systematic review of the literature to evaluate TENS for the treatment of cancer-related pain. Two randomized controlled trials (n=64) met inclusion criteria. Meta-analysis was not conducted due to the disparities between patient population, mode of TENS, treatment duration, and outcome measures prevented meta-analysis. There is insufficient evidence to support TENS for the treatment of cancer-related pain.

Mulvey et al. (2010) conducted a systematic review of randomized controlled trials to assess the effectiveness of TENS for the treatment of phantom pain and stump pain following amputation in adults. No studies were identified. Johnson et al. (2015b) conducted an update of this Cochrane review and found no new randomized controlled trials evaluating TENS for the treatment of phantom pain and stump pain. Rheumatoid Arthritis: In a systematic review of the literature, Brosseau et al. (2003) evaluated the effectiveness of TENS for the treatment of rheumatoid arthritis of the hand. Three randomized controlled trials (n=78) met inclusion criteria. Conventional TENS (C-TENS) and acupuncture-TENS (acu-TENS) were compared to either placebo or each other. Pain outcomes on the effect of TENS were conflicting. Acu-TENS was beneficial for reducing pain intensity and improving muscle power scores compared to placebo. No clinical benefit on pain was reported with C-TENS compared to placebo. C-TENS resulted in a clinical benefit on the patients' assessment of change compared to acu-TENS. The authors concluded that more well designed studies with a standardized protocol and adequate numbers of subjects were needed to fully identify the effect of TENS for the treatment of RA of the hand.

Dissanayaka et al. (2016) compared the effectiveness of transcutaneous electrical nerve stimulation and interferential therapy (IFT) both in combination with hot pack, myofascial release, active range of motion exercise, and a home exercise program on myofascial pain syndrome patients with upper trapezius myofascial trigger point. Following randomization of patients into three groups (hot pack, active range of motion exercises, myofascial release, and a home exercise program with postural advice), transcutaneous electrical nerve stimulation-standard care and IFT-standard care-were administered eight times during 4 weeks at regular intervals. Pain intensity and cervical range of motions (cervical extension, lateral flexion to the contralateral side, and rotation to the ipsilateral side) were measured at baseline, immediately after the first treatment, before the eighth treatment, and 1 week after the eighth treatment. Immediate and short-term improvements were marked in the transcutaneous electrical nerve stimulation group (n = 35) compared with the IFT group (n = 35) and the control group (n = 35) with respect to pain intensity and cervical range of motions ($P < 0.05$). The IFT group showed significant improvement on these outcome measurements than the control group did ($P < 0.05$). Authors concluded that TENS with standard care facilitates recovery better than IFT does in the same combination.

Page et al. (2016) completed a Cochrane Database Systematic Review on electrotherapy modalities for rotator cuff disease. Examples included therapeutic ultrasound, low-level laser therapy (LLLT), transcutaneous electrical nerve stimulation (TENS), and pulsed electromagnetic field therapy (PEMF). These modalities are usually delivered as components of a physical therapy intervention. Authors synthesized the available evidence regarding the benefits and harms of electrotherapy modalities for the treatment of people with rotator cuff disease. Randomized controlled trials (RCTs) and quasi-randomized trials, including adults with rotator cuff

disease (e.g. subacromial impingement syndrome, rotator cuff tendinitis, calcific tendinitis), and comparing any electrotherapy modality with placebo, no intervention, a different electrotherapy modality or any other intervention (e.g. glucocorticoid injection) were included. Trials investigating whether electrotherapy modalities were more effective than placebo or no treatment, or were an effective addition to another physical therapy intervention (e.g. manual therapy or exercise) were the main comparisons of interest. Main outcomes of interest were overall pain, function, pain on motion, patient-reported global assessment of treatment success, quality of life and the number of participants experiencing adverse events. Most trials (n = 43) included participants with rotator cuff disease without calcification (four trials included people with calcific tendinitis). Sixteen (34%) trials investigated the effect of an electrotherapy modality delivered in isolation. Only 23% were rated at low risk of allocation bias, and 49% were rated at low risk of both performance and detection bias (for self-reported outcomes). The trials were heterogeneous in terms of population, intervention and comparator, so none of the data could be combined in a meta-analysis. Authors were uncertain whether transcutaneous electrical nerve stimulation (TENS) was more or less effective than glucocorticoid injection with respect to pain, function, global treatment success and active range of motion because of the very low quality evidence from a single trial. Authors concluded that uncertainty exists as to whether TENS is superior to placebo, and whether any electrotherapy modality provides benefits over other active interventions (e.g. glucocorticoid injection) because of the very low quality of the evidence. Further trials of electrotherapy modalities for rotator cuff disease should be based upon a strong rationale and consideration of whether or not they would alter the conclusions of this review.

In an article by Vance et al. (2014) titled "Using TENS for pain control: the state of the evidence," Transcutaneous electrical nerve stimulation (TENS) is described as a nonpharmacological intervention that activates a complex neuronal network to reduce pain by activating descending inhibitory systems in the central nervous system to reduce hyperalgesia. Within the article, authors describe the current mechanisms of TENS reduction on analgesia, which is thought to be more complex than previously described. More specifically, TENS activates a complex neuronal network to result in a reduction in pain. At frequencies and intensities used clinically, TENS activates large diameter afferent fibers. This afferent input is sent to the central nervous system to activate descending inhibitory systems to reduce hyperalgesia. Specifically, blockade of neuronal activity in the periaqueductal gray (PAG), rostral ventromedial medulla (RVM) and spinal cord inhibit the analgesic effects of TENS showing that TENS analgesia is maintained through these pathways. In parallel, studies in people with fibromyalgia show that TENS can restore central pain modulation, a measure of central inhibition. Therefore, TENS appears to reduce hyperalgesia through both peripheral and central mechanisms. Authors do report that the evidence for TENS efficacy is conflicting. Sluka et al. (2013) suggests that certain factors should be considered when evaluating the research. These include dosing of TENS, negative interactions with long-term opioid use, the population and outcome assessed, timing of outcome measurement, and comparison groups. Population-specific systemic reviews and meta-analyses are emerging, indicating both high frequency (HF) and low frequency (LF) TENS being shown to provide analgesia, specifically when applied at a strong, non-painful intensity. They conclude that additional research is necessary to determine if TENS has effects specific to mechanical stimuli and/or beyond reduction of pain and will improve activity levels, function and quality of life. These authors are considered experts in the area of TENS research and they offer these interesting practice points:

- High frequency (HF) and low frequency (LF) transcutaneous electrical nerve stimulation (TENS) activate different opioid receptors. Both applications have been shown to provide analgesia specifically when applied at a strong, non-painful intensity. HF TENS may be more effective for people taking opioids.
- Effective analgesia for chronic pain conditions may be limited by the development of tolerance to TENS if repeated application of either LF or HF TENS at the same frequency and intensity is used daily (i.e., same dose). Strategies to prolong analgesia may include varying these parameters.
- Targeting the use of TENS during movement or activity may be most beneficial.
- TENS may be effective in restoration of central pain modulation, a measure of central inhibition.
- A clearer picture of TENS effectiveness will emerge as trials with attention to optimal dosing and appropriate outcome measures increase in numbers.

Gibson et al. (2019) provided an overview of evidence from Cochrane Reviews of the effectiveness of TENS to reduce pain in adults with chronic pain (excluding headache or migraine). They included nine reviews investigating TENS use in people with defined chronic pain or in people with chronic conditions associated with ongoing pain. The evidence reported within each review was consistently rated as very low quality. since we

would predict these different comparisons may be estimating different true effects. Authors found the methodological quality of the reviews was good, but quality of the evidence within them was very low. They were therefore unable to conclude with any confidence that, in people with chronic pain, TENS is harmful, or beneficial for pain control, disability, health-related quality of life, use of pain-relieving medicines, or global impression of change. Pietrosimone et al. (2020) aimed to determine the effect of TENS + therapeutic exercise (TE) on patient-reported function, quadriceps strength, and voluntary activation, as well as physical performance compared with sham TENS + TE (Sham) and TE alone in individuals with symptomatic knee OA and quadriceps voluntary activation failure (QVAF). Ninety individuals participated in a double-blinded randomized controlled trial. Everyone received 10 standardized TE sessions of physical therapy. TENS + TE and Sham groups applied the respective devices during all TE sessions and throughout activities of daily living over 4 wk. Improvements in WOMAC subscales, quadriceps strength, and voluntary activation, 20-m walk times, chair-stand repetitions, and stair-climb time were found at post 1 and post 2 compared with baseline for all groups ($P < 0.05$). WOMAC Pain and Stiffness improved in the TENS + TE group compared with TE alone at post 1 ($P < 0.05$); yet, no other between-group differences were found. Authors concluded that TE effectively improved patient-reported function, quadriceps strength, and voluntary activation, as well as physical performance in individuals with symptomatic KOA and QVAF, but augmenting TE with TENS did not improve the benefits of TE.

A Best Practices for Chiropractic Management of Patients with Chronic Musculoskeletal Pain: A Clinical Practice Guideline authored by Hawk et al. (2020), for chronic low back pain, TENS or interferential current may be beneficial as part of a multimodal approach, at the beginning of treatment to assist the patient in becoming or remaining active. For chronic neck pain, they recommend TENS and interferential current in the same manner as for chronic low back pain.

Rapazo et al. (2021) investigated the effectiveness of electrical stimulation (ES) for neck pain (NP). Main results showed evidence of moderate quality that ES combined with other intervention significantly decreases the pain intensity compared to other intervention immediately post-treatment and at short-term follow-up; evidence of low quality showed significant effects of ES combined with other intervention in decreasing neck disability compared to other intervention immediately post-treatment; evidence of very-low quality that ES increased the pressure pain threshold compared to placebo immediately post-treatment and that ES + other intervention also increased the pressure pain threshold compared to other intervention at short-term follow-up. Authors concluded that ES combined with other intervention seems to be useful to relieve pain and to improve disability in people with NP, however, more studies are needed.

Dias et al. (2021) compared the immediate analgesic effect of transcutaneous nerve stimulation (TENS) and interferential current (IFC), with different combinations of parameters, in individuals with chronic low back pain (CLBP). 280 individuals with CLBP were included in the study, both genders, randomized in 8 groups. All individuals underwent a single application of TENS or IFC for 30min. The assessments were carried out prior to the intervention, as well as immediately after, with the following outcomes: pain intensity (Numeric Pain Rating Scale-NPRS), qualitative pain characteristics (McGill Pain Questionnaire-MPQ), and pressure pain threshold (PPT) by pressure algometry (PA) in 4 points of the low back region. Authors concluded that both TENS and IFC presented immediate analgesic effect in CLBP, with emphasis on the interferential current of 4 KHz modulated at 100Hz.

According to the National Institute for Health and Care Excellence (NICE) review (2021), they report the following for TENS:

- TENS versus sham TENS and usual care
 - Quality of life
 - Moderate quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and sham TENS at ≤ 3 months.
 - Quality of life Moderate to low quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and usual care at ≤ 3 months.
 - Pain reduction
 - Very low-quality evidence from 2 studies with 242 participants showed a clinically important difference for TENS compared to sham TENS at ≤ 3 months.
 - Moderate quality evidence from 1 study with 40 participants showed a clinically important difference for TENS at > 3 months compared to sham TENS.
 - Low quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and usual care at ≤ 3 months.

- Physical function
 - High quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and sham TENS at ≤ 3 months.
 - High quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and usual care at ≤ 3 months.
- Psychological distress
 - Moderate to low quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and sham TENS at ≤ 3 months.
 - Moderate to low quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and usual care at ≤ 3 months.
- Pain interference
 - Low quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and sham TENS at ≤ 3 months.
 - Low quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and usual care at ≤ 3 months.
- Pain self-efficacy
 - High quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and sham TENS at ≤ 3 months.
 - High quality evidence from 1 study with 202 participants showed no clinically important difference between TENS and usual care at ≤ 3 months.

Paley et al. (2021) critically appraised the characteristics and outcomes of systematic reviews evaluating the clinical efficacy of TENS for any type of acute and chronic pain in adults. Authors included 169 reviews consisting of eight overviews, seven hybrid reviews and 154 systematic reviews with 49 meta-analyses. Only three meta-analyses pooled sufficient data to have confidence in the effect size estimate (i.e., pooled analysis of >500 events). Lower pain intensity was found during TENS compared with control for chronic musculoskeletal pain and labour pain, and lower analgesic consumption was found post-surgery during TENS. The appraisal revealed repeated shortcomings in RCTs that have hindered confident judgements about efficacy, resulting in stagnation of evidence. Authors concluded that this appraisal reveals examples of meta-analyses with 'sufficient data' demonstrating benefit. There were no examples of meta-analyses with 'sufficient data' demonstrating no benefit. Therefore, they recommend that TENS should be considered as a treatment option.

Reichenbach et al. (2022) sought to determine the effectiveness of TENS at relieving pain and improving physical function as compared to placebo TENS, and to determine its safety, in patients with knee osteoarthritis. 220 participants with knee osteoarthritis were recruited between October 15, 2012, and October 15, 2014. Patients were randomized to 3 weeks of treatment with TENS (n = 108) or placebo TENS (n = 112). The primary endpoint was knee pain at the end of 3-weeks treatment assessed with the WOMAC pain subscale. Secondary outcome measures included WOMAC physical function subscale and safety outcomes. There was no difference between TENS and placebo TENS in WOMAC pain at the end of treatment, nor throughout the trial duration. Subgroup analyses did not indicate an interaction between patient/treatment characteristics and treatment effect on WOMAC pain at the end of treatment (P-interaction ≥ 0.22). The occurrence of adverse events was similar across groups, with 10.4% and 10.6% of patients reporting events in the TENS and placebo TENS groups, respectively (P = 0.95). No relevant differences were observed in secondary outcomes. Authors concluded that TENS does not improve knee osteoarthritis pain when compared to placebo TENS. Therapists should consider other potentially more effective treatment modalities to decrease knee osteoarthritis pain and facilitate strengthening and aerobic exercise. Wu et al. (2022) evaluated the effects of Transcutaneous Electric Nerve Stimulation (TENS) on pain, function, walking ability and stiffness in people with Knee osteoarthritis (KOA). Twenty-nine studies were found (1398 people, age range 54-85, 74% are female) and fourteen were included in this review. Intervention duration was divided as short term (immediately after intervention), medium term (<four weeks) and long term (\geq four weeks). Active TENS showed greater improvement in Visual Analogue Scale (VAS) than sham TENS. Combining TENS with other interventions produced superior outcomes compared with other interventions for VAS in all the terms. In the meanwhile, TENS combined with other interventions was superior to other interventions for the pain subgroup of Western Ontario and McMaster Universities Arthritis Index in the medium term and long term. TENS combined with other interventions was superior to other interventions for function in the medium term and long term. Authors concluded that TENS could significantly relieve pain, decrease dysfunction and improve walking ability in people with KOA, but it is not effective for stiffness.

Johnson et al. (2022) investigated the efficacy and safety of transcutaneous electrical nerve stimulation (TENS) for relief of pain in adults in a systematic review and meta-analysis. The review included 381 RCTs (24, 532 participants). Pain intensity was lower during or immediately after TENS compared with placebo (moderate-certainty evidence). Methodological (eg, sample size) and pain characteristics (eg, acute vs chronic, diagnosis) did not modify the effect. Pain intensity was lower during or immediately after TENS compared with pharmacological and non-pharmacological treatments used as part of standard of care (low-certainty evidence). Levels of evidence were downgraded because of small-sized trials contributing to imprecision in magnitude estimates. Data were limited for other outcomes including adverse events which were poorly reported, generally mild and not different to comparators. Authors concluded that there was moderate-certainty evidence that pain intensity is lower during or immediately after TENS compared with placebo and without serious adverse events.

Wu et al. (2022) evaluated the effects of Transcutaneous Electric Nerve Stimulation (TENS) on pain, function, walking ability and stiffness in people with Knee osteoarthritis (KOA). Twenty-nine studies were found (1398 people, age range 54-85, 74% are female) and fourteen were included in this review. Intervention duration was divided as short term (immediately after intervention), medium term (<four weeks) and long term (\geq four weeks). Active TENS showed greater improvement in Visual Analogue Scale (VAS) than sham TENS. Combining TENS with other interventions produced superior outcomes compared with other interventions for VAS in all the terms. In the meanwhile, TENS combined with other interventions was superior to other interventions for the pain subgroup of Western Ontario and McMaster Universities Arthritis Index in the medium term and long term. TENS combined with other interventions was superior to other interventions for function in the medium term and long term. Authors concluded that TENS could significantly relieve pain, decrease dysfunction and improve walking ability in people with KOA, but it is not effective for stiffness.

Beltran-Alacreu et al. (2022) determined if the use of PENS is more effective and should be recommended when compared to TENS for the reduction of musculoskeletal pain intensity. Nine RCTs were included in the qualitative analysis, with seven of them in the quantitative analysis ($n = 527$). The overall effect of PENS on pain was statistically but not clinically superior to TENS with a high level of heterogeneity. When only studies with a lower risk of bias ($n = 3$) were analyzed, the heterogeneity decreased, and no difference was observed between TENS and PENS with a moderate recommendation level according to GRADE. There were no data concerning adverse effects. There is low-quality of evidence for more pain intensity reduction with PENS, but the difference was not clinically significant. However, when only studies with low risk of bias are meta-analyzed, there is a moderate quality of evidence that there is no difference when TENS or PENS is applied for pain intensity.

Evans et al. (2022) summarized the reported efficacy of transcutaneous single nerve stimulators in management of migraine frequency and severity. Fourteen studies, which treated 995 patients, met inclusion criteria, including 7 randomized controlled trials and 7 uncontrolled clinical trials. Transcutaneous nerve stimulators reduced headache frequency in episodic migraines (2.81 fewer headache days per month, 95% CI 2.18-3.43, $I^2 = 21\%$) and chronic migraines (2.97 fewer headache days per month). Transcutaneous nerve stimulators reduced headache severity in episodic headaches (2.23 fewer pain scale points). Authors concluded that preventive use of transcutaneous nerve stimulators provided clinically significant reductions in headache frequency in individuals with chronic or episodic migraines. Individuals with episodic migraines also experienced a reduction in headache pain severity following preventive transcutaneous nerve stimulation.

