

Medical Coverage Policy



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Electrical Stimulation Therapy and Home Devices

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Overview

This Coverage Policy addresses outpatient electrical stimulation therapy (e.g., wound care therapy, auricular electroacupuncture, transcutaneous electrical modulation pain reprocessing) and the use of in-home devices, conductive garments and other related supplies for the treatment of multiple conditions.

Coverage Policy

Electrical Stimulation Therapies

Chronic Wound Healing

Electrical stimulation (HCPCS Code G0281) is considered medically necessary for the treatment of a chronic wound when ALL of the following criteria are met:

- Presence of **ANY** of the following chronic wound types:
 - Stage 3 or stage 4 pressure ulcer
 - arterial ulcer
 - neuropathic (diabetic) ulcer
 - venous stasis ulcer
- Failure to demonstrate measurable signs of improved healing (e.g., signs of epithelialization and reduction in ulcer size) with a 30-day trial of conventional wound management, including optimization of nutritional status, moist dressings and debridement.
- Electrical stimulation therapy is performed under the direct supervision of a medical professional with expertise in wound evaluation and management.

The use of electrical stimulation in the home setting for wound healing in the absence of direct supervision by a health care provider is considered experimental, investigational or unproven.

Electrical stimulation therapy for any other chronic wound indication including but not limited to prevention of a pressure ulcer or pressure sore is considered experimental, investigational or unproven.

Other Electrical Stimulation Therapies

Each of the following electrical stimulation therapies is considered experimental, investigational or unproven:

- auricular electroacupuncture (e.g., PStim™) (HCPCS Code S8930)
- transcutaneous electrical modulation pain reprocessing (TEMPR) (e.g., Scrambler therapy, Calmare®) (CPT Code® 0278T)

Home Electrical Stimulation Devices (Electrical Stimulators)

Coverage for Durable Medical Equipment (DME) including in-home electrical stimulation devices varies across plans. Please refer to the customer's benefit plan document for coverage details.

If coverage for an in-home electrical stimulation device is available, the following conditions of coverage apply.

Neuromuscular Electrical Stimulation (NMES)

Neuromuscular electrical stimulation (NMES) (HCPCS Code E0745) and related supplies (HCPCS Code A4595) are considered medically necessary when used as one component of a comprehensive rehabilitation program for the treatment of disuse atrophy when the nerve supply to the atrophied muscle is intact.

Neuromuscular electrical stimulation (NMES) and related supplies (HCPCS Code A4595) for ANY other indication (e.g., idiopathic scoliosis [HCPCS Code E0744], heart failure) are considered experimental, investigational or unproven.

Transcutaneous Electrical Nerve Stimulation (TENS)

A transcutaneous electrical nerve stimulator (TENS) (HCPCS Code E0720, E0730) and related supplies (HCPCS Code A4595) are considered medically necessary for in-home use as an adjunct to conventional post-operative pain management within 30 days of surgery.

TENS (HCPCS Code E0720, E0730, K1016) and related supplies (HCPCS Code A4595, K1017) for ANY other indication, including a device for the treatment of migraine headaches (e.g., Cefaly), are considered experimental, investigational or unproven.

Conductive Garment

A conductive garment (HCPCS Code E0731) is considered medically necessary when used in conjunction with a medically necessary in-home NMES or TENS device for ANY of the following clinical situations:

- The use of conventional electrodes, tapes or lead wires is not feasible either because the individual has a large area requiring treatment or a large number of sites requiring stimulation.
- The site(s) requiring stimulation (i.e., back) is/are difficult to reach with conventional electrodes, tapes or lead wires.
- A co-existing medical condition (e.g., skin problems) precludes the use of conventional electrodes, tapes, or lead wires.

A conductive garment for any other in-home indication is considered not medically necessary.