Fertout et al. (2022) assessed the efficacy of transcutaneous electrical nerve stimulation (TENS) for the management of temporomandibular disorders (TMD) and to determine the indications and most appropriate application modalities in a systematic review. Fourteen articles were retained, corresponding to a total of 532 patients, among which, 285 had a TMD. Immediately after a TENS session, significant relief of pain (19.2% to 77%), significant functional improvement (mouth opening amplitude increased by between 8.7% and 19.46%), and reduced electromyographic activity of the anterior temporalis and masseter muscles were observed. However, studies comparing TENS to other physical medicine modalities (ultrasound and laser) reported equivalent results. Authors concluded that further randomized comparative clinical trials will be necessary to optimize the use of TENS (program, duration of sessions, duration of treatment) for different types of TMD.

Vance et al. (2022) addressed the continued uncertainty about the clinical efficacy of TENS to alleviate pain, despite years of research and note that this uncertainty is related to the quality of the clinical trials included in systematic reviews. This summary of the evidence includes only trials with pain as the primary outcome. In comparison with their 2014 review, there appears to be improvement in adverse events and parameter reporting. Importantly, stimulation intensity has been documented as critical to therapeutic success.

Examinations of the outcomes beyond resting pain, analgesic tolerance, and identification of TENS responders remain less studied areas of research. This literature review supports the conclusion that TENS may have efficacy for a variety of acute and chronic pain conditions, although the magnitude of the effect remains uncertain due to the low quality of existing literature. In order to provide information to individuals with pain and to clinicians treating those with pain, authors suggest that resources for research should target larger, high-quality clinical trials including an adequate TENS dose and adequate timing of the outcome and should monitor risks of bias. Systematic reviews and meta-analyses should focus only on areas with sufficiently strong clinical trials that will result in adequate sample size.

Davison et al. (2022) systematically reviewed and evaluated available literature examining the effectiveness of using electrical stimulation to promote clinical outcomes after hip fractures. They identified 432 records through database searching. Initial screening indicated 24 articles were appropriate for full-text review, and four articles met the inclusion criteria. In included studies, electrical stimulation (i.e. TENS) reduced pain, improved range of motion (ROM), and accelerated functional recovery immediately after hip fracture. Conflicting evidence existed when using neuromuscular electrical stimulation to improve muscle strength and other functional outcomes (e.g. mobility); however, nine experts advised that longer-term interventions might be necessary to achieve significant improvement in muscle strength. Authors concluded that available evidence, albeit limited, supports the early application of noninvasive electrical stimulation (e.g. TENS) for improving clinical outcomes (i.e. reducing pain, improving ROM, and accelerating functional recovery after hip fractures). They could not find conclusive evidence on the effectiveness of using electrical stimulation to improve muscle strength. This review establishes the need for future additional high-quality trials in this field.

Leemans et al. (2022) estimated the effects of musculoskeletal rehabilitation interventions on movement-evoked pain and to explore the assessment methods/protocols used to evaluate movement-evoked pain in adults with musculoskeletal pain. Meta-analysis was conducted for outcomes with homogeneous data from at least 2 trials. The mean change in movement-evoked pain was the primary outcome measure. Thirty-eight trials were included, and 60 different interventions were assessed. There was moderate-certainty evidence of a beneficial effect of exercise therapy compared to no treatment on movement-evoked pain in adults with musculoskeletal pain. There was low-certainty evidence of a beneficial effect of transcutaneous electrical nerve stimulation compared to no treatment. There was no benefit of transcutaneous electrical nerve stimulation when compared to sham transcutaneous electrical nerve stimulation.

Verville et al. (2023) evaluated benefits and harms of transcutaneous electrical nerve stimulation (TENS) for chronic primary low back pain (CPLBP) in adults to inform a World Health Organization (WHO) standard clinical guideline. Seventeen RCTs (adults, n = 1027; adults ≥ 60 years, n = 28) out of 2010 records and 89 full text RCTs screened were included. The evidence suggested that TENS resulted in a marginal reduction in pain compared to sham (9 RCTs) in the immediate term (2 weeks), and a reduction in pain catastrophizing in the short term (3 months) with TENS versus no intervention or interventions with TENS specific effects (1 RCT). For other outcomes, little or no difference was found between TENS and the comparison interventions. The certainty of the evidence for all outcomes was very low. Authors concluded that on very low certainty evidence, TENS resulted in brief and marginal reductions in pain (not deemed clinically important) and a short-term reduction in pain catastrophizing in adults with CPLBP, while little to no differences were found for other outcomes.

DeJesus et al. (2023) provided a systematic review of the literature to analyze the effects of transcutaneous electrical nerve stimulation (TENS) on analgesia on sensitization measures, in studies with chronic musculoskeletal pain and in studies with acute experimental pain. Among 22,252 manuscripts found, 58 studies were included in the systematic review and 35 in the meta-analysis. Thirty-four studies assessed pain intensity; 24 studies investigated hyperalgesia; temporal summation was only evaluated in 2 studies; and conditioned pain modulation was not observed in the included studies. Meta-analyses favored TENS, despite its limitations and heterogeneity. Primary hyperalgesia in studies with musculoskeletal pain presented a high level of evidence, while other outcomes presented moderate evidence in the studies that were included. It is not possible to infer results about both temporal summation and conditioned pain modulation. Moderate evidence suggests that TENS promotes analgesia by reducing both central and peripheral sensitization, as shown by the reduction in primary and secondary hyperalgesia, pain intensity at rest, and during movement in experimental acute pain and chronic musculoskeletal pain. Overall, both types of studies analyzed in this review presented meta-analyses favorable to the use of TENS (compared to placebo TENS), showing reductions in both primary and secondary hyperalgesia, as well as decreases in pain intensity at rest and in motion. Authors conclude that this article presents data from the literature on the effect of TENS through sensitization assessments in individuals

with chronic musculoskeletal pain, or acute experimental pain. These data contribute to knowledge about pain neuroscience research, using TENS technology.

Microcurrent Electrical Nerve Stimulation

There is insufficient evidence in the published peer-reviewed scientific literature to support the safety and effectiveness of MENS including frequency specific microcurrent (FSM). Studies include small patient populations and short-term follow-ups with conflicting outcomes and in some cases reported outcomes were no better than placebo (Rajpurohit et al., 2010; Zuim et al., 2006). More recently, microcurrent, using very small electrical devices contained within wound dressings, has been evaluated as a therapy to speed the closure of chronic wounds. However, research published to date has not produced findings that suggest this form of ES can accelerate wound closure (Houghton, 2014). Nair (2018) did not see some positive findings for wound healing, however more research is needed to confirm results. Iijima and Takahashi (2021) summarized the level of knowledge regarding the effects of microcurrent therapy (MCT) on musculoskeletal pain in adults. Randomized controlled trials (RCTs) investigating the effects of MCT on musculoskeletal pain were included. Additionally, non-RCTs were included to assess the adverse events. The primary outcomes were pain and adverse events related to MCT. A comprehensive assessment of 4 RCTs and 5 non-RCTs that met the inclusion criteria revealed that MCT significantly improved shoulder pain (1 study, 40 patients) and knee pain (1 study, 52 patients) compared with sham MCT without any severe adverse events. MCT has clinically significant benefits for knee pain. This study also revealed a clinically significant placebo response in treating knee pain. This evidence highlights the substantial effect of placebo response in clinical care. Authors concluded that the findings of this meta-analysis highlight the effect of placebo response in treating knee pain. MCT is a potential, core nonpharmacologic treatment option in clinical care with minimal adverse events and should be further investigated.

Gikaro et al. (2023) studied the effectiveness of electrophysical agents in fibromyalgia. The primary outcomes were pain, functional status, and mood. Fifty-four studies involving 3045 patients with fibromyalgia were eligible for qualitative synthesis and 47 (pain), 31 (functional status), and 26 (mood) for network meta-analysis. The network consistency model revealed that, when compared with true control, transcutaneous electrical nerve stimulation and microcurrent improved pain symptoms; repetitive transcranial magnetic stimulation improved patient functional status; and microcurrent, repetitive transcranial magnetic stimulation, and no treatment significantly improved mood after intervention. Surface under the cumulative ranking indicated that microcurrent was most likely to be the best for managing pain and mood; low-level laser therapy for pain and mood; and repetitive transcranial magnetic stimulation for improving functional status and mood. Authors concluded that this review found low to moderate quality evidence that microcurrent, laser therapy, and repetitive transcranial magnetic stimulation are the most effective electrophysical agents for improving at least one outcome in fibromyalgia.

H-WAVE®

There is insufficient evidence in the published peer reviewed scientific literature to support the safety and effectiveness of the H-WAVE® electrical stimulators. Blum et al. (2008) conducted a systematic review and meta-analysis of randomized and nonrandomized controlled trials to evaluate the safety and efficacy of H-WAVE® therapy. Five studies (n=6535) met inclusion criteria. H-WAVE® was shown to decrease pain across various chronic soft tissue inflammation and neuropathic pain conditions, decrease pain medication intake (n=2 studies) and increase functionality (n=2 studies). However, author-noted limitations of the studies included the heterogeneity of the studies, inconsistency of the effects (e.g., reduction in pain medication, functionality), data were obtained from cross-sectional studies, data were subjective in nature (i.e., there were no formal examination findings, test results and/or laboratory values), various outcome measures, potential selection bias of publications for this review, and due to a lack of reported data it was not possible to statistically evaluate the safety of the therapy. Williamson et al. (2021) systematically searched human clinical studies on H-Wave® device stimulation (HWDS) was conducted as well as a comprehensive review of articles articulating possible HWDS mechanisms of action. Studies unrelated to H-Wave were excluded. Multiple clinical studies have reported significant benefits for diabetic and non-specific neuropathic pain, where function also improved, and pain medication usage substantially dropped. Authors concluded that low- to moderate-quality HWDS studies have reported reduced pain, restored functionality, and lower medication use in a variety of disorders, although higher-quality research is needed to verify condition-specific applicability. HWDS has enough reasonable evidence to be considered as an adjunctive component of non-opioid multi-modal pain management, given its

excellent safety profile and relative low cost. It is important to consider that two authors have a conflict of interest as they are consultants for Electronic Waveform Lab Inc. and have an interest in a positive outcome.

Allen et al. (2023) compared the relative effects of various forms of electric stimulation (ES) on functional and pain outcomes. Authors report that varying forms of ES have markedly different technical parameters, applications, and indications, based on clinically meaningful impact on pain perception, function improvement, and medication reduction. Authors explain that there is limited quality evidence for most forms of ES, although there are several notable exceptions for treatment of specific indications. Neuromuscular electrical stimulation (NMES) has well-demonstrated beneficial effects for rehabilitation of selective spinal cord injured (SCI), post-stroke, and debilitated inpatients. Functional electrical stimulation (FES) has similarly shown effectiveness in rehabilitation of some stroke, SCI, and foot drop outpatients. H-Wave® device stimulation (HWDS) has moderate supportive evidence for treatment of acute and refractory chronic pain, consistently demonstrating improvements in function and pain measures across diverse populations. Interestingly, transcutaneous electrical nerve stimulation (TENS), the most widely used form of ES, demonstrated insignificant or very low levels of pain and functional improvement. Authors concluded that ten of 13 reviewed forms of ES have only limited quality evidence for clinically significant reduction of pain or improvement of function across different patient populations. NMES and FES have reasonably demonstrated effectiveness, albeit for specific clinical rehabilitation indications. HWDS was associated with the most clinically significant outcomes, in terms of functional improvement combined with reduction of pain and medication use. More rigorous long-term clinical trials are needed to further validate appropriate use and specific indications for most forms of ES. Limitations of this study include that data was collected by the device manufacturer where there is a potential conflict of interest.

Norwood et al. (2024) conducted a retrospective independent statistical analysis on Patient-Reported Outcome Measures (PROMs) data for users of H-Wave® device stimulation (HWDS) for chronic low back pain (cLBP) collected by the device manufacturer over a period of 4 years. Final surveys for 34,192 pain management patients were filtered for pain chronicity limited to 3-24 months and device use of 22-365 days, resulting in 11,503 patients with "all diagnoses"; this number was then reduced to 2711 patients with nonspecific cLBP, sprain, or strain. Reported pain was reduced by 3.12 points (0-10 pain scale), with significant ($\geq 20\%$) relief in 85.28%. Function/activities of daily living (ADL) improved in 96.36%, while improved work performance was reported in 81.61%. Medication use decreased or stopped in 64.41% and sleep improved in 59.76%. Over 96% reported having expectations met or exceeded, service satisfaction, and confidence in device use, while no adverse events were reported. Subgroup analyses found positive associations with longer duration of device use, home exercise participation, and working, whereas older age and longer pain chronicity resulted in reduced benefit. Similar analysis of the larger all-diagnoses cohort demonstrated near-equivalent positive outcomes. Authors concluded that outcomes directly reported by cLBP HWDS patients demonstrated profound positive effects on function and ADL, robust improvement in pain perception, and additional benefits like decreased medication use, better sleep, and improved work performance, representing compelling new evidence of treatment efficacy. Limitations of this study include that data was collected by the device manufacturer where there is a potential conflict of interest.

Threshold Electrical Stimulation (TES)

Dali et al. (2002) sought to determine whether a group of stable children with cerebral palsy would improve their motor skills after 12 months of TES. Two thirds received active and one third received inactive stimulators. Fifty seven of 82 outpatients who were able to walk at least with a walker, completed all 12 months of treatment. Results demonstrated that there was no significant difference between active and placebo treatment in any of the tested groups, nor combined. Authors concluded that TES in these patients did not have any significant clinical effect during the test period. Kerr et al. (2006) investigated the efficacy of NMES and TES in strengthening the quadriceps muscles of both legs in children with cerebral palsy (CP). Sixty children were randomized to one of the following groups: NMES (n=18), TES (n=20), or placebo (n=22). Thirty-four children walked unaided, 17 used posterior walkers, six used crutches, and the remaining three used sticks for mobility. Peak torque of the left and right quadriceps muscles, gross motor function, and impact of disability were assessed at baseline and end of treatment (16wks), and at a 6-week follow-up visit. No statistically significant difference was demonstrated between NMES or TES versus placebo for strength or function. Statistically significant differences were observed between NMES and TES versus placebo for impact of disability at the end of treatment, but only between TES and placebo at the 6-week follow-up. In conclusion, further evidence is

required to show whether NMES and/or TES may be useful as an adjunct to therapy in ambulatory children with diplegia who find resistive strengthening programmes difficult.

Interferential Current (IFC)

Studies for IFC are primarily in the form of case reports, case series and some randomized controlled trials with small patient populations, short-term treatment sessions and short-term follow-ups. Randomized controlled trials with large patient populations and long-term follow-ups comparing IFT to established treatment options are lacking. The California Technology Assessment Forum (2005) evaluated the literature on IFT for the treatment of musculoskeletal pain and concluded that this treatment modality has not been shown to be as beneficial as alternative treatments such as nonsteroidal anti-inflammatory drugs and exercise therapy. Although IFT was found to be a generally safe technique, it did not meet the CTAF technology assessment criteria for the treatment of musculoskeletal pain. Fuentes et al. (2010) conducted a systematic review and meta-analysis of randomized controlled trials (n=20) to evaluate the pain-reducing effectiveness of IFC in the management of musculoskeletal pain. Twenty studies met inclusion criteria. Seven studies assessed IFC for joint pain (e.g., osteoarthritis), nine for muscle pain (e.g., low back pain, neck pain), three for soft tissue shoulder pain (e.g., tendinitis) and one for postoperative pain. Three studies were considered to be of poor methodological quality, 14 of moderate quality and three of high quality. Methodological issues included small sample sizes, heterogeneity of patient population, inappropriate handling of withdrawals and dropouts, and lack of appropriate randomization, concealment of allocation and blinding of patients and assessors. Fourteen studies (n=1114) were used for meta-analysis. Only three studies reported adverse events (e.g., blisters, burns, bruising, swelling). The authors concluded that the analgesic effect that IFC is superior to that of the concomitant interventions was unknown; IFC alone was not significantly better than placebo or other therapy at discharge or follow-up; the heterogeneity across studies and methodological limitations prevented conclusive statements regarding analgesic efficacy; and the results should be viewed with caution due to the limited number of studies that used IFC as a monotherapy. The American College of Physicians and the American Pain Society Joint Clinical Practice Guideline for the Diagnosis and Treatment of LBP (Chou and Huffman 2007) concluded that there was not enough evidence to support the use of interferential therapy, TENS, traction, ultrasound, or short wave diathermy for acute or chronic LBP. These results were based on systematic reviews and randomized trials of one or more of the aforementioned therapies for treatment of acute or chronic LBP that reported pain outcomes, back specific function, general health status, work disability or patient satisfaction. In a review by Poitras and Brosseau (2008), they determined that due to limited studies of sufficient quality, no recommendations could be made for the use of ultrasound, interferential current, or electrical muscle stimulation for the treatment of chronic LBP. Facci et al. (2011) compared the effects of TENS and interferential current among patients with nonspecific chronic low back pain. One hundred and fifty patients were randomly divided into three groups: TENS (group 1), interferential current (group 2) and controls (group 3). The patients designated for electrotherapy received ten 30-minute sessions, while the control group remained untreated. All patients and controls were evaluated before and after treatment using a visual analog scale and the McGill Pain and Roland Morris questionnaires, and regarding their use of additional medications. Results showed no statistically significant difference between the TENS and interferential current groups. The only difference was found between these groups and the controls, with noted improvement in outcome measures for the treatment groups. According to the AHRQ publication on Non-Invasive Treatments for Low Back Pain (2016), insufficient evidence from four trials exists regarding the effectiveness of interferential therapy versus other interventions, or interferential therapy plus another intervention versus the other interventions alone for low back pain, due to methodological limitations and imprecision. According to the American College of Physician's Noninvasive Treatments for Acute, Subacute, and Chronic Low Back Pain clinical practice guideline (2017), evidence was insufficient to determine the effectiveness of electrical muscle stimulation and inferential therapy.

Rutjes et al. (2009) conducted a systematic review of randomized or quasi-randomized controlled trials of electrical stimulation, including IFT (n=4 studies), for the treatment of osteoarthritis of the knee. Due to the poor methodological and reporting quality of the studies, the effectiveness of IFT could not be confirmed. Zeng et al. (2015) investigated the efficacy of different electrical stimulation (ES) therapies in pain relief of patients with knee osteoarthritis (OA). 27 trials and six kinds of ES therapies, including high-frequency transcutaneous electrical nerve stimulation (h-TENS), low-frequency transcutaneous electrical nerve stimulation (l-TENS), neuromuscular electrical stimulation (NMES), interferential current (IFC), pulsed electrical stimulation (PES), and noninvasive interactive neurostimulation (NIN), were included. IFC was the only significantly effective treatment in terms of both pain intensity and change pain score at last follow-up time point when compared with the control group. Meanwhile, IFC showed the greatest probability of being the best option among the six

treatment methods in pain relief. However, the evidence of heterogeneity and the limitation in sample size of some studies could be a potential threat to the validity of results. Authors also state that although the recommendation level of the other ES therapies is either uncertain (h-TENS) or not appropriate (l-TENS, NMES, PES and NIN) for pain relief, it is likely that none of the interventions is dangerous. Almeida et al. (2018) investigated the effects of transcutaneous electrical nerve stimulation and interferential current on acute and chronic pain. Eight studies with a pooled sample of 825 patients were included. In general, both transcutaneous electrical nerve stimulation and interferential current improved pain and functional outcomes without a statistical difference between them. Authors concluded that transcutaneous electrical nerve stimulation and interferential current have similar effects on pain outcome. The low number of studies included in this meta-analysis indicates that new clinical trials are needed.

Kadi et al. (2019) evaluated IFS for treating pain after total knee arthroplasty surgery. A total of 113 individuals were randomized to IFS (n=57) or sham treatment (n=56). There were 98 individuals (87%) who completed the study. After 30 days, there was no significant difference between groups in pain assessed by a VAS, 0.278. Pain medication use (paracetamol) also did not differ significantly between groups after treatment and neither did outcome measures assessing range of motion or edema. In this study, IFS was not beneficial at improving outcomes after total knee arthroplasty. Hussein et al. (2022) aimed to analyze the recently available information regarding the efficacy of IFC in alleviating the pain of musculoskeletal origin. This review included 35 trials of variable methodological quality from which 19 trials were selected for the meta-analysis. In general, IFC alone versus placebo demonstrated a significant pain-relieving effect. On the other hand, IFC showed no significant difference when added to standard treatment compared to placebo plus standard treatment or standard treatment alone. Similarly, IFC showed no significant difference when compared to other single interventions (laser, TENS, cryotherapy). Authors concluded that IFC alone is better than placebo at discharge. However, the low number of studies raises suspicions about this conclusion. IFC alone or added to other interventions is not more effective than comparative treatments in relieving musculoskeletal pain. Rampazo et al. (2022) discussed the literature findings on the analgesic efficacy of IFC therapy. Authors concluded that according to the literature, IFC therapy shows significant analgesic effects in patients with neck pain, low back pain, knee osteoarthritis and post-operative knee pain. Most of the IFC parameters seem not to influence its analgesic effects. We encourage further studies to investigate the mechanism of action of IFC therapy.

Chen et al. (2022) conducted a systematic review and meta-analysis to assess the effectiveness of interferential current therapy (IFC) in patients with knee osteoarthritis. They included randomized controlled trials (RCTs) in which IFC was applied to knee osteoarthritis patients and the outcomes of pain scores or functional scales were assessed. Ten RCTs with 493 patients met the inclusion criteria. Nine RCTs were included in the meta-analysis. The IFC groups exhibited significant improvements relative to the control groups for short-term pain scores, long-term pain scores, and short-term Western Ontario and McMaster Universities Osteoarthritis Index scores. All included studies did not observe any obvious adverse effects of IFC. IFC can be recommended as a treatment for knee osteoarthritis because it improves short- and long-term pain and short-term function. However, large-scale and high-quality RCTs with longer follow-up are required to establish an appropriate standardized treatment.

Rampazo et al. (2023) investigated the effectiveness of IFC in patients with chronic non-specific low back pain. Thirteen RCTs were considered eligible for this systematic review (pooled n = 1367). Main results showed moderate-quality evidence and moderate effect sizes that IFC probably reduces pain intensity and disability compared to placebo immediately post-treatment, but not at intermediate-term follow-up. Low-quality evidence with small effect size showed that IFC may reduce pain intensity compared to TENS immediately post-treatment, but not for disability. There is very low-quality evidence that IFC combined with other interventions (massage or exercises) may not further reduce pain intensity and disability compared to the other interventions provided in isolation immediately post-treatment. Authors concluded that moderate-quality evidence shows that IFC is probably better than placebo for reducing pain intensity and disability immediately post-treatment in patients with chronic non-specific low back pain.

High Volt Galvanic Stimulation (HVGS)

The few studies identified in the literature addressing HVGS were mostly randomized clinical trials and case studies published before 1997 with small patient populations and short-term follow-up. Patient selection criteria were lacking. More recently, Snyder et al. (2010) systematically reviewed the basic-science literature regarding

the effects of high-voltage pulsed stimulation (HVPS) for edema control. Included studies investigated HVPS and its effect on acute edema formation and included outcome measures specific to edema. Eleven studies met the inclusion criteria. Studies were critiqued by electrical stimulation treatment parameters: mode of stimulation, polarity, frequency, duration of treatment, voltage, intensity, number of treatments, and overall time of treatments. According to Snyder et al., (2010), the available evidence indicates that HVPS administered using negative polarity, pulse frequency of 120 pulses/s, and intensity of 90% visual motor contraction may be effective at curbing edema formation. In addition, according to authors, evidence suggests that treatment should be administered in either four 30-min treatment sessions (30-min treatment, 30-min rest cycle for 4 h) or a single, continuous 180-min session to achieve the edema-suppressing effects. Often such treatment occurs in an athletic training room for college athletes and may not be feasible in an outpatient clinical setting. Authors suggest that findings supported by the basic science research provides a general list of treatment parameters that may successfully manage the formation of edema after acute injury in animal subjects. They believe this should facilitate further research related to HVPS and the effects on edema in humans. At this time, there is insufficient evidence in the published peer reviewed scientific literature to support the safety and efficacy of HVG/HVPS stimulation.

PENS and PNT

There is insufficient evidence in the published peer-reviewed literature to support the safety and effectiveness of PENS or PNT as a treatment option for chronic pain. Overall, studies have included small patient populations and short term follow-ups. For low back pain, most of the literature is of poor quality with all trials evaluating chronic low back pain. In a technology brief, Hayes (2017) investigated the effectiveness of PENS for the treatment of low back pain (LBP). Three randomized controlled trials (n=34 to 200) evaluated the efficacy and safety of PENS for chronic LBP (CLBP) in adults and one study evaluated PNT for subacute radiating LBP. Hayes rated the studies as very low-quality of evidence. There was no clinically significant improvement with the use of PENS. When compared with other therapies, PENS monotherapy was favored over treatment with PENS followed by TENS or TENS alone at one month; however, the difference was not maintained at two months. Another study reported no difference in outcomes with PENS vs. sham. There is insufficient evidence to support PENS for the treatment of LBP. Weiner et al. (2008) conducted a randomized controlled trial (n=200) to evaluate the efficacy of PENS in adults with chronic low back pain. Patients were randomized to either 1) PENS, 2) brief electrical stimulation to control for treatment expectance (control-PENS), 3) PENS plus general conditioning and aerobic exercise (GCAE) or to 4) control-PENS plus GCAE. Treatment was delivered twice a week for six weeks to the 50 participants in each group. All groups reported significantly reduced pain (McGill Pain Questionnaire short form) and disability and improved gait velocity, which was sustained at six months. Significantly fewer fear avoidance beliefs were reported in the CGAE group compared to the non-CGAE group. Comparable reduced pain and function were reported by the PENS and control-PENS group, whether delivered for five minutes or 30 minutes. Thus, the exact dose of electrical stimulation needed for analgesia could not be determined. PENS and GCAE were more effective than PENS alone in reducing fear avoidance beliefs, but not in reducing pain or in improving physical function. There was a statistically significant improvement in chair rise time in the control-PENS plus CGAE compared to control-PENS alone. The overall drop-out rate was 8%. In the Agency for Healthcare Research and Quality (AHRQ) publication "Noninvasive Treatments for Low Back Pain" by Chou et al. (2016), the two studies on PENS that were of fair quality contradicted one another, as one found that PENS plus exercise was superior to sham plus exercise, while the other did not. Some studies looked at LBP with radicular signs while others did not or were unclear. Overall, the literature doesn't support PENS for treatment of chronic low back pain without radicular symptoms. There was insufficient evidence to determine effects of PENS versus sham, PENS plus exercise versus exercise alone, or PENS versus other interventions (TENS), due to methodological limitations and imprecision. Harms were poorly reported in trials of PENS.

Kang et al. (2007) conducted a single-blinded, randomized study of 63 patients with knee pain secondary to osteoarthritis. Twenty-eight patients were randomly assigned to the sham group and 35 to the live treatment group. The study investigated the efficacy of PNT in reducing knee pain and medication consumption during the first week following treatment. Pain levels were rated on a 100-mm visual analog pain scale. The live group had greater efficacy than the sham group in all time periods; however, only in the immediate post-treatment period did it reach statistical significance (p=0.0361). The overall median pain intensity difference over all periods was 14.5 for the live group and 6.5 for the sham group and reached statistical significance. At one week follow-up, the live group reported significantly less medication use than the sham group. Plaza-Manzano et al. (2020) evaluated the effects of percutaneous electrical stimulation (PENS) alone or as an adjunct with other interventions on pain and related disability in musculoskeletal pain conditions. Sixteen studies were included and included heterogeneous musculoskeletal conditions with short- or midterm follow-ups. The risk of bias was

generally low; but the heterogeneity of the results downgraded the level of evidence. Authors concluded that there is low level of evidence suggesting the effects of PENS alone or in combination for pain, but not related disability, in musculoskeletal pain.

Beltran-Alacreu et al. (2022) aimed to determine if the use of PENS was more effective and should be recommended when compared to TENS for the reduction of musculoskeletal pain intensity. Studies published until 31/12/2020, comparing the effectiveness of PENS and TENS, were considered. The main outcome was pain assessed with a visual analog scale or numerical pain rating scale. Nine RCTs were included in the qualitative analysis, with seven of them in the quantitative analysis (n = 527). The overall effect of PENS on pain was statistically but not clinically superior to TENS with a high level of heterogeneity. When only studies with a lower risk of bias (n = 3) were analyzed, no difference was observed between TENS and PENS with a moderate recommendation level according to GRADE. There were no data concerning adverse effects. There was low-quality of evidence for more pain intensity reduction with PENS, but the difference was not clinically significant. However, when only studies with low risk of bias are meta-analyzed, there was a moderate quality of evidence that there is no difference when TENS or PENS is applied for pain intensity. According to National Institute for Health and Care Excellence (NICE), regarding PENS:

- PENS versus sham PENS
 - Quality of life
 - Low quality evidence from 1 study with 89 participants showed a clinically important benefit of PENS compared to sham PENS at ≤3 months.
 - Very low to low quality evidence from 1 study with 24 participants showed a clinically important benefit of PENS compared to usual care at ≤3 months.
 - Pain reduction
 - Low quality evidence from 1 study with 89 participants showed a clinically important benefit of PENS compared to sham PENS at ≤3 months.
 - Low quality evidence from 1 study with 24 participants showed a clinically important benefit of PENS compared to usual care at ≤3 months.

NMES and FES

Orthopedic Conditions

Electric stimulated muscle contraction/neuromuscular electric stimulation (NMES) has been found to enhance muscle function post surgically. Patients who have received an ACL reconstruction have demonstrated accelerated recovery and greater muscle function when NMES is used in combination with exercise; however the impact on functional outcomes is inconsistent (Cameron, 2017). Similar results were noted with knee OA patients and for other inflammatory conditions of the knee. Most research studied the use of NMES on the quadriceps muscle, however clinically NMES may be used for other joints and muscle groups (Cameron, 2017). NMES has been shown to be part of an effective rehabilitative regimen for patients following ligament/knee surgery. It may help prevent muscle atrophy associated with knee immobilization, may enable patients to ambulate sooner, and may reduce the use of pain medication as well as length of hospital stay (Arvidsson, 1986; Lake, 1992; Gotlin et al, 1994; Snyder-Mackler et al, 1991 and 1995). Bax et al (2005) systematically reviewed the available evidence for the use of NMES in increasing strength of the quadriceps femoris. The authors concluded that limited evidence suggests that NMES can improve strength in comparison with no exercise, but volitional exercises appear more effective in most situations. The authors' cautious conclusions reflect the general poor quality of the included studies. It is also important to understand that at the time NMES is used, it is to re-education the neuromuscular system and engage more motor units with muscle contraction. Given this, the mechanism of strength increase is likely due to improved neuromuscular action vs. a true strength increase of the muscle.

Monaghan et al. (2010) completed a Cochrane review regarding the effectiveness of NMES as a means of increasing quadriceps strength in patients before and after total knee replacement. Only two studies were identified for inclusion in the review. No significant differences were reported in either study for maximum voluntary isometric torque or endurance between the NMES group and the control group but significantly better quadriceps muscle activation was reported in the exercise and neuromuscular stimulation group compared with the exercise group alone in the second study. This difference was significant at the mid training (six week) time point but not at the twelfth week post training time point. Both studies carried a high risk of bias. Mean values were not given for strength, endurance, cross sectional area or quality of life. Pain outcomes, patient satisfaction or adverse effects were not reported in either study. The results were presented as percentage improvements from baseline and the number of subjects in each group was unclear. Authors concluded that the studies found

in this review do not permit any conclusions to be made about the application of neuromuscular stimulation for the purposes of quadriceps strengthening before or after total knee replacement. At that time the evidence for the use of neuromuscular stimulation for the purposes of quadriceps strengthening in this patient group is unclear.

Kim et al. (2010) performed a systematic review of RCTs assessing the effects of NMES on quadriceps strength, functional performance, and self-reported function after ACL reconstruction. Eight randomized controlled trials were included. Authors concluded that NMES combined with exercise may be more effective in improving quadriceps strength than exercise alone, whereas its effect on functional performance and patient-oriented outcomes is inconclusive. Inconsistencies were noted in the NMES parameters and application of NMES. Imoto et al. (2011) systematically evaluated the effectiveness of electrical stimulation on rehabilitation after ligament and meniscal injuries. Seventeen studies evaluating ES after anterior cruciate ligament reconstruction and two studies evaluating ES after meniscectomy were included. There was a statistically significant improvement in quadriceps strength through ES and in functional outcomes six to eight weeks after surgical reconstruction of the anterior cruciate ligament. Authors concluded that there is evidence that ES coupled with conventional rehabilitation exercises may be effective in improving muscle strength and function two months after surgery. Maddocks et al. (2013) evaluated the effectiveness of NMES for improving muscle strength in adults with advanced disease and to examine the acceptability and safety of NMES, and changes in muscle function (strength or endurance), muscle mass, exercise capacity, breathlessness and health-related quality of life. They included randomized controlled trials (RCTs) in adults with advanced chronic obstructive pulmonary disease (COPD), chronic heart failure, cancer or human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) comparing a program of NMES as a sole or adjunct intervention to no treatment, placebo NMES or an active control. Eleven studies involving a total of 218 participants met the inclusion criteria across COPD, chronic heart failure and thoracic cancer. Authors concluded NMES appears an effective means of improving muscle weakness in adults with progressive diseases such as COPD, chronic heart failure and cancer. Further research is needed to confirm findings and determine most effective parameters.

Bemner et al. (2016) completed a critically appraised topic on the effectiveness of neuromuscular electrical stimulation in improving voluntary activation of the quadriceps. Four randomized controlled trials (RCTs) met the inclusion criteria and were included. Of the included studies, one reported statistically significant improvements in quadriceps voluntary activation in the intervention group relative to a comparison group, but the statistical significance was not true for another study consisting of the same sample of participants with a different follow-up period. One study reported a trend in the NMES group, but the between group differences were not statistically significant in three of the four RCTs. Current evidence does not support the use of NMES for the purpose of enhancing quadriceps voluntary activation in patients with orthopedic knee conditions. There is level B evidence that the use of NMES alone, or in conjunction with therapeutic exercise, does not enhance quadriceps voluntary activation in patients with orthopedic knee conditions (e.g., anterior cruciate ligament injuries, osteoarthritis, total knee arthroplasty).

Jones et al. (2016) updated a Cochrane Database review on the effectiveness of neuromuscular electrical stimulation for quadriceps muscle weakness in adults with advanced disease. Programs of NMES appear to be acceptable to patients and have led to improvements in muscle function, exercise capacity, and quality of life. However, estimates regarding the effectiveness of NMES based on individual studies lack power and precision. Randomized controlled trials in adults with advanced chronic respiratory disease, chronic heart failure, cancer, or HIV/AIDS comparing a program of NMES as a sole or adjunct intervention to no treatment placebo NMES, or an active control were included. Eighteen studies (20 reports) involving a total of 933 participants with COPD, chronic respiratory disease, chronic heart failure, and/or thoracic cancer met the inclusion criteria for this update, an additional seven studies since the previous version of this review. All but one study that compared NMES to resistance training compared a program of NMES to no treatment or placebo NMES. Most studies were conducted in a single center and had a risk of bias arising from a lack of participant or assessor blinding and small study size. The quality of the evidence using GRADE comparing NMES to control was low for quadriceps muscle strength, moderate for occurrence of adverse events, and very low to low for all other secondary outcomes. The included studies reported no serious adverse events and a low incidence of muscle soreness following NMES. NMES led to a statistically significant improvement in quadriceps muscle strength. An increase in muscle mass was also observed following NMES, though the observable effect appeared dependent on the assessment modality used. Across tests of exercise performance, mean differences compared to control were statistically significant for the 6-minute walk, but not for the incremental shuttle walk, endurance shuttle

walk, or for cardiopulmonary exercise testing with cycle ergometry. Authors concluded that NMES may be an effective treatment for muscle weakness in adults with advanced progressive disease, and could be considered as an exercise treatment for use within rehabilitation programs. Further research is very likely to have an important impact on the confidence in the estimate of effect and may change the estimate. Further research to understand the role of NMES as a component of, and in relation to, existing rehabilitation approaches is needed.