Other Electrical Stimulation Therapies

In-home use of ANY of the following electrical stimulation devices is considered experimental, investigational, or unproven for the treatment of any condition:

- bioelectric nerve block (electroceutical therapy) (HCPCS Code E1399)
- combination therapy (e.g., Neufit Neubie, Flex-MT+) (HCPCS code E1399)
- cranial electrical stimulation (cranial electrotherapy stimulation) (HCPCS Code K1002)
- electrical sympathetic stimulation therapy (HCPCS Code E1399)
- electrotherapeutic point stimulation (ETPSSM) (HCPCS Code E1399)
- functional electrical stimulation (FES) (HCPCS Codes E0764, E0770)
- H-WAVE electrical stimulation (HCPCS Code E1399)
- high-voltage galvanic stimulation (HVG) (HCPCS Code E1399)
- interferential therapy (IFT) (HCPCS Codes S8130, S8131)
- microcurrent electrical nerve stimulation (MENS), including frequency-specific microcurrent (FSM) stimulation (HCPCS Code E1399)
- pelvic floor electrical stimulation (PFES) (HCPCS Code E0740)
- percutaneous electrical nerve stimulation (PENS) (HCPCS Code K1018, K1019)
- percutaneous neuromodulation therapy (PNT) (HCPCS Code E1399)
- percutaneous nerve field stimulation (PNFS) (e.g., NSS-2 Bridge, IB-Stim) (CPT Code 64999)
- threshold/therapeutic electrical stimulation (TES) (HCPCS Code E1399)
- transcutaneous electrical acupoint stimulation (TEAS) (HCPCS Code E0765)
- transcutaneous electrical joint stimulation (HCPCS Code E0762)

Note: For electrical stimulation therapies in the outpatient setting please refer to the Cigna/American Specialty Health (ASH) Coverage Policy “Electric Stimulation for Pain, Swelling and Function in a Clinical Setting”.

General Background

Electrical stimulation (ES) therapy involves the application of electrodes to affected areas of the body for the purpose of delivering electrical current. ES is used for neuromuscular relaxation and contraction and for wound healing. ES devices (e.g., transcutaneous electrical stimulators [TENS]) are devices proposed for use by the patient at home. There are numerous ES devices and proposed indications.

According to the National Institute of Health Pain Consortium (2021), pain care and management disparities exist between certain racial, ethnic, and socioeconomic groups. Contributing factors to these disparities include bias in pain treatment, socioeconomic status, language barriers, and access to care. The consortium concluded that Black patients were more likely than white patients to have more referrals for substance abuse, fewer referrals to a pain specialist, and increased urine drug testing. Additionally, Blacks are less likely to receive analgesic pain medication than whites and compared to other sociodemographic groups, primary care providers are more likely to underestimate pain levels in Blacks. Patients in the highest socioeconomic status were more likely to be prescribed opioid pain medication during emergency room visits while people living below the poverty line were more likely to report pain. Those patients who are non-native English speakers may have health literacy limitations, difficulty navigating the healthcare system, and difficulty understanding healthcare providers. Minority neighborhood pharmacies are less likely to carry sufficient prescription pain medications than those in white neighborhoods.

Electrical Stimulation Therapy

Chronic Wounds

Chronic wounds are wounds that have not completed the healing process in the expected time frame, usually 30 days, or have proceeded through the healing phase without establishing the expected functional results. These wounds generally do not heal without intervention and are sometimes unresponsive to conventional therapies. Neuropathic diabetic foot ulcers, pressure ulcers, venous leg ulcers, and arterial ulcers are examples of chronic wounds. Electrical stimulation (ES) has been proposed as an adjuvant therapy in the treatment of stage 3 and stage 4 pressure ulcers, arterial ulcers, neuropathic (diabetic) ulcers and venous stasis ulcers that are nonresponsive to conventional therapies.

Studies have not adequately evaluated the safety and effectiveness of unsupervised home use of electrical stimulation devices by a patient for the treatment of chronic wounds. Risks are uncommon but may occur with unsupervised treatments, including rashes at the site of electrode placement or, in rare cases, burns on the skin. Evaluation of the wound is an integral part of wound therapy. It is recommended that when ES is used as an adjunctive treatment for chronic wound healing, treatment should be conducted under the direct supervision of a medical professional with expertise in wound evaluation and management (Centers for Medicare and Medicaid [CMS], 2002).

A pressure ulcer, also known as a decubitus ulcer or bedsore, is the result of pathologic changes in blood supply to the dermal and underlying tissues, usually because of compression of the tissue over a bony prominence, such as the sacrum, heels, hips and elbows (Thomas, 2011, CMS, 2002).