Gatewood et al. (2017) aimed to investigate the efficacy of device modalities used following arthroscopic knee surgery. Outcome measures included: muscle strength, range of motion, swelling, blood loss, pain relief, narcotic use, knee function evaluation and scores, patient satisfaction and length of hospital stay. Twenty-five studies were included in this systematic review, nineteen of which found a significant difference in outcomes. Authors concluded that NMES improve quadriceps strength and overall knee functional outcomes following knee surgery. Yue et al. (2018) assessed the evidence relative to the comparative effectiveness of neuromuscular electrical stimulation (NMES), transcutaneous electrical nerve stimulation (TENS), and electroacupuncture (EA) for improving patient rehabilitation following total knee arthroplasty (TKA). Data were analyzed from 17 randomized controlled trials involving 1285 procedures: 8 NMES studies (608 procedures), 7 TENS studies (560 procedures), and 2 EA studies (117 procedures). Qualitative analysis suggested that NMES was associated with higher quadriceps strength and functional recovery after TKA. Recovery benefits were maximal when the stimulation was performed once or twice a day for 4-6 weeks at an intensity of 100-120 mA and frequency of 30-100 Hz. The electrode should be sufficiently large (100-200 cm²) to reduce discomfort. TENS at an intensity of 15-40 mA and frequency of 70-150 Hz provided effective analgesia after TKA. EA at an intensity of 2 mA and frequency of 2 Hz may also provide postoperative analgesia of TKA. Authors concluded that as adjunct modalities, NMES and TENS can effectively improve rehabilitation after TKA without triggering significant intolerance, and maximal benefits depend on optimized parameters and intervention protocols. EA may be an effective adjunct modality for analgesia after TKA.

Novak et al. (2020) sought to provide guidelines for treatment parameters regarding electrical stimulation by investigating its efficacy in improving muscle strength and decreasing pain in patients with knee osteoarthritis. Nine randomized control trials were included in the review. First, the review confirmed that neuromuscular electrical stimulation is the most effective electrical stimulation treatment in the management of knee OA, and its efficiency is higher when combined with a strengthening program. Second, frequency of at least 50 Hz and no more than 75 Hz with a pulse duration between 200 and 400 μ s and a treatment duration of 20 mins is necessary for successful treatment. Peng et al. (2021) evaluated the effect of neuromuscular electrical stimulation (NMES) on quadriceps muscle strength, pain, and function outcomes following total knee arthroplasty (TKA). Nine RCTs that involved 691 patients were included in the meta-analysis. Pooled analysis showed that NMES improved quadriceps muscle strength after TKA within 1 month, 1-2 months, 3-4 months, and 12-13 months; pain between 1 and 2 months and between 3 and 6 months, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) between 3 and 4 months, timed up and go test (TUG) within 1 month, 3 minute walk test between 3 and 6 months, and SF-36 MCS between 3 and 6 months after TKA. Authors concluded that as a supplementary treatment after TKA, postoperative NMES could improve the short-term to long-term quadriceps muscle strength, mid-term pain, and mid-term function following TKA. However, many outcomes failed to achieve statistically meaningful changes and minimal clinically important difference (MCID), thus the clinical benefits remained to be confirmed.

Labanca et al. (2022) investigated whether adding NMES to TKA rehabilitation leads to a better quadriceps strength recovery in comparison with standardized rehabilitation. A second aim was to investigate which are the most commonly used NMES pulse settings and their effectiveness. Intervention studies evaluating the effects of a rehabilitation intervention based on quadriceps NMES in patients undergoing TKA were retrieved. Four studies met the inclusion criteria. Due to the limited number and the heterogeneity of the selected studies, it was not appropriate to carry out a meta-analysis. All the studies reported higher quadriceps strength in patients undergoing quadriceps NMES, particularly early after TKA. The addition of NMES or traditional strength training shows similar long-term effects. Short duration and low-intensity NMES have limited effects on quadriceps strength. Heterogeneity was found on NMES methodologies and pulse settings. In conclusion, NMES is effective for quadriceps strength recovery following TKA. NMES intensity and duration are essential for good NMES outcomes on quadriceps strength. Further studies on NMES methodologies, pulse features and settings are required to address the gaps in knowledge on NMES following TKA.

Culvenor et al. (2022) synthesized the evidence for effectiveness of rehabilitation interventions following ACL and/or meniscal tear on symptomatic, functional, clinical, psychosocial, quality of life and reinjury outcomes.

Authors included 22 systematic reviews (142 trials of mostly men) evaluating ACL-injured individuals and none evaluating isolated meniscal injuries. We synthesized data from 16 reviews evaluating 12 different interventions. Moderate-certainty evidence was observed for: (1) neuromuscular electrical stimulation to improve quadriceps strength; (2) open versus closed kinetic chain exercises to be similarly effective for quadriceps strength and self-reported function; (3) structured home-based versus structured in-person rehabilitation to be similarly effective for quadriceps and hamstring strength and self-reported function; and (4) postoperative knee bracing being ineffective for physical function and laxity. There was low-certainty evidence that: (1) preoperative exercise therapy improves self-reported and physical function postoperatively; (2) cryotherapy reduces pain and analgesic use; (3) psychological interventions improve anxiety/fear; and (4) whole body vibration improves quadriceps strength. There was very low-certainty evidence that: (1) protein-based supplements improve quadriceps size; (2) blood flow restriction training improves quadriceps size; (3) neuromuscular control exercises improve quadriceps and hamstring strength and self-reported function; and (4) continuous passive motion has no effect on range of motion. Authors concluded that the general level of evidence for rehabilitation after ACL or meniscal tear was low. Moderate-certainty evidence indicates that several rehabilitation types can improve quadriceps strength, while brace use has no effect on knee function/laxity.

According to a 2024 manuscript by Arhos et al., using NMES to augment quadriceps strength training in patients after knee injury and surgery is critical to improving functional outcomes and reducing the risk of reinjury. Setting up NMES with appropriate parameters and dosage to maximum tolerance at each visit is essential for ensuring patients are achieving the optimal treatment effect. With the use of NMES at an early postinjury timepoint, clinicians can attenuate the detrimental long-term effects of quadriceps weakness and inhibition in patients after knee injuries.

Carvalho et al. (2024) examined the effectiveness of neuromuscular electrical stimulation (NMES) added to the exercise or superimposed on voluntary contractions on patient-reported outcomes measures (PROMs) in people with knee osteoarthritis (KOA). Authors described the effects of intervention according to each PROMs (scores for Pain; Self-reported functional ability; Symptoms (hear clicking, swelling, catching, restricted range of motion, and stiffness); Daily living function; Sports function; and Quality of life) to examine the impact of NMES plus exercise on pain compared with exercise in people with knee OA. Six RCTs ($n = 367$) were included. In the qualitative synthesis, the systematic literature analysis showed improvement in pain after NMES plus exercise compared with exercise alone in three studies. The other three studies revealed no difference between groups in pain, although similar improvement after treatments. In the meta-analysis, NMES at a specific joint angle combined with exercise was not superior to exercise alone in pain management. There was no additional effect of NMES on exercise on self-reported functional ability, stiffness, and physical function compared with exercise alone. In only one study, symptoms, activities of daily living, sports function, and quality of life improved after whole-body electrostimulation combined with exercise. Authors concluded that this review found insufficient evidence for the effectiveness of NMES combined with exercise in treating knee OA considering PROMs. While pain relief was observed in some studies, more high-quality clinical trials are needed to support the use of NMES added to the exercise in clinical practice.

Moezy et al. (2024) assessed the effectiveness of NMES and exercise therapy, for improving pain, muscle weakness and function among patients with KOA. A randomized controlled trial was conducted with 75 female patients diagnosed with KOA. Participants were divided into three intervention groups: NMES-only, exercise therapy (Exs) alone, and a combination of NMES and exercise (NMES + Exs). All patients underwent 12 supervised treatment sessions, three times a week. Outcome measures included pain intensity measured by visual analog scale (VAS), knee flexion range of motion (FROM), thigh muscle girth (TG), thickness of the Vastus Medialis Oblique (VMO), timed up and go test (TUG), six-minute walk test (6MWT), and WOMAC scores. Statistical analyses (ANOVA and Kruskal-Wallis) methods were done to compare the amounts at the baseline, immediately after treatment and after 12 weeks. The NMES group exhibited a significant reduction in pain at the 12-week follow-up compared to the other groups. The NMES + Exs group showed better outcomes in terms of FROM, TG, and VMO thickness post-intervention and at the 12-week follow-up. Additionally, NMES was superior in improving TUG and 6MWT post-intervention and during the follow-up assessments. The NMES + Exs group achieved better WOMAC stiffness scores at both post-intervention and follow-up evaluations. Furthermore, at the 12-week follow-up, NMES + Exs group outperformed the others in WOMAC pain and function subscales ($p = 0.003$, $p = 0.017$, respectively), while the NMES group demonstrated better WOMAC total scores compared to the other groups. Authors concluded that the combination of NMES and exercise seems to be an efficient approach for managing KOA, as it enhances knee flexion range and TG, increases

VMO thickness, and improves WOMAC scores. On the other hand, NMES alone was found to be effective in improving the physical function of KOA patients.

Neurological Conditions

The main goal of stroke rehabilitation is to improve function to allow patients greater independence in their activities of daily living, resulting in an improvement in quality of life. Typical treatment techniques of stroke rehabilitation comprise various combination of range of motion (ROM) and muscle strengthening exercises, mobilization activities, and compensatory techniques. Other key therapies include neurophysiological and/or developmental based methods in which the treatment program incorporates neuromuscular re-education techniques. It is in these situations that FES is used for stroke rehabilitation. It has been utilized to manage contracture of joints, maintain ROM, facilitate voluntary motor control, and reduce spasticity. However, there is insufficient evidence that FES is effective as a rehabilitative tool for patients who suffered strokes. In particular, there are little data supporting the long-term effectiveness of this modality for stroke rehabilitation and other neurologic conditions. In a Cochrane review, Price and Pandyan (2000) ascertained the effectiveness of any form of surface electric stimulation in the prevention and/or treatment of pain around the shoulder at any time after stroke. These investigators concluded that the evidence from randomized controlled studies so far does not confirm or refute that ES around the shoulder after stroke influences reports of pain, but there do appear to be benefits for passive humeral lateral rotation. A possible mechanism is through the reduction of glenohumeral subluxation. The authors stated that further studies are needed. Van Peppen et al (2004) determined the evidence for physical therapy interventions aimed at improving functional outcome after stroke. 151 studies were included in this systematic review; 123 were randomized controlled trials (RCTs) and 28 controlled clinical trials (CCTs). Researchers reported that while strong evidence was found regarding use of NMES for glenohumeral subluxation, no or insufficient evidence in terms of functional outcome was found for FES and NMES aimed at improving dexterity or gait performance. Furthermore, in a review on therapeutic orthosis and electric stimulation for upper extremity hemiplegia after stroke, Aoyagi and Tsubahara (2004) stated that despite a number of studies suggesting the effectiveness of electrical stimulation for reducing shoulder subluxation or improving the function of wrist and finger extensors in the short term, the long term effectiveness after discontinuation as well as the motor recovery mechanism remains unclear. More research is needed to determine the evidence-based effectiveness of electrical stimulation for stroke survivors. Koyuncu et al. (2010) conducted a randomized controlled trial to evaluate FES for the treatment of 50 hemiplegic patients with shoulder subluxation and pain secondary to stroke. All patients received conventional rehabilitation and the study group also received FES stimulation to the supraspinatus and posterior deltoid muscles on the hemiplegic side, five times a day, one hour each for four weeks. Comparison of the resting AROM vs. PROM VAS value changes showed no significant difference between the groups. There was a significant difference between the two groups for the amount of change in shoulder subluxation in favor of the study group, indicating increased stability of the shoulder. Authors suggest that that applying FES treatment to the supraspinatus and posterior deltoid muscles in addition to conventional treatment when treating the subluxation in hemiplegic patients is more beneficial than conventional treatment by itself. Gu and Ran (2016) reviewed the evidence for the effect of functional electrical stimulation (FES) on shoulder subluxation, pain, upper arm motor function, daily function, and quality of life in patients with stroke when added to conventional therapy. The results of this meta-analysis showed a significant difference in shoulder subluxation between the FES group and the placebo group, only if FES was applied early after stroke. And a significant difference was observed posttreatment in the Fugl-Meyer Motor Assessment between the FES group and the placebo group. No effects were found on pain, upper arm motor function, daily function, and quality of life outcomes. Authors concluded that FES can be used to prevent or reduce shoulder subluxation early after stroke. However, findings did not support the efficacy of use of FES for pain reduction, improvement in arm strength, movement, functional use, daily function, or quality of life after stroke.

FES has been proposed for improving ambulation in patients with gait disorders such as drop foot, hemiplegia due to stroke, cerebral injury, or incomplete spinal cord injury. As an example, FES can be applied to the anterior tibialis muscle to assist in dorsiflexion during gait for patients with foot drop. Several small studies support the integration of FES for patients with spinal cord injury or who have sustained a stroke for various activities. As long as the peripheral nervous system is intact, any patients with central nervous system dysfunction may benefit from FES use. Effectiveness of FES may be likely due to the direct effect of muscle strengthening in addition to increased excitability of the motor neuron pool produced by the motor level electrical stimulation (Cameron, 2017).

The Parastep I System is a FES device proposed to promote ambulation. Several publications authored by the same group of researchers in 1997 evaluated this system relative to bone density, oxygen uptake and other physiologic measures. Jacobs et al. (1997) examined the task-nonspecific effects of functional neuromuscular stimulation (FNS)-assisted ambulation training on the physiological responses of persons with paraplegia to upper extremity exercise challenge. Twelve men and three women with motor- and sensory-complete thoracic-level SCI (T4-T11), mean age 28.2 +/- 6.8yrs (range, 21.1 to 45.2yrs), mean injury duration 3.7 +/- 3.0yrs (range, 7 to 8.8yrs). Thirty-two sessions of FNS ambulation training using a commercial six-channel system (Parastep 1). This system is composed of a microprocessor-controlled electrical stimulation unit and a walking frame outfitted with finger switches that allow the user to independently control the system and stimulation parameters. Outcome measures included peak and subpeak physiological responses to arm ergometry testing and upper extremity strength measures, obtained before and after the FNS ambulation training. Statistically significant increases in peak values for time to fatigue, peak power output, and peak VO₂ (all $p < .001$). Heart rate was significantly lower throughout subpeak levels of arm ergometry after the ambulation training ($p < .05$). Values of upper extremity strength were not significantly altered after training. Authors concluded that FNS ambulation by persons with SCI paraplegia results in task-nonspecific training adaptations. Central cardiovascular adaptations were indicated as the primary source of these beneficial alterations in exercise responses.

Additionally the group provided data on ambulation and standing. Klose et al. (1997) described performance parameters and effects on anthropometric measures in spinal cord injured subjects training with the Parastep 1 system. Thirteen men and 3 women with thoracic (T4-T11) motor-complete spinal cord injury: mean age, 28.8yrs; mean duration postinjury, 3.8yrs. Thirty-two functional neuromuscular stimulation ambulation training sessions using a commercially available system (Parastep-1). The hybrid system consists of a microprocessor-controlled stimulator and a modified walking frame with finger-operated switches that permit the user to control the stimulation parameters and activate the stepping. Distance walked, time spent standing and walking, pace, circumferential (shoulders, chest, abdomen, waist, hips, upper arm, thigh, and calf) and skinfold (chest, triceps, axilla, subscapular, supraillium, abdomen, and thigh) measurements, body weight, thigh cross-sectional area, and calculated lean tissue were outcome measures. Statistically significant changes in distance, time standing and walking, and pace were found. Increases in thigh and calf girth, thigh cross-sectional area, and calculated lean tissue, as well as a decrease in thigh skinfold measure, were all statistically significant. Authors concluded that the Parastep 1 system enables persons with thoracic-level spinal cord injuries to stand and ambulate short distances but with a high degree of performance variability across individuals. The factors that influence this variability have not been completely identified. Chaplin et al. (1996) also evaluated use of the device for ambulation. A total of 84 of 91 participants were able to take steps and of these, 31 were able to ambulate without assistance from another person. This was a case series study, which is uncontrolled and over lower methodologic quality.

Brissot et al. (2000) investigated the motor performances of use of Parastep I regarding energy expenditure and to evaluate its advantages and limitations, especially in social activities involving ambulation. This study was conducted in 15 thoracic spine-injured patients. The lesion was complete except in two patients. The gait ability and the functional use were judged clinically. Energy cost was evaluated from heart rate, peak oxygen uptake, and lactatemia. Thirteen patients completed the training (mean: 20 sessions) and achieved independent ambulation with a walker. The mean walking distance, without rest, was 52.8 +/- 69 m, and the mean speed was 0.15 +/- 0.14 m/sec. One patient with incomplete lesion, who had been nonambulatory for 8 months after the injury, became able to walk without functional electrical stimulation after five sessions. The follow-up was 40 +/- 11 months. Five patients pursued using functional electrical stimulation-assisted gait as a means of physical exercise but not for ambulation in social activities. The patients experienced marked psychological benefits, with positive changes in their way of life. In three subjects, a comparison of physiologic responses to exercise between a progressive arm ergometer test and a walking test with the Parastep (Sigmedics, Inc., Northfield, IL) at a speed of 0.1 m/sec was performed, showing that the heart rate, the peak oxygen uptake, and lactatemia during gait were close to those obtained at the end of the maximal test on the ergometer. Authors concluded that in spite of its ease of operation and good cosmetic acceptance, the Parastep approach has very limited applications for mobility in daily life, because of its modest performance associated with high metabolic cost and cardiovascular strain. However, it can be proposed as a resource to keep physical and psychological fitness in patients with spinal cord injury.