When evaluating pressure ulcers, a staging system is typically used that measures tissue destruction by classifying wounds according to the tissue layers involved. In 2016, the National Pressure Ulcer Advisory Panel (NPUAP) updated the stages of pressure ulcers. The stages that are supported by the literature for use of electrical stimulation when conventional therapies fail are stages 3 and 4 which are described as follows:

- **Stage 3: Pressure Injury: Full-thickness skin loss:** Full thickness loss of skin in which adipose (fat) is visible in the ulcer and granulation tissue and epibole (rolled wound edges) are often present. Slough and/or eschar may be visible. The depth of tissue damage varies by anatomical location; areas of significant adiposity can develop deep wounds. Undermining and tunneling may occur. Fascia, muscle, tendon, ligament, cartilage and/or bone are not exposed. If slough or eschar obscures the extent of tissue loss this is an Unstageable Pressure Injury.

- **Stage 4: Pressure Injury: Full-thickness skin and tissue loss:** Full thickness tissue loss with exposed or directly palpable fascia, muscle, tendon, ligament, cartilage or bone in the ulcer. Slough or eschar may be present. Epibole (rolled edges), undermining and/or tunneling often occur. Depth varies by anatomical location. If slough or eschar obscures the extent of tissue loss this is an Unstageable Pressure Injury.

Arterial (ischemic) ulcers of the lower limb are caused by inadequate arterial blood supply resulting in tissue ischemia and necrosis. Arterial ulcers may be associated with conditions such as arteriosclerosis obliterans, thromboangiitis obliterans (Buerger's disease), necrotizing vasculitides (e.g., polyarteritis nodosa, rheumatoid arthritis, systemic lupus), sickle cell anemia and diabetes mellitus. Reestablishment of an adequate vascular supply is a key factor to support proper healing. Medical management includes control of diabetes, control of hypertension, smoking cessation, and moderate exercise (CMS, 2002; Bello, 2000).

Venous stasis ulcers result from venous hypertension, which is usually caused by valvular incompetence or can develop as a result of thrombosis, obstruction, dilation (varicosities) or hemorrhage. The underlying pathophysiology is venous insufficiency. Treatment regimens focus on increasing venous return and decreasing edema. Generally treatment consists of compression stockings or wraps, combined with frequent elevation of the extremity and avoidance of prolonged standing (Burns, et al., 2007).

The major contributors to the formation of diabetic ulcers include neuropathy, foot deformity and ischemia. The neuropathy, both sensory and motor, is secondary to persistently elevated blood glucose levels. Therefore, maintaining optimal blood sugar levels is important. Treatment options include antibiotics if osteomyelitis is present, relief of pressure at the wound site, surgical debridement, control of infection, and arterial reconstruction. Other therapeutic options may include Becaplermin (Regranex®), bioengineered skin substitutes and a variety of synthetic dressings (Barbul, 2005).

U.S. Food and Drug Administration (FDA): According to the Centers for Medicare & Medicaid Services (CMS) decision memorandum (2002), the FDA granted premarket application (PMA) approvals for electrical stimulators as Class III devices for the indications of bone stimulation and deep brain stimulation. FDA has also cleared electrical stimulators as Class II devices when indicated for muscle stimulation. However, the FDA has not cleared or approved the use of ES for the treatment of wounds. The FDA concluded that the use of these devices for the treatment of wounds is significantly different than the use of these devices for the indications currently covered under a 510(k) clearance. They are considered Class III devices and, as such, require approval via the PMA process. Manufacturers cannot market electrical stimulators for wound healing. However, lack of approval does not preclude physicians and other healthcare providers from providing this therapy as an off-label use.