Morawietz and Moffat (2013) provided an overview of, and evaluate the current evidence on, locomotor training approaches for gait rehabilitation in individuals with incomplete spinal cord injury to identify the most effective

therapies. Only randomized controlled trials evaluating locomotor therapies after incomplete spinal cord injury in an adult population were included. Eight articles were included in this review. Five compared body-weight-supported treadmill training (BWSTT) or robotic-assisted BWSTT with conventional gait training in acute/subacute subjects (≤ 1 y postinjury). The remaining studies each compared 3 or 4 different locomotor interventions in chronic participants (> 1 y postinjury). Sample sizes were small, and study designs differed considerably impeding comparison. Only minor differences in outcomes measures were found between groups. Gait parameters improved slightly more after BWSTT and robotic gait training for acute participants. For chronic participants, improvements were greater after BWSTT with functional electrical stimulation and overground training with functional electrical stimulation/body-weight support compared with BWSTT with manual assistance, robotic gait training, or conventional physiotherapy. Authors concluded that evidence on the effectiveness of locomotor therapy is limited. All approaches show some potential for improvement of ambulatory function without superiority of 1 approach over another. More research on this topic is required.

Yan and colleagues (2005) evaluated whether FES was more effective in promoting motor recovery of the lower extremity and walking ability than standard rehabilitation alone. A total of 46 patients were assigned randomly to one of three groups receiving standard rehabilitation with FES or placebo stimulation or alone (control). They received treatment for 3 weeks, starting shortly after having the stroke. Outcome measurements included composite spasticity score, maximum isometric voluntary contraction of ankle dorsi-flexors and planter-flexors, and walking ability. After 3 weeks of treatment, those receiving FES plus standard rehabilitation did better on several measures of lower limb functioning compared to the other 2 groups. All patients in the FES group were able to walk after treatment, and 84.6 % of them returned home, in comparison with the placebo (53.3 %) and control (46.2 %) groups. However, these authors stated that generalization of the results from this study should be performed with caution because of subject selection criteria, which did not cover all stroke categories or subjects aged younger than 45 or older than 85 years. Randomized controlled trials and case series have primarily included small patient populations ($n=14-64$) with short-term follow-ups and heterogeneous treatment regimens and outcome measures (Esnour, et al., 2010; Nooijen, et al., 2009; Everaert, et al., 2010; Stein, et al., 2010; Barrett, et al., 2010; Postans, et al., 2004).

In a Cochrane review on electrostimulation for promoting recovery of movement or functional ability after stroke, Pomeroy et al (2006) sought to find out whether electrostimulation improved functional motor ability to do activities of daily living. Twenty-four trials were included in the review. Authors reported that electrostimulation improved some aspects of functional motor ability and some aspects of motor impairment and normality of movement over no treatment. For electrostimulation compared with placebo, this review found that electrostimulation improved an aspect of functional motor ability. For electrostimulation compared with conventional physical therapy, they found that electrostimulation improved an aspect of motor impairment. There were no statistically significant differences between electrostimulation and control treatment for all other outcomes. Authors caution that these results need to be interpreted with reference to the following: (1) the majority of analyses only contained one trial; (2) variation was found between included trials in time after stroke, level of functional deficit, and dose of electrostimulation; and (3) the possibility of selection and detection bias in the majority of included trials. Researchers conclude that data were insufficient to inform clinical use of electrostimulation for neuromuscular re-training. Research is needed to address specific questions about the type of electrostimulation that might be most effective, in what dose and at what time after stroke. Pereira et al. (2012) conducted a systematic review of randomized controlled trials to evaluate the effectiveness of FES in improving lower limb function in chronic stroke patients (mean time since stroke ≥ 6 mos). Seven RCTs including a pooled sample size of 231 participants met inclusion criteria. Analysis revealed a small but significant treatment effect in favor of FES on the 6 minute walk test. Authors conclude that FES may be an effective intervention in the chronic phase post stroke. However, its therapeutic value in improving lower extremity function and advantage over other gait training approaches remains uncertain.

Howlett et al. (2015) conducted a systematic review and meta-analysis to investigate the effectiveness of FES in improving activity following a stroke and to determine if FES is more effective than training alone. Eighteen randomized and non-randomized comparisons studies ($n=485$) met inclusion criteria. One study had three arms which was counted as a separate comparison group ($n=19$ comparisons). Because of incomplete data, all trials were not included in the meta-analysis. Only measures that reflected the International Classification of Function domain of activity performance were used in analyses. In some trials only one measure was available and in trials with more than one measure the reviewers chose the measure that most closely reflected the task being trained. Various outcome measures were used for lower-limb and upper-limb activity assessments. FES had a small to moderate effect on activity compared to no FES or placebo and had a moderate effect on activity

compared to training alone. However, due to the lack of available data, the authors were unable to determine if FES improved subject participation or if the benefits of FES are long-term. Author-noted limitations of the studies included: the lack of blinding of therapist and participants; the potential of small trial bias with 25 being the average number of participants per trial; and combining data for the meta-analysis that was collected using different outcome measures. There was also heterogeneity of subject characteristics including time after stroke, the limb that was trained, and the severity of stroke. In a randomized controlled study, Bethoux et al. (2015) compared changes in gait quality and function between FES and ankle-foot orthoses (AFOs) in individuals with foot drop post-stroke over a 12-month period. They completed a follow-up analysis on a multi-center unblinded RCT that had been conducted at 30 rehabilitation centers. Subjects continued to wear their randomized device for all home and community ambulation for another 6 months to final 12-month assessments. Primary outcomes were the 10 Meter Walk Test (10MWT) and device-related serious adverse event rate. Secondary outcome measures were the 6-Minute Walk Test (6MWT), GaitRite Functional Ambulation Profile, and the Modified Emory Functional Ambulation Profile (mEFAP). A total of 495 subjects were randomized, and 384 completed the 12-month follow-up. Both FES and AFO groups showed statistically and clinically significant improvement for 10MWT. No significant between-group differences were found. At 12 months, both FES and AFOs continue to demonstrate equivalent gains in gait speed. Results suggest that long-term FES use may lead to additional improvements in walking endurance and functional ambulation; further research is needed to confirm these findings.

Prenton et al. (2016) conducted a systematic review and meta-analysis of randomized controlled trials to compare the effects of FES and ankle foot orthoses (AFO) for foot drop of central neurological origin. Five synthesized randomized controlled trials (n=815) were included. Orthotics included customized and off-the-shelf AFOs. Meta-analysis of the outcomes of the 10-meter (m) walking speed (5 trials) (n=789) and functional exercise capacity (3 trials) (n=761) showed between-group comparable improvements which were not significant (p=0.79; p=0.31, respectively). There were no significant differences in meta-analysis for the 10-meter (m) walk test using data at short- (4 trials; n=771) and longer-term (3 trials; n=713) time-points for FES vs. AFO. There was a significant difference (p=0.04) in favor of the AFO for the medium-term 10-m test. Analyses revealed between-group comparable improvements in functional exercise capacity. The timed up-and-go test was reported in two studies and both reported between-group comparable improvements (p=0.812 and p=0.539). The mobility domain of the Stroke Impact Scale (SIS) was reported by three trials (n=701) and showed comparable between-group improvements (p=0.80). This meta-analysis indicates that AFOs have positive combined-orthotic effects on walking that are equivalent to FES for foot-drop caused by stroke regardless of length of use. The fact that the reviewed trials only included subjects age 18 years and older who had experienced a stroke prevents the results from being generalized to other populations. Other limitations of the analysis included the risk of bias in the studies and the heterogeneity of the AFO and FES devices used.

Stein et al. (2015) conducted a systematic review (n=29 studies; 940 subjects) and meta-analysis (n=14 studies; 383 subjects) of randomized controlled trials to evaluate the effect of NMES on spastic muscles after stroke. The primary outcome was spasticity, assessed by the Modified Ashworth Scale. The secondary outcome was range of motion (n=13 studies), assessed by a goniometer. Outcomes were conflicting. Some studies reported an improvement in spasticity (n=12 studies) and range of motion (n=13 studies) with NMES when used as an adjunctive therapy and some studies did not. Based on sensitivity analysis, no effects on spasticity and range of motion were seen on wrists and no effect on spasticity of elbows. The degree of spasticity and the criteria for spasticity assessment varied. Most studies showed evidence of bias. Other study limitations included: heterogeneity of outcome measures; time of treatment following stroke (1.5 months to more than 12 months); various degrees of chronic tissue changes; heterogeneity of conventional therapies used (e.g., active leg cycling, occupational therapy, stretching, Botulinum Toxin A), missing data; and heterogeneity of stimulation frequency and pulse duration. Large scale and high-quality randomized controlled trials are needed to establish the true efficacy of NMES in this patient population. Sharififar et al. (2018) aimed to determine the effect on motor function of extremities of adding an electrical sensory modality without motor recruitment before or with routine rehabilitation for hemiparesis after stroke by a comprehensive systematic review and meta-analysis. Authors concluded that electrical sensory input can contribute to routine rehabilitation to improve early post-stroke lower-extremity impairment and late motor function, with no change in spasticity. Prolonged periods of sensory stimulation such as TENS combined with activity can have beneficial effects on impairment and function after stroke.

Kristensen et al. (2021) sought to determine the effectiveness of neuromuscular electrical stimulation (NMES) toward improving activities of daily living (ADL) and functional motor ability post-stroke and to investigate the

influence of paresis severity and the timing of treatment initiation for the effectiveness of NMES. The inclusion criteria were randomized controlled trials exploring the effect of NMES toward improving ADL or functional motor ability in survivors of stroke. The search identified 6064 potential articles with 20 being included. Data from 428 and 659 participants (mean age, 62.4 years; 54% male) for outcomes of ADL and functional motor ability, respectively, were pooled in a random-effect meta-analysis. The analysis revealed a significant positive effect of NMES toward ADL, whereas no effect on functional motor ability was evident. Subgroup analyses showed that application of NMES in the subacute stage and in the upper extremity improved ADL, whereas a beneficial effect was observed for functional motor abilities in patients with severe paresis. Authors concluded that the results of the present meta-analysis are indicative of potential beneficial effects of NMES toward improving ADL post stroke, whereas the potential for improving functional motor ability appears less clear. Furthermore, subgroup analyses indicated that NMES application in the subacute stage and targeted at the upper extremity is efficacious for ADL rehabilitation and that functional motor abilities can be positively affected in patients with severe paresis.

Johnston et al. (2021) provided evidence to guide clinical decision-making for the use of either ankle-foot orthosis (AFO) or functional electrical stimulation (FES) as an intervention to improve body function and structure, activity, and participation as defined by the International Classification of Functioning, Disability and Health (ICF) for individuals with poststroke hemiplegia with decreased lower extremity motor control within this clinical practice guideline. A review of literature published through November 2019 was performed across 7 databases for all studies involving stroke and AFO or FES. Data extracted included time post-stroke, participant characteristics, device types, outcomes assessed, and intervention parameters. Outcomes were examined upon initial application and after training. Recommendations were determined on the basis of the strength of the evidence and the potential benefits, harm, risks, or costs of providing AFO or FES. One-hundred twenty-two meta-analyses, systematic reviews, randomized controlled trials, and cohort studies were included. Strong evidence exists that AFO and FES can each increase gait speed, mobility, and dynamic balance. Moderate evidence exists that AFO and FES increase quality of life, walking endurance, and muscle activation, and weak evidence exists for improving gait kinematics. AFO or FES should not be used to decrease plantarflexor spasticity. Studies that directly compare AFO and FES do not indicate overall superiority of one over the other. But evidence suggests that AFO may lead to more compensatory effects while FES may lead to more therapeutic effects. Due to the potential for gains at any phase post-stroke, the most appropriate device for an individual may change, and reassessments should be completed to ensure the device is meeting the individual's needs. It is important to note that this CPG cannot address the effects of one type of AFO over another for the majority of outcomes, as studies used a variety of AFO types and rarely differentiated effects. The recommendations also do not address the severity of hemiparesis, and most studies included participants with varied baseline ambulation ability. Authors summarize that this CPG suggests that AFO and FES both lead to improvements post-stroke. Future studies should examine timing of provision, device types, intervention duration and delivery, longer term follow-up, responders versus nonresponders, and individuals with greater impairments.

van der Scheer et al. (2021) summarized and appraise evidence on functional electrical stimulation (FES) cycling exercise after spinal cord injury (SCI), in order to inform the development of evidence-based clinical practice guidelines. Ninety-two studies met the eligibility criteria, comprising 999 adults with SCI representing all age, sex, time since injury, lesion level and lesion completeness strata. For muscle health (e.g., muscle mass, fiber type composition), significant improvements were found in 3 out of 4 Level 1-2 studies, and 27 out of 32 Level 3-4 studies (GRADE rating: 'High'). Although lacking Level 1-2 studies, significant improvements were also found in nearly all of 35 Level 3-4 studies on power output and aerobic fitness (e.g., peak power and oxygen uptake during an FES cycling test) (GRADE ratings: 'Low'). Authors concluded that the evidence indicates that FES cycling exercise improves lower-body muscle health of adults with SCI and may increase power output and aerobic fitness. Mahmoudi et al. (2021) systematically reviewed the effect of functional electrical stimulation (FES) on balance as compared to conventional therapy alone in post-stroke. Nine papers were included in this review. The total number of participants in this review study was 255. The age of participants ranged from 20 to 80 years. Stroke patients were in chronic phase (n = 5) and in subacute phase (n = 4). Various parameters, including the target muscles, the treatment time per session (20 min-2 h), number of treatment sessions (12-48) and FES frequency (25-40 Hz), were assessed. Among the studies, significant between-group improvement favoring FES in combination with conventional therapy was found on the Berg Balance Scale (n = 7) and Timed Up and Go Scale (n = 4) when compared to conventional therapy alone. There was no adverse effect reported by any studies. Authors concluded that FES was reported to be more beneficial in balance improvement among stroke patients when combined with conventional balance therapy. The studies

were limited by low-powered, small sample sizes ranging from 9 to 48, and lack of blinding, and reporting of missing data.

Electrical stimulation has been employed as a safe and effective therapy for improving arm function after stroke. Contralaterally controlled functional electrical stimulation (CCFES) is a unique method that has progressed from application in small feasibility studies to implementation in several randomized controlled trials. However, no meta-analysis has been conducted to summarize its efficacy. Loh et al. (2022) summarized the effect size of CCFES through measures of upper extremity motor recovery compared with that of neuromuscular electrical stimulation (NMES). Six RCTs were selected and 267 participants were included. The Upper Extremity Fugl-Meyer assessment (UEFMA) was included in all studies, the Box and Blocks test (BBT) and active range of motion (AROM) were included in 3 and 4 studies, respectively. The modified Barthel Index (mBI) and Arm Motor Abilities Test (AMAT) were included in 2 and 3 studies, respectively. The CCFES group demonstrated greater improvement than the NMES did in UEFMA, AROM, and mBI. However, the results for AMAT did not differ significantly. Authors concluded that contralaterally controlled functional electrical stimulation produced greater improvements in upper extremity hemiplegia in people with stroke than NMES did.

Ye et al. (2021) comprehensively and critically appraised the clinical benefits and engineering designs of functional electrical stimulation (FES)-rowing for management of individuals with spinal cord injury (SCI). Comparison of peak oxygen consumption ($\dot{V}O_{2peak}$) rates showed that $\dot{V}O_{2peak}$ during FES-rowing was significantly higher than arm-only exercise; FES-rowing training improved $\dot{V}O_{2peak}$ by 11.2% on average, with a 4.1% increase in $\dot{V}O_{2peak}$ per month of training. FES-rowing training reduced bone density loss with increased time postinjury. The rowing ergometer used in 2 studies provided motor assistance during rowing. Studies preferred manual stimulation control (n=20) over automatic (n=4). Authors concluded that results suggest FES-rowing is a viable exercise for individuals with SCI that can improve cardiovascular performance and reduce bone density loss. Further randomized controlled trials are needed to better understand the optimal set-up for FES-rowing that maximizes the rehabilitation outcomes. Karamian et al. (2022) summarized the various forms of electrical stimulation technology that exist and their applications for SCI. With regards to FES and NMES, authors report positive findings for improvement in muscle function and functional activities.

Chiu et al. (2014) conducted a systematic review to determine the effectiveness of FES vs. activity training alone in children with cerebral palsy. Five randomized controlled trials met inclusion criteria. The experimental group had to receive FES while performing an activity such as walking. The studies used outcome measures of activity that best reflected the activity used in the study. When continuous data (e.g., walking speed) were not available, ordinal data (e.g., Gross Motor Function Measurement) were used. A statistically significant between-group difference in activity in the FES groups was reported for the three studies that compared FES with no FES. Improvements were seen immediately after the intervention period, but long-term follow-up was not reported. The two studies investigating the effects of FES vs. activity training reported no significant differences between the groups. The results reported that FES is better than no FES but that FES is not more effective than activity training. Outcomes could not be pooled for meta-analysis due to incomplete data and the large difference in baseline scores. Due to the inability to conduct a meta-analysis, the authors stated that firm conclusions could not be made. Limitations of the studies included the heterogeneous patient populations and the variations in the frequency, intensity and duration of the interventions. Bosques et al. (2016) discussed the potential clinical applicability, while clarifying the differences in electrical stimulation (ES) treatments and the theory behind potential benefits to remediate functional impairments in youth in a comprehensive review. The synthesis of the literature suggests that improvements in various impairments may be possible with the integration of ES. Most studies were completed on children with cerebral palsy (CP). Electrical stimulation may improve muscle mass and strength, spasticity, passive range of motion (PROM), upper extremity function, walking speed, and positioning of the foot and ankle kinematics during walking. Sitting posture and static/dynamic sitting balance may be improved with ES to trunk musculature. Bone mineral density may be positively affected with the use of Functional Electrical Stimulation (FES) ergometry. ES may also be useful in the management of urinary tract dysfunction and chronic constipation. Among all reviewed studies, reports of direct adverse reactions to electrical stimulation were rare. In conclusion, NMES and FES appear to be safe and well tolerated in children with various disabilities. Authors suggested that physiatrists and other healthcare providers better understand the indications and parameters in order to utilize these tools effectively in the pediatric population.

Springer and Khamis (2017) completed a systematic review on the orthotic and therapeutic effects of functional electrical stimulation on gait in people with multiple sclerosis (MS). Twelve relevant studies were reviewed.

Eleven studies reported the effects of peroneal stimulation. Most found a significant orthotic effect (measured during stimulation), mainly on walking speed. Only three assessed the therapeutic effect (carry-over), which was not significant. Authors concluded that the evidence suggests that FES has a positive orthotic effect on walking in patients with MS. Yet, more robust trials are needed to substantiate this finding. Therapeutic efficacy of FES was not demonstrated.

Ou et al. (2022) assessed the effects of neuromuscular electrical stimulation on the upper limbs of patients with cerebral palsy. Eight randomized controlled trials (N = 294) were included in the meta-analysis. Compared with traditional physical therapy, sensorimotor training and task-oriented training, constraint-induced movement therapy, dynamic bracing, and conventional robot-assisted therapy, neuromuscular electrical stimulation in combination with these therapies resulted in significantly greater functional scale scores, muscle strength of upper limbs, and spasticity of upper limbs but did not improve the wrist range of motion. In addition, the effect of neuromuscular electrical stimulation on functional scale scores remained after 3-mo follow-up. Authors concluded that neuromuscular electrical stimulation effectively improved hand function, muscle strength, and spasticity in patients with cerebral palsy.

Tenberg et al. (2023) investigated the comparative effectiveness of various exercise interventions of the upper limb for individuals with an acute or subacute stroke. The primary outcome was upper limb motor function, secondary outcomes were activities of daily living and social participation, both assessed at post-intervention and follow-up. Nonspecific/multimodal active upper limb therapy was the standard comparator. This review involved 145 randomized controlled trial on 6432 participants and 45 different treatment categories. The network meta-analysis analyzed 119 randomized controlled trials on 5553 participants and 41 different treatment categories. Electrical stimulation combined with task-specific training, high-volume constraint-induced movement therapy, and strength training were the most effective interventions. Authors concluded that electrical stimulation combined with task-specific training (low evidence), high-volume constraint-induced movement therapy (moderate evidence), and strength training (low evidence) were the most effective interventions in improving upper limb motor function in individuals with a stroke. As the results were sensitive against a high risk of bias, likewise, these interventions should receive more attention in research and practice. Due to the heterogeneous use, electrical stimulation in combination with task-specific training should be further investigated in well-designed studies alongside other successful interventions (eg, constraint-induced movement therapy).

Wu et al. (2023) analyzed and discussed the efficacy of various electrical stimulation therapy (EST) treatments in alleviating pain among MS patients. Ten RCTs containing 315 participants were included. The pooled data from 8 trials including 267 participants showed that the EST was superior in alleviating pain evaluated by the visual analog scale. In subgroup analysis, medium-term EST treatment showed the highest effect size compared to short-term and long-term treatment. However, no significant differences were found in terms of pain-related quality of life, depression, fatigue, and pain-related disability. No adverse events related to EST were reported. A high risk of bias was identified in three of the ten included studies. Authors concluded that EST is effective and safe for alleviating pain in MS, but it should be noted that limited sample sizes and methodological issues were present in the included studies. More robust assessment criteria and high-quality RCTs are required for patients with MS.

Hwang and Song (2023) summarized the rehabilitative effects of electrical stimulation therapy on gait performance in stroke patients. This review included randomized controlled trials (RCT) investigating the therapeutic effects of electrical stimulation in stroke patients throughout five databases. This review qualitatively synthesized 20 studies and quantitatively analyzed 11 RCTs. Functional electrical stimulation (FES) was the most commonly used electrical stimulation type to improve postural stability and gait performance in stroke patients. The clinical measurement tools commonly used in the three studies to assess the therapeutic effects of FES were Berg balance scale (BBS), 10-meter walk test (10MWT), 6-minute walk test (6mWT), and gait velocity. The BBS score and gait velocity had positive effects in the FES group compared with the control group, but the 10MWT and 6mWT showed the same effects between the two groups. The heterogeneity of BBS scores was also high. Authors concluded that the results of this review suggest that electrical stimulation shows little evidence of postural stability and gait performance in stroke patients, although some electrical stimulations showed positive effects on postural stability and gait performance.

Máté et al. (2023) examined the evidence regarding the potential of hybrid functional electrical stimulation (FES) cycling for improving cardiorespiratory fitness for people with a mobility disability related to a central nervous system (CNS) disorder. From a total of 280 articles, 13 were studies included. During acute bouts of exercise,

hybrid FES cycling was moderately more effective than arm crank exercise (ACE) in increasing $\dot{V}O_{2peak}$ from rest. There was a large effect on the increase of $\dot{V}O_{2peak}$ from rest for hybrid FES cycling compared with FES cycling. Longitudinal training with hybrid FES cycling showed a significant improvement in $\dot{V}O_{2peak}$ from pre to post intervention with a large, pooled effect size of 0.83. Authors concluded that hybrid FES cycling produced higher $\dot{V}O_{2peak}$ compared with ACE or FES cycling during acute bouts of exercise. Hybrid FES cycling can improve cardiorespiratory fitness in people with SCI. Additionally, there is emerging evidence that hybrid FES cycling might increase aerobic fitness in people with mobility disability related to CNS disorders.

Andreopoulou et al. (2023) conducted an umbrella review of systematic reviews on functional electrical stimulation (FES) to improve walking in adults with an upper motor neuron lesion. The methodological quality of the 24 eligible reviews (stroke, $n = 16$; spinal cord injury (SCI), $n = 5$; multiple sclerosis (MS); $n = 2$; mixed population, $n = 1$) ranged from critically low to high. Stroke reviews concluded that FES improved walking speed through an orthotic (immediate) effect and had a therapeutic benefit (i.e., over time) compared to usual care (low certainty evidence). There was low-to-moderate certainty evidence that FES was no better or worse than an Ankle Foot Orthosis regarding walking speed post 6 months. MS reviews concluded that FES had an orthotic but no therapeutic effect on walking. SCI reviews concluded that FES with or without treadmill training improved speed but combined with an orthosis was no better than orthosis alone. FES may improve quality of life and reduce falls in MS and stroke populations. Authors concluded that FES has orthotic and therapeutic benefits. Certainty of evidence was low-to-moderate, mostly due to high risk of bias, low sample sizes, and wide variation in outcome measures. Future trials must be of higher quality, use agreed outcome measures, including measures other than walking speed, and examine the effects of FES for adults with cerebral palsy, traumatic and acquired brain injury, and Parkinson's disease.

Ibitoye et al. (2023) examined the effectiveness of leg exercises on bone mineral density and muscle cross-sectional area based on their clinical efficacy in persons with SCI. The primary outcome targeted was the change in muscle mass/volume and bone mineral density as measured by CT, MRI and similar devices. Relevant studies indicated that persons with SCI that undertook FES- and frame-supported leg exercise exhibited better improvement in muscle and bone health preservation in comparison to those who were confined to frame-assisted leg exercise only. However, this observation is only valid for exercise initiated early (i.e., within 3 months after injury) and for ≥ 30 min/day for \geq thrice a week and for up to 24 months or as long as desired and/or tolerable. Consequently, apart from the positive psychological effects on the users, leg exercise may reduce fracture rate and its effectiveness may be improved if augmented with FES.

Zhu et al. (2022) summarized and analyzed the relationship between functional electrical stimulation treatment and gait parameter changes in children with cerebral palsy. Nine papers were included in the analysis, with a total of 282 children with cerebral palsy, including 142 patients in the functional electrical stimulation treatment group and 140 patients in the comfort treatment, general nursing, or other physical therapy. The results showed that functional electrical stimulation could increase the walking speed of children with cerebral palsy and increase the walking step length of children with cerebral palsy. Authors concluded that functional nerve stimulation treatment could increase the gait speed and step length of children with cerebral palsy, which could improve the walking of children with cerebral palsy. Furthermore, this study needs more research data to support our findings.

Dysphagia

Electrical stimulation (ES) has been examined for the treatment of dysphagia. However, there is currently insufficient evidence to support the effectiveness of ES in treating this condition. No peer-reviewed literature was found for DPNS specifically, but rather is limited to electrical stimulation, FES, or NMES. In a non-concurrent cohort study, Blumenfeld et al. (2006) assessed the effectiveness of ES in treating persons with dysphagia and aspiration. The charts of 40 consecutive subjects undergoing ES and 40 consecutive persons undergoing traditional dysphagia therapy (TDT) were reviewed. The swallow severity scale improved from 0.50 to 1.48 in the TDT group ($p < 0.05$) and from 0.28 to 3.23 in the ES group ($p < 0.001$). After adjusting for potential confounding factors, persons receiving ES did significantly better in regard to improvement in their swallowing function than persons receiving TDT ($p = 0.003$). The authors concluded that the findings suggested that dysphagia therapy with transcutaneous ES is superior to traditional dysphagia therapy alone in individuals in a long-term acute care facility. They also stated that confirmation of these findings with a prospective, placebo-controlled, randomized clinical trial is needed before a definitive determination regarding the effectiveness of ES dysphagia therapy can be made. Kiger et al. (2006) compared the outcomes using transcutaneous neuromuscular electrical stimulation (VitalStim[®] therapy) to outcomes using traditional swallowing therapy for deglutition disorders. A total of 22 patients had an initial and a follow-up video-

fluoroscopic swallowing study or fiberoptic endoscopic evaluation of swallowing and were divided into an experimental group that received VitalStim® treatments and a control group that received traditional swallowing therapy. Outcomes were analyzed for changes in oral and pharyngeal phase dysphagia severity, dietary consistency restrictions, and progression from non-oral to oral intake. Results of chi-square analysis showed no statistically significant difference in outcomes between the experimental and control groups.

Huckabee and Doeltgen (2007) reviewed NMES as an emerging modality in an attempt to advise the New Zealand medical community about the application of it as a treatment for pharyngeal swallowing impairment (dysphagia). Authors conclude that there are potential benefits of the use of this treatment but key concerns for patient safety and long term outcomes exist. Shaw et al. (2007) sought to evaluate the effectiveness of VitalStim® therapy in a heterogeneous group of dysphagic patients. They performed a retrospective analysis of 18 patients who received this therapy at an urban tertiary referral center. All patients underwent pre-therapy evaluation by speech-language pathologists, including modified barium swallow and/or functional endoscopic evaluation of swallowing and clinical evaluation of swallowing that included assessment of laryngeal elevation, diet tolerance, and swallowing delay, and were then assigned an overall dysphagia severity score. After therapy, all patients underwent the same assessments. Twelve of the 18 also underwent a functional swallowing telephone survey months (range, 1 to 21 months) after their therapy to assess whether the improvement was worthwhile and sustained. Eleven of the 18 patients (61%) demonstrated some improvement in their swallowing. Six of the 18 patients (33%) were improved enough to no longer require a feeding tube. However, of the 5 patients categorized as having "severe dysphagia" before therapy, only 2 showed any improvement, and these patients still required a feeding tube for adequate nutrition. Telephone surveys did confirm that those who improved with their therapy seemed to maintain their progress and that most patients were satisfied with their therapy. Authors concluded that VitalStim therapy seems to help those with mild to moderate dysphagia. However, the patients with the most severe dysphagia in the study did not gain independence from their feeding tubes but could potential help those with mild to moderate dysphagia. Carnaby-Mann and Crary (2007) examined the evidence on neuromuscular electrical stimulation for swallowing rehabilitation. A total of 81 studies were reviewed. Seven were accepted for analysis. A significant summary effect size was identified for the application of NMES for swallowing. Best-evidence synthesis showed indicative findings in favor of NMES for swallowing. The analysis revealed a small but significant summary effect size for NMES for swallowing. Because of the small number of studies and low methodological grading for these studies, caution should be taken in interpreting this finding. These results support the need for more rigorous research in this area. This is in agreement with the observation of Steel et al (2007) who noted that although ES approaches to the restoration and rehabilitation of swallowing is an exciting area of research which holds promise for future clinically relevant technology and/or therapy, implementation of ES in clinical swallowing rehabilitation settings still remains pre-mature.

Clark et al. (2009) systematically reviewed the literature examining the effects of NMES on swallowing and neural activation. The review was conducted as part of a series examining the effects of oral motor exercises (OMEs) on speech, swallowing, and neural activation. Out of 899 citations initially identified for the broad review of OMEs, 14 articles relating to NMES qualified for inclusion. Most of the studies (10/14) were considered exploratory research, and many had significant methodological limitations. Authors concluded that the review revealed that surface NMES to the neck has been most extensively studied with promising findings, yet high-quality controlled trials are needed to provide evidence of efficacy. Surface NMES to the palate, faucial pillars, and pharynx has been explored in Phase I research, but no evidence of efficacy is currently available. Intramuscular NMES has been investigated in a single Phase I exploratory study. Additional research is needed to document the effects of such protocols on swallowing performance. Christiaanse et al. (2011) compared the change in swallowing function in pediatric patients with dysphagia who received neuromuscular electrical stimulation (NMES) to a control group who received usual oral motor training and dietary manipulations without NMES. Children were classified into two groups based on the etiology of their dysphagia (primary vs. acquired). Only the treatment group who had acquired dysphagia improved more than the similar subgroup of control children. Authors concluded that NMES treatment of anterior neck muscles in a heterogeneous group of pediatric patients with dysphagia did not improve the swallow function more than that seen in patients who did not receive NMES treatment. However, there may be subgroups of children that will improve with NMES treatment. Geeganage et al. (2012) assessed the effectiveness of interventions for the treatment of dysphagia and nutritional and fluid supplementation in patients with acute and subacute stroke. Authors included 33 studies involving 6779 participants. Swallowing therapies included the following: acupuncture, drug therapy, neuromuscular electrical stimulation, pharyngeal electrical stimulation, physical stimulation (thermal, tactile), transcranial direct current stimulation, and transcranial magnetic stimulation. Authors conclude that there

remains insufficient data on the effect of swallowing therapy, feeding, and nutritional and fluid supplementation on functional outcome and death in dysphagic patients with acute or subacute stroke. Behavioural interventions and acupuncture reduced dysphagia, and pharyngeal electrical stimulation reduced pharyngeal transit time.

Tan et al. (2013) assessed the overall efficacy by comparing the two treatment protocols in a meta-analysis. Studies that compared the efficacy of treatment and clinical outcomes of NMES versus traditional treatment (TT) in dysphagia rehabilitation were assessed. Seven studies were eligible for inclusion, including 291 patients, 175 of whom received NMES and 116 of whom received TT. Of the seven studies, there were two randomized controlled trials, one multicentre randomized controlled trial and four clinical controlled trials. The change scores on the Swallowing Function Scale of patients with dysphagia treated with NMES were significantly higher compared with patients treated with TT. However, subgroup analysis according to etiology showed that there were no differences between NMES and TT in dysphagia post-stroke. No studies reported complications of NMES. Authors concluded that NMES is more effective for treatment of adult dysphagia patients of variable etiologies than TT. However, in patients with dysphagia post-stroke, the effectiveness was comparable. Miller et al (2014) performed a systematic review of the literature on the use of neuromuscular electrostimulation (NMES) in otorhinolaryngology that have been published in German or English. The search identified 180 studies. These were evaluated and relevant studies were included in the further evaluation. The authors concluded that the evidence collected to date is encouraging; particularly for the treatment of certain forms of dysphagia and laryngeal paresis. Terré and Mearin (2015) evaluated the effectiveness of neuromuscular electrical stimulation (NMES) treatment in patients with oropharyngeal dysphagia secondary to acquired brain injury. Twenty patients with neurological oropharyngeal dysphagia (14 stroke and six severe traumatic brain injury) were enrolled in a prospective randomized study, with patients and assessors blinded (to group allocation): 10 patients underwent NMES and conventional swallowing therapy and 10 patients underwent sham electrical stimulation (SES) and conventional swallowing therapy. Both groups completed 20 sessions. Feeding swallowing capacity was evaluated using the functional oral intake scale (FOIS). After treatment, the NMES group increased by 2.6 points (4.5 points) compared with only 1 point (3.1 points) for the SES group. At 3 months of follow-up, mean scores were 5.3 and 4.6 respectively; thus, both groups improved similarly. At that time point (3 months), tracheal aspiration persisted in six patients in each group. However, a significant improvement in relation to the bolus viscosity at which aspiration appeared was found in the NMES group versus the SES group. Also, a significant increase in pharyngeal amplitude contraction was observed at the end of treatment (1 month) in the NMES group compared with the SES group. Authors concluded that NMES significantly accelerated swallowing function improvement in patients with oropharyngeal dysphagia secondary to acquired brain injury. Chen et al. (2016) evaluated whether swallow treatment with neuromuscular electrical stimulation is superior to that without neuromuscular electrical stimulation, and whether neuromuscular electrical stimulation alone is superior to swallow therapy. Eight studies were identified. Authors concluded that swallow treatment with neuromuscular electrical stimulation seems to be more effective than that without neuromuscular electrical stimulation for post-stroke dysphagia in the short term considering the limited number of studies available. Evidence was insufficient to indicate that neuromuscular electrical stimulation alone was superior to swallow therapy. Alamer et al. (2020) summarized the latest best scientific evidence on the efficacy of neuromuscular electrical stimulation on swallowing function in dysphagic stroke patients. Evidence of overall quality was graded from moderate to high. Eleven RCTs involving 784 patients were analyzed. The primary outcome measures of this review were functional dysphagia scale (FDS) and standard swallowing assessment. This review found neuromuscular electrical stimulation (NMES) coupled with traditional swallowing therapy could be an optional intervention to improve swallowing function after stroke in rehabilitation department.

Liang et al. (2021) explored the clinical efficacy of VitalStim electrical stimulation combined with swallowing function training for patients with dysphagia following an acute stroke. Seventy-two patients with dysphagia following an acute stroke were admitted to our hospital and were further divided into two groups using prospective research methods. There were 36 cases in each group according to the random number table method. The control group received conventional medical treatment and swallowing function training while the experimental group received conventional medical treatment and VitalStim electrical stimulation combined with swallowing function training. The overall response rate of the experimental group (94.44%) was higher than that of the control group (77.78%), and the difference was statistically significant. Compared with before treatment, the upward and forward movement speeds of the hyoid bone, anterior movement speed, the grading score of the Kubota drinking water test, Caiteng's grading score, serum superoxide dismutase, 5-hydroxytryptamine, and norepinephrine levels, Fugl-Meyer Assessment score, and multiple quality of life scores of the two groups showed improvement after treatment. While the standard swallowing assessment score, serum malondialdehyde level, and National Institutes of Health Stroke Scale score decreased, the aforementioned

indices showed a significant improvement in the experimental group. Authors concluded that the results of this study indicate that VitalStim electrical stimulation combined with swallowing function is effective for treating dysphagia following an acute stroke. It can effectively improve swallowing, neurological, and limb motor functions, reduce complications, promote physical recovery, and improve overall quality of life of patients.

Propp et al. (2022) aimed to determine the effectiveness of neuromuscular electrical stimulation (NMES) for treatment of oropharyngeal dysphagia in children. Studies of children (≤ 18 years) diagnosed with oropharyngeal dysphagia using NMES in the throat/neck region were included. A meta-analysis was not conducted due to clinical heterogeneity in studies. Ten studies were included (5 RCTs, 4 case series, 1 cohort study; including 393 children, mean or median age below 7 years, including children with neurologic impairments). In all studies, swallowing function improved after NMES treatment. Eight of 10 studies reported on the child's feeding ability, and, with one exception, there was improvement in feeding ability. The studies demonstrated moderate to high risk of bias. Authors concluded that NMES treatment may be beneficial in improving swallowing function for children with dysphagia, however, given the quality of the studies, inadequate outcome reporting, and short follow-up duration, uncertainty remains. Well-designed RCTs are needed to establish its effectiveness before its adoption in clinical practice.

Miller et al. (2022) evaluated recent studies regarding a potential effectiveness of transcutaneous NMES applied to the anterior neck as a treatment for dysphagia. Eighteen studies were identified with varying patient groups, stimulation protocols, electrode placement and therapy settings. However, 16 studies have reported of beneficial outcomes in relation with NMES. It could generally be concluded that there is a considerable amount of level 2 studies which suggest that NMES is an effective treatment option, especially when combined with traditional dysphagia therapy for patients with dysphagia after stroke and patients with Parkinson's disease, or with different kinds of brain injuries. Further research is still necessary in order to clarify which stimulation protocols, parameters and therapy settings are most beneficial for certain patient groups and degrees of impairment.

Wang et al. (2024) evaluated the impact of NMES on dysphagia in stroke patients. Research outcomes included Swallowing Quality of Life (SWAL-QoL), Penetration-Aspiration Scale (PAS), Functional Oral Intake Scale (FOIS), Dysphagia Outcomes and Severity Scale (DOSS), the Repeat Salivary Swallowing Test (RSST), and Water Swallowing Test (WST). Nine randomized controlled trials (RCTs) and quasi-RCTs were included, and remarkable differences were found between patients treated with or without NMES in respect of FOIS scores, PAS scores, and SWAL-QoL scores. No significant difference was manifested in WST, RSST, and DOSS. Evidence suggests that NMES is more effective for post-stroke dysphagia patients than treatment without NMES.

Heart Conditions

Literature does not support the use of NMES for the treatment of heart failure. (Arena et al., 2010) conducted a systematic review of the literature to evaluate the evidence supporting NMES and inspiratory muscle training (IMT) for the treatment of systolic heart failure. Thirteen NMES studies met inclusion criteria, ten were randomized controlled trials. Although the studies reported improvement in aerobic capacity, peak oxygen uptake and strength and endurance of muscle groups, the studies were limited by patient population (i.e., mostly males), diverse NMES training protocols, variation in the type of muscle contraction elicited (i.e., titanic vs. twitch), the use of different muscle groups and different comparators. The percent improvement in peak oxygen uptake was consistently greater with conventional therapy (i.e., bicycle/treadmill). Sillen et al. (2009) conducted a systematic review of randomized controlled trials to analyze the role of NMES in strength, exercise capacity, and disease-specific health status in patients with congestive heart failure (n=9 studies) and chronic obstructive pulmonary disease (n=5 studies) with disabling dyspnea, fatigue, and exercise intolerance. The limited number of studies, heterogeneous patient populations and variability in NMES methodology prohibited the use of meta-analysis. Although some of the studies reported significant improvements with NMES compared to no exercise or usual care, outcomes, including adverse events, were conflicting. Additional studies are indicated to provide sufficient evidence to establish the clinical utility of NMES in this patient population.

Pelvic Floor Stimulation (electric or electromagnetic)

Stewart et al. (2017) assessed the effects of electrical stimulation with non-implanted devices, alone or in combination with other treatment, for managing stress urinary incontinence or stress-predominant mixed urinary incontinence in women. Eligible trials (n=56) included adult women with SUI or stress-predominant mixed urinary incontinence (MUI). Authors concluded that electrical stimulation (ES) probably improves incontinence-specific quality of life (QoL) compared to no treatment but there may be little or no difference between electrical

stimulation and pelvic floor muscle training (PFMT). Consistent with other reviews, it is uncertain whether adding electrical stimulation to PFMT makes any difference in terms of quality of life, compared with PFMT alone. The impact of electrical stimulation on subjective cure/improvement and incontinence-specific QoL, compared with vaginal cones, PFMT plus vaginal cones, or drug therapy, is uncertain. Comparisons of different types of ES to each other and of ES plus surgery to surgery are also inconclusive in terms of subjective cure/improvement and incontinence-specific QoL. Authors concluded that the current evidence base indicated that electrical stimulation is probably more effective than no active or sham treatment, but it is not possible to say whether ES is similar to PFMT or other active treatments in effectiveness or not. Overall, the quality of the evidence was too low to provide reliable results. Pan et al. (2018) evaluated the value of magnetic stimulation (MS) in patients with pelvic floor dysfunction (PFD). A total of 20 studies including 1019 patients were eligible for inclusion whose level of evidence for the included studies was low. Meta-analysis of four trials comparing MS with sham intervention showed that MS was not associated with significant improvement in outcomes or QoL, or number of leakages. Narrative review showed that there were no convincing evidences that MS was effective for chronic pelvic floor pain, detrusor overactivity, or overactive bladder. Authors concluded that there is no convincing evidence to support the benefits of using MS in the management of PFD. The applicability of MS in the treatment of PFD remains uncertain, so larger, well-designed trials with longer follow-up periods adopted relevant and comparable outcomes are needed to be further explored to provide a definitive conclusion.

Ignácio et al. (2022) sought to determine what the effect is of an intravaginal electrical stimulation regimen on their ability to contract the pelvic floor muscles and on self-reported urinary incontinence in women who are unable to contract their pelvic floor muscles voluntarily. Sixty-four women with pelvic floor muscle function assessed by bi-digital palpation to be grade 0 or 1 on the Modified Oxford Scale. For 8 weeks, participants randomised to the experimental group received weekly 20-minute sessions of intravaginal electrical stimulation with instructions to attempt pelvic floor muscle contractions during the bursts of electrical stimulation in the final 10 minutes of each session. The control group received no intervention. The primary outcome was ability to voluntarily contract the pelvic floor muscles, evaluated through vaginal palpation using the Modified Oxford Scale. Secondary outcomes were prevalence and severity of urinary incontinence symptoms assessed by the International Consultation on Incontinence Questionnaire on Urinary Incontinence-Short Form (ICIQ-UI-SF) score from 0 to 21. Sixty-one participants provided outcome data. After the intervention, the ability to contract the pelvic floor muscles was acquired by 36% of the experimental group and 12% of the control. The experimental group also improved by a mean of 2 points more than the control group on the ICIQ-UI-SF score. Authors concluded that in women who are unable to contract their pelvic floor muscles voluntarily, 8 weeks of intravaginal electrical stimulation with voluntary contraction attempts improved their ability to contract their pelvic floor muscles and reduced the overall severity and impact of urinary incontinence on quality of life. Although the main estimates of these effects indicate that the effects are large enough to be worthwhile, the precision of these estimates was low, so it is not possible to confirm whether the effects are trivial or worthwhile.

Zhu et al. (2022) evaluated the efficacy and safety of pelvic floor muscle training (PFMT) combined with biofeedback (BF), electrical stimulation (ES) therapy, or both for postpartum lower urinary tract symptoms (LUTS). Seventeen studies were included. The results of the meta-analysis showed that PFMT plus ES with or without BF was more effective than PFMT alone. Patients receiving PFMT plus ES and BF achieved greater improvement than controls receiving PFMT alone in incontinence quality of life scores, pelvic floor muscle strength, and urodynamic parameters (maximum urethral closure pressure, abdominal leak point pressure, and maximum urinary flow rate), and 1-h urine leakage also decreased. Authors concluded that PFMT plus ES with or without BF exhibited better efficacy and safety for early postpartum LUTS than PFMT alone. Ali et al. (2022) sought to determine the effects of nonsurgical, minimally or noninvasive therapies on urge urinary incontinence (UUI) symptoms and quality of life (QoL) in individuals with neurogenic bladder (NGB). Randomized controlled trials that compared therapies such as intravaginal electrical stimulation (IVES), transcutaneous electrical nerve stimulation (TENS), neuromuscular electrical stimulation (NMES), transcutaneous tibial nerve stimulation (TTNS), pelvic floor muscle training (PFMT), and behavioural therapy (BT) to control were included. Meta-analyses revealed a significant effect of electrical stimulation on UUI due to multiple sclerosis and stroke. The pooled analyses of TTNS and revealed significant effects of these interventions on QoL in people with Parkinson's disease. However, meta-analyses revealed nonsignificant effects for PFMT and BT on UUI due to Parkinson's disease. Authors concluded that their meta-analyses found electrical stimulation to be beneficial for improving the symptoms of UUI among people with multiple sclerosis and those with stroke. The review also revealed that TTNS and BT might improve QoL for people with NGB due to Parkinson's disease, although the effects of PFMT and BT on UUI warrant further investigation.

Sarmiento et al. (2022) perform an updated and comprehensive literature review focused on the effects of pelvic floor electrical stimulation. Regarding the studied populations, the results demonstrated heterogeneity between human and animal populations. Articles comprised studies that investigated the therapeutic effects of electrical stimulation on pelvic floor dysfunctions in humans, totaling 1303 participants. From these, only the research performed by 25 included men in the study population, which investigated 96 patients with urinary incontinence post-radical prostatectomy. Authors concluded that non-invasive electrical stimulation has shown promise in the clinical improvement of disorders associated with pelvic floor fragility. The vast majority of studies addressed in this review showed that electrostimulation improves urination control and sexual quality, in addition to providing greater collagen production and maintaining the effectiveness of sphincter contraction.

Learnardo et al. (2022) compared biofeedback-assisted pelvic muscle floor training (PFMT) and pelvic electrical stimulation (ES) as an intervention group, with PFMT or bladder training (BT) as the control group, in women with an overactive bladder (OAB) in a meta-analysis. Eight studies involving 562 patients (comprising 204 patients with biofeedback-assisted PFMT, 108 patients with pelvic ES, and 250 patients who received PFMT alone or BT and lifestyle recommendations only, as the control group) were included. The ES group showed significant differences in terms of changes to QoL, episodes of incontinence, and the number of participants cured or improved, while the biofeedback group resulted in nonsignificant changes in QoL, episodes of incontinence, and the number of participants cured or improved, both compared to the control group respectively. Authors concluded that this meta-analysis shows that low-frequency pelvic ES appears to be sufficient and effective as an additional intervention for women with OAB in clinical practice according to improvements in the subjects' QoL and reduction of symptoms. Meanwhile, biofeedback-assisted PFMT does not appear to be a significant adjuvant for conservative OAB therapy.

Todhunter-Brown et al. (2022) summarized Cochrane Reviews that assessed the effects of conservative interventions for treating urinary incontinence (UI) in women. The common types of UI are stress (SUI), urgency (UUI) and mixed (MUI). A wide range of interventions can be delivered to reduce the symptoms of UI in women. Conservative interventions are generally recommended as the first line of treatment. Authors included reviews that compared a conservative intervention with 'control' (which included placebo, no treatment or usual care), another conservative intervention or another active, but non-conservative, intervention. They included 29 relevant Cochrane Reviews. Seven focused on physical therapies; five on education, behavioural and lifestyle advice; one on mechanical devices; one on acupuncture and one on yoga. Fourteen focused on non-conservative interventions but had a comparison with a conservative intervention. There were 112 unique trials (including 8975 women) that had primary outcome data included in at least one analysis. For UUI, (five reviews): Conservative intervention versus control: there was moderate to high-certainty evidence demonstrating that PFMT plus feedback, PFMT plus biofeedback, electrical stimulation and bladder training were more beneficial than control for curing or improving UI. Women using electrical stimulation plus PFMT had higher quality of life than women in the control group. One conservative intervention versus another conservative intervention: for cure or improvement, there was moderate certainty evidence that electrical stimulation was more effective than laseropuncture. There was high or moderate certainty evidence that PFMT resulted in higher quality of life than electrical stimulation and electrical stimulation plus PFMT resulted in better cure or improvement and higher quality of life than PFMT alone. For all types of urinary incontinence (13 reviews): Conservative intervention versus control: there was moderate to high certainty evidence of better cure or improvement with PFMT, electrical stimulation, weight loss and cones compared to control. Specific to electrical stimulation and exercise, authors concluded that there is high certainty that PFMT is more beneficial than control for all types of UI for outcomes of cure or improvement and quality of life and electrical stimulation is beneficial for women with UUI. Most evidence within the included Cochrane Reviews is of low certainty.

Stania et al. (2022) sought to determine the therapeutic efficacy of intravaginal electrical stimulation (ES) in women with SUI. Of the 686 records identified, a total of 10 articles met the inclusion criteria. A meta-analysis revealed significant differences between the ES and no active treatment groups in the pooled objective cure rates and subjective cure or improvement rates. No significant differences were found in the pooled number of incontinence episodes per 24 h, the pooled Incontinence Quality of Life Questionnaire scores or the pooled number of adverse effects between the ES and other conservative treatment groups. Authors concluded that there was insufficient evidence for or against the use of intravaginal ES therapy for women with SUI, partly due to the variability in the interventions of the included trials and the small number of trials included.

Fernández-Pérez et al. (2023) evaluated the effectiveness of physical therapy interventions for the treatment of female dyspareunia. Of the 19 articles selected, six applied multimodal physiotherapy treatments; five,

electrotherapy; three, Thiele's massage; two, interdisciplinary interventions or pelvic floor muscle training; and one, extracorporeal shockwave therapy. The meta-analysis showed significant results for the variables pain and quality of life with the interventions based on electrotherapy and electrotherapy combined with pelvic floor muscle training. These interventions did not show significant results for the improvement of sexual function. Authors concluded that physiotherapy techniques are effective and procedures have been identified with reliable results in improving pain and quality of life in patients with dyspareunia. One of the most important aspects is the strengthening of the perineal musculature and the application of Transcutaneous Electrical Nerve Stimulation. Furthermore, manual trigger point release therapy and Thiele massage, optimize and guarantee the reduction of pain intensity.

Huang et al. (2023) investigated the comparative efficacy of neuromodulation technologies for overactive bladder (OAB) syndrome in adults. The search selected clinical trials with random allocation to percutaneous tibial nerve stimulation (PTNS), transcutaneous tibial nerve stimulation (TTNS), vaginal electrical stimulation (VES), sacral neuromodulation (SNM), parasacral stimulation (PS), pudendal neuromodulation, or placebo. The main outcomes were the voiding diary, OAB-related quality of life, and positive response rate. The study included 21 randomized controlled trials involving 1433 participants, and all trials were used for the meta-analysis. In the network meta-analyses, five of six neuromodulation technologies, including PTNS, TTNS, VES, SNM, and PS, were related to higher efficacy than the placebo. Ranking probability showed that SNM was the most efficacious therapy for improving OAB-related quality of life, urinary episodes, and urinary frequency. For urgency incontinence episodes and the number of pads, PTNS and TTNS were the most efficacious modalities, respectively. Authors concluded that neuromodulation technologies, including PTNS, TTNS, VES, SNM, and PS, may be effective and safe solutions for OAB syndrome in adults. Moreover, SNM is the most efficacious regimen for OAB-related quality of life, urinary episodes, and urinary frequency. PTNS and TTNS are the most efficacious modalities for reducing urgency incontinence episodes and the number of pads, respectively. Future studies should pay more attention to the quality of study design and report, patients who may benefit the most from neuromodulation, and the long-term effect, cost-effectiveness, and satisfaction of neuromodulation.

Zhang et al. (2023) described and synthesized non-pharmacological and nonsurgical interventions for male urinary incontinence from the existing literature. A total of 4602 studies were identified, of which 87 studies were included. Approximately 78% were randomized controlled trials. More than 88% of the participants were men with prostate cancer. Exercising pelvic floor muscles 30 times per day for 12 weeks was the most frequently reported. Parameters of electrical stimulation were typically set up to 50 Hz and 300 μ s for frequency and width of pulse, respectively, and lasted for 15 min. Pure pelvic floor muscle training, Pilates, Yoga, whole body vibration, diaphragm/abdominal muscle training, micturition interruption exercise, acupuncture, and auriculotherapy showed positive effects on reducing urinary incontinence. Authors concluded that findings suggest implementing pelvic floor muscle training alone before or after surgery can both prompt the recovery of continence in men after prostate cancer surgery. The decision to use biofeedback or electrical stimulation to enhance the therapeutic effect of pelvic floor muscle training should be approached with caution. More rigorous designed studies are needed to validate the effectiveness of Traditional Chinese Medicine techniques and diverse novel methods.

Jiang et al. (2024) assessed the efficacy of transcutaneous electrical nerve stimulation (TENS) for neurogenic bladder after spinal cord injury (SCI). The primary outcomes were maximum cystometric capacity (MCC) and residual urine volume (RUV). Secondary outcomes included maximum detrusor pressure, flow rate, and bladder diary. Eleven trials involving 881 participants were included. Meta-analysis showed that TENS in addition to conventional treatment had larger MCC and lower RUV than did conventional treatment only. Compared with magnetic stimulation, no differences were observed with TENS for MCC and RUV. There also were no differences in MCC and when compared with solifenacin succinate and pelvic floor biofeedback, respectively. Authors concluded that TENS may be an effective treatment option for neurogenic bladder after SCI.

Cranial Electrotherapy Stimulation

O'Connell et al. (2018) evaluated the efficacy of non-invasive cortical stimulation techniques in the treatment of chronic pain. Non-invasive brain stimulation techniques aim to induce an electrical stimulation of the brain in an attempt to reduce chronic pain by directly altering brain activity. They include repetitive transcranial magnetic stimulation (rTMS), cranial electrotherapy stimulation (CES), transcranial direct current stimulation (tDCS), transcranial random noise stimulation (tRNS) and reduced impedance non-invasive cortical electrostimulation (RINCE). Outcomes of interest were pain intensity measured using visual analogue scales or numerical rating scales, disability, quality of life and adverse events. A total of 94 trials were included in this review (involving 2983 randomised participants). Authors concluded that there is very low-quality evidence that single doses of

high-frequency rTMS of the motor cortex and tDCS may have short-term effects on chronic pain and quality of life but multiple sources of bias exist that may have influenced the observed effects. They did not find evidence that low-frequency rTMS, rTMS applied to the dorsolateral prefrontal cortex and CES are effective for reducing pain intensity in chronic pain. There remains a need for substantially larger, rigorously designed studies. Gatzinsky et al. (2020) surveyed the literature regarding the efficacy and safety of primary motor cortex (M1) rTMS, and the accuracy to predict a positive response to epidural motor cortex stimulation (MCS) which is supposed to give a more longstanding pain relief for chronic neuropathic pain (NP). Data on 5-20 Hz (high-frequency) rTMS vs. sham was extracted from 24 blinded randomised controlled trials which were of varying quality, investigated highly heterogeneous pain conditions, and used excessively variable stimulation parameters. The difference in pain relief between active and sham stimulation was statistically significant in 9 of 11 studies using single-session rTMS, and in 9 of 13 studies using multiple sessions. Baseline data could be extracted from 6 single and 12 multiple session trials with a weighted mean pain reduction induced by active rTMS, compared to baseline, of -19% for single sessions, -32% for multiple sessions with follow-up <30 days, and -24% for multiple sessions with follow-up ≥30 days after the last stimulation session. For single sessions the weighted mean difference in pain reduction between active rTMS and sham was 15 percentage points, for multiple sessions the difference was 22 percentage points for follow-ups <30 days, and 15 percentage points for follow-ups ≥30 days. Authors concluded that rTMS targeting M1 can result in significant reduction of chronic NP which, however, is transient and shows a great heterogeneity between studies; very low certainty of evidence for single sessions and low for multiple sessions. Multiple sessions of rTMS can maintain a more longstanding effect. rTMS seems to be a fairly good predictor of a positive response to epidural MCS and may be used to select patients for implantation of permanent epidural electrodes. More studies are needed to manifest the use of rTMS for this purpose. Pain relief outcomes in a longer perspective, and outcome variables other than pain reduction need to be addressed more consistently in future studies to consolidate the applicability of rTMS in routine clinical practice.

Lloyd et al. (2020) systematically reviewed the most up-to-date literature and perform a meta-analysis of the effects of tDCS on pain intensity in fibromyalgia. Meta-analysis was conducted on studies investigating pain intensity after tDCS in participants with fibromyalgia and analyzed using standardized mean difference and 95% confidence intervals. Fourteen clinical studies were included. Ten were controlled trials and 4 were within-subjects crossover studies. Meta-analysis of data from 8 controlled trials provides tentative evidence of pain reduction when active tDCS is delivered compared to sham. However, substantial statistical heterogeneity and high risk of bias of primary studies prevent more conclusive recommendations being made. Authors concluded that tDCS is a safe intervention with the potential to lower pain intensity in fibromyalgia. However, there is a need for more empirical research of the neural target sites and optimum stimulation parameters to achieve the greatest effects before conducting further clinical studies. Alwardat et al. (2020) evaluated the effectiveness of tDCS on pain reduction and related disability in patients with non-specific chronic low back pain (CLBP). Nine RCTs (411 participants) were included in the systematic review according to inclusion criteria, while only five studies could be included in the meta-analysis. The primary motor cortex (M1) was the main stimulated target. The meta-analysis showed non-significant effect of multiple sessions of tDCS over M1 on pain reduction and disability post-treatment respectively. No significant adverse events were reported. The current results do not support the clinical use of tDCS for the reduction of pain and related disability in non-specific CLBP. However, the limited number of available evidence limits our conclusions on the effectiveness of these approaches.

Szymoniuk et al. (2023) aimed to give an up-to-date overview of brain stimulation methods, including transcranial direct current stimulation (tDCS), repetitive transcranial magnetic stimulation (rTMS), cranial electrotherapy stimulation (CES), and reduced impedance non-invasive cortical electrostimulation (RINCE) as a potential treatment for chronic pain in a narrative review. According to authors, the majority of studies on the use of brain stimulation in chronic pain are of poor methodology with small sample sizes. Because tDCS and rTMS demonstrated successful results on chronic pain relief with a low rate of side effects, their clinical use is the most beneficial among discussed techniques. Additionally, research on adverse effects is continued to further increase the safety of these methods. Regarding CES and RINCE, further high quality research is needed to confirm findings. There are only a few studies that suggest CES therapy to be beneficial and most clinical trials showed no benefit. RINCE was proven effective in managing chronic pain, but data referred only to one study, so there was the risk of bias due to the small sample size. In summary, rTMS and tDCS represent the most promising therapeutic options for chronic pain among discussed brain stimulation methods. However, due to the low quality of evidence provided by available studies, large multi-center RCTs with long-term follow-ups are necessary to verify the safety and clinical outcomes of non-invasive as well as invasive brain stimulation.

Gómez-García et al. (2023) evaluated the efficacy of transcranial direct current stimulation in patients with dysphagia in post-stroke patients. Of the 9 investigations analyzed, all applied transcranial direct current stimulation in combination with conventional dysphagia therapy to the experimental group. All the studies analyzed identified improvements in swallowing function and meta-analysis confirmed their strong effect on reducing the risk of penetration and aspiration. The results showed that participants who received transcranial direct current stimulation significantly improved swallowing function. Authors concluded that transcranial direct current stimulation has positive effects in the treatment of poststroke dysphagia by improving swallowing function, oral and pharyngeal phase times and the risk of penetration and aspiration. Furthermore, its combination with conventional dysphagia therapy, balloon dilatation with catheter or training of the swallowing muscles ensures improvement of swallowing function.

Ahmed et al. (2023) compared the efficacy of non-invasive brain stimulation (NiBS) such as transcranial direct current stimulation (tDCS), repetitive transcranial magnetic stimulation (rTMS), theta-burst stimulation (TBS), and transcutaneous vagus nerve stimulation (taVNS) in upper limb stroke rehabilitation. Eighty-seven RCTs with 3750 participants were included. Pairwise meta-analysis showed that all NiBS except continuous TBS (cTBS) and cathodal tDCS were significantly more efficacious than sham stimulation for motor function, whereas taVNS, anodal tDCS, and both low and high frequency rTMS were significantly more efficacious than sham stimulation for ADLs. NMA showed that taVNS was more effective than cTBS, cathodal tDCS, and Physical rehabilitation alone for improving motor function. P-score found that taVNS is best ranked treatment in improving motor function and ADLs after stroke. After taVNS, excitatory stimulation protocols (intermittent TBS, anodal tDCS, and HF-rTMS) are most effective in improving motor function and ADLs after acute/sub-acute and chronic stroke. Authors concluded that evidence suggests that excitatory stimulation protocols are the most promising intervention in improving upper limb motor function and performance in ADLs. taVNS appeared to be a promising intervention for stroke patients, but further large RCTs are required to confirm its relative superiority.

Neufit Neubie device

There is a paucity of published literature to support the use of the Neufit Neubie device for electrical stimulation and therefore conclusions about the safety and efficacy of the device or combination units cannot be made.

RST-SANEXAS neoGEN® Electric cell-Signaling Treatments (EcST)

There is no peer reviewed published literature to support the use of the RST-SANEXAS neoGEN® Electric cell-Signaling Treatment (EcST) and therefore conclusions about the safety, and efficacy cannot be made.

Transcutaneous electrical modulation pain reprocessing (TEMPR) (e.g., Scrambler therapy, Calmare®)

There is insufficient evidence in the published peer reviewed scientific literature to support the efficacy of TEMPR. Studies comparing TEMPR to conventional treatment options and to sham therapy are lacking. Available studies are primarily in the form of case series with small, heterogeneous patient populations and short-term follow-ups investigating TEMPR for the treatment of various types of pain including cancer pain. In some cases, pain relief was not maintained following therapy (Ricci, et al., 2019; Lee, et al., 2016; Notaro, et al., 2016; Coyne, et al., 2013; Ricci, et al., 2011; Smith, et al., 2020; Sabato, et al., 2005; Marineo, et al., 2003).

Marineo et al. (2012) conducted a randomized controlled trial to compare the effects of Scrambler therapy (n=26) to guideline-based drug management (n=26) (control group) for the treatment of pain (i.e., postsurgical neuropathic pain, postherpetic neuralgia or spinal canal stenosis). Scrambler therapy included one 45-minute session a day for ten days at the maximally tolerated stimulus. The primary outcome was change in visual analogue scale (VAS) pain scores at one month. Secondary outcomes included VAS pain scores at two and three months, pain medication usage and allodynia. At the one-month, two-month and three-month follow-up visits, there was a significant reduction in the mean VAS score for the treatment group compared to the control group ($p < 0.0001$, each). More relapses occurred in patients with polyradicular pain than monoradicular pain. Relapses in the test group were significant ($p < 0.001$) but not in the control group ($p > 0.05$). No adverse effects were observed. Compared to the control group, allodynia significantly reduced in the Scrambler group at one, two and three months ($p = 0.0017$, $p = 0.0094$, $p = 0.0644$, respectively). Scrambler therapy was also associated with significant pain medication reduction and dosage variation was statistically significant ($p < 0.0001$). Author-noted limitations included: lack of a sham comparator, the type of treatment provided to the control group, and the small sample size. Other limitations are the short-term follow-up and heterogeneity of the patient population.

Hou et al. 2018 conducted a systematic review of the literature to assess the safety and efficacy of medical and pharmacological therapies for the treatment of chemotherapy-induced peripheral neuropathy (CIPN). Studies

with adult subjects (age \geq 18 years) were included if they were randomized controlled trials (RCTs), prospective non-randomized studies, case-control, cohort, cross-over or retrospective. Case reports, case series, abstracts, review articles, letters to the editor, and animal studies were excluded. In total, 13 RCTs, 18 prospective studies, and four retrospective studies met the inclusion criteria. The studies investigated the use of pharmacotherapy and other numerous modalities including laser therapy, scrambler therapy, magnetic field therapy, dietary therapy, long-wave diathermy therapy, and acupuncture. The primary outcome measures were highly variable across the included studies. The authors' focus was pain relief and change in the severity of CIPN symptoms. Due to the low quality of the studies and the paucity of evidence no recommendation could be made for acupuncture-like transcutaneous nerve stimulation (ALTENS), electro-acupuncture, percutaneous auricular neurostimulation, interferential therapy, low-frequency magnetic field therapy and scrambler therapy. The limitations of this systematic review included: heterogeneity of the studies with variations in timing of treatment, primary outcomes, and chemotherapeutic agents. Most of the included studies had small sample sizes and short term follow-up periods.

Hayes (2020) evaluated Scrambler/Calmare for the treatment of chronic nonmalignant pain. Nine studies including three randomized controlled trials, one repeated-measure time series (observational studies), three pretest/posttest study and two retrospective reviews were included in the Brief. Outcomes were measured using visual analog scale (VAS), numeric rating scale (NRS), and the Brief Pain Inventory (BPI). No adverse events were reported. Although limited evidence suggested improvement in pain, "substantial uncertainty" remains due to the lack of well-designed comparative studies. The overall quality of the evidence was rated low to very low and Hayes concluded that there was insufficient evidence to assess the impact of Scrambler/Calmare on health outcomes or patient management.

Hayes (2020) also evaluated the literature on Scrambler/Calmare for the management of chronic pain related to cancer or cancer treatment. There was a paucity of "very-low-quality" evidence for cancer-related pain in adult patients. Twelve studies including two randomized controlled trials, nine single arm studies, and one retrospective review meet the inclusion criteria. It is proposed that Scrambler Therapy (ST) may be used as an adjunct to conventional treatments. The long-term durability of relief of pain using ST is unclear. Limitations of the studies included: small patient populations ($n=11-83$), short term follow-ups, lack of a control group, limited reporting of outcomes, lack of statistical rigor and analyses, lack of blinding, and substantial attrition. There is insufficient evidence to support the safety and effectiveness of Scrambler/Calmare for pain related to cancer and cancer treatment.

Kashyap and Bhatnagar (2020) aimed to detect possible gaps in the literature regarding the efficacy of ST for cancer pain and formulate recommendations for research through a systematic review of the literature. Twenty-seven studies were retrieved. Ten were articles that were categorized as literature reviews, including 7 general literature reviews not following a specific review methodology, 1 editorial, and 2 systematic reviews. Seventeen were original studies, including 2 single-arm trials, 1 randomized controlled trial, 4 pilot trials, 4 case reports, 2 retrospective studies, and 4 prospective studies. By and large, the available literature supports the use of ST as an effective therapy for the management of refractory cancer pain. However, the level of evidence for its application to cancer pain is not particularly strong, and improvement in pain with ST may even be owing to a placebo effect. Authors concluded that methodologically sound, large randomized control trials are needed in this area.

Wang et al. (2022) aimed to summarize the evidence regarding 4 major types of neuromodulation devices for the treatment of painful diabetic neuropathy (PDN). They focused on spinal cord stimulators (SCS), peripheral nerve stimulators (PNS), transcutaneous electrical nerve stimulators (TENS), and scrambler therapy devices (ST) because they are often used for refractory neuropathic pain. Seventeen studies met inclusion criteria, 10 of which were regarding SCS. Only 3 of the 10 were randomized controlled trials. We found no studies assessing contemporary PNS. Four studies assessed TENS, but the devices varied widely in voltages and waveforms. Two case reports described ST. Authors concluded that the evidence for neuromodulation devices for the treatment of PDN mostly comprises open-label prospective trials or case reports. SCS has the most volume of evidence for efficacy. Studies regarding TENS show mixed results, possibly due to numerous device varieties. PNS and ST may hold promise based on their proposed mechanisms of action, but prospective controlled trials are needed.

Jin et al. (2022) aimed to investigate the efficacy of scrambler therapy (ST) for the management of chronic pain in a meta-analysis. Out of 348 studies, a total of 7 RCTs ($n = 287$ patients) that met the inclusion criteria were

included in the final analysis. Overall, ST marginally decreased pain scores after the end of the treatment compared with the control group, with substantial heterogeneity. A subgroup meta-analysis found that the use of ST significantly reduced analgesic consumption compared to the control group. However, no significant efficacy was observed in the subgroup meta-analyses by methodological quality, type of diseases causing pain, and follow-up period. The included trials have a small sample size and low methodological quality. Authors concluded that ST seems to be effective in the management of patients with chronic pain. However, further, large RCTs are warranted to confirm our findings.

Karri et al. (2023) performed a systematic review based on the use of Scrambler Therapy (ST) in treating chronic pain syndromes. Primary outcome parameters collected were analgesic benefit, adverse effects, and other metrics such as sensorimotor testing. A total of 21 studies met the final criteria for study inclusion and comprised randomized controlled trials (n = 8), prospective observational studies (n = 10), and retrospective cohort studies (n = 3). Nearly all the reported studies explored the use of ST for the treatment of neuropathic pain, with chemotherapy-induced peripheral neuropathy being the most studied condition. Most studies were limited by small cohorts but reported ST being safe, well tolerated, and providing clinically meaningful pain reduction. The duration of posttreatment follow-up ranged from ten to 14 days (concordant with completion of typical ST protocols) to three months. Secondary benefits such as medication reduction and improvement of sensory and motor symptoms were noted by some studies. Authors concluded that ST is regarded as a safe intervention with potential for significant analgesic benefit for neuropathic pain conditions. Although the available evidence is most robust for treating chemotherapy-induced peripheral neuropathy, ST has also been shown to be effective in treating other neuropathic pain syndromes. Evidence for ST use in nociceptive pain conditions is limited but appears promising. The favorable safety profile and increasing evidence basis for ST warrant more extensive recognition and consideration for use in clinical care.

Coding Information

Notes:

1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare & Medicaid Services (CMS) code updates may occur more frequently than policy updates.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
97014	Application of a modality to 1 or more areas; electrical stimulation (unattended)
97032	Application of a modality to 1 or more areas; electrical stimulation (manual) each 15 minutes

HCPCS Codes	Description
G0283	Electrical stimulation unattended, to one or more areas for indication(s) other than wound care, as part of a therapy plan of care

***Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.**

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