Literature Review: ES is an established treatment option for chronic stage 3 and stage 4 pressure ulcers, venous stasis ulcers, arterial ulcers, and neuropathic diabetic foot ulcers. Although there is a limited number of studies investigating ES for the treatment of chronic wounds, meta-analysis (n=12 studies), systematic reviews, randomized controlled trials (n=34–63) and a nonrandomized comparative study (n=80) reported significant improvement in healing and decrease in wound size or complete healing compared to placebo or no stimulation. Follow-ups occurred for up to three months. There is high variability as to which type of electrical current and application protocol is the most effective for the ulcer type (Smith, et al., 2013; Houghton, et al., 2010; Regan, et al., 2009; Jünger, et al., 2008; Janković, et al. 2008; Adunsky, et al., 2005; Houghton, et al., 2003; Akai, et al., 2002; Peters, et al.; 2001).

Professional Societies/Organizations:

The American College of Foot and Ankle Surgeons (ACFA) (2006) Clinical Consensus Statement for diabetic foot disorders stated that the rationale for using electrical stimulation in wound healing stems from the fact that the body has an endogenous bioelectric system that enhances healing of bone fractures and soft tissue wounds. According to ACFA clinical studies provide support for the use of electrical stimulation in wound care.

Electrical Stimulation In-Home Devices (Electrical Stimulators)

Neuromuscular Electrical Stimulation (NMES)

NMES is the application of electrical current through electrodes on the skin to targeted muscles to elicit muscle contraction and relaxation. NMES is proposed to promote muscle restoration and to prevent or diminish muscle atrophy and spasms 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. Protocols in the literature recommend no more than two hours of NMES treatment within a 24-hour period and the treatment plan is typically re-evaluated every 30 days. Compared to transcutaneous electrical neurostimulation (TENS), NMES delivers a stronger current with a wider pulse width.

U.S. Food and Drug Administration (FDA): Neuromuscular electrical stimulators are 510(k) FDA approved as Class II devices. An example of a NMES device is the EMS 7500 (Koalaty Products, Ind., Roswell, GA). The device is approved for “(1) relaxing muscle spasms, (2) increasing local blood circulation, (3) immediate post-surgical stimulation of calf muscles to prevent venous thrombosis, (4) muscle re-education, (5) maintaining or increasing range of motion, and (6) preventing or retarding disuse atrophy.” Another example is the Kneehab XP Type 412/421 (Bio-Medical Research Ltd., West Galway, Ireland) that focuses on quadriceps stimulation to “maintain or increase range of motion, prevention or retardation of disuse atrophy, re-educate muscles, early post-surgical strengthening and knee stability, relax muscle spasms, and increase blood circulation.”

Literature Review - Disuse Atrophy: Systematic reviews and randomized controlled trials support NMES for the treatment of disuse atrophy and reported that NMES was as effective as, or more effective than, exercise (Bax, 2005; Lieber, et al., 1996). NMES is a well-established treatment modality for disuse atrophy when the nerve supply to the muscle is intact.

Literature Review – Other Indications: There is insufficient evidence to support the effectiveness of NMES in the prevention and/or management of multiple conditions including: aerobic NMES for diabetes mellitus and obesity; cancer; congestive heart failure; chronic obstructive pulmonary disease (COPD); deep vein thrombosis; knee rehabilitation following injury or surgical intervention; muscular dystrophy; muscle wasting and weakness associated with cancers; cerebral palsy; stroke; swallowing; toning, strengthening and firming of abdominal muscles; osteoarthritis (e.g., of the knee); rheumatoid arthritis; fecal incontinence; low back pain; Bell’s palsy; sensory stimulation for coma patients; motor disorders; and chronic ulcers. Overall, studies in the form of randomized controlled trials and case series included small, heterogeneous patient populations and short-term follow-ups. Some systematic reviews have reported that no improvement was seen with NMES, outcomes were conflicting and/or in some cases, when improvement was noted, the effects did not last. Heterogeneity of treatment regimens and outcome measures make it difficult to establish that NMES resulted in meaningful clinical outcomes (e.g., decrease pain, functional improvement, improvement in quality of life and ability to carry out activities of daily living) for these other conditions and indications.

Advanced Disease: Maddocks et al. (2013) conducted a Cochrane systematic review of randomized controlled trials to investigate the effectiveness of NMES in improving muscle strength in adults with advanced disease. Eleven studies evaluating NMES to no exercise or placebo NMES for the treatment of advanced COPD (8 studies; n=126), chronic heart failure (2 studies; n=76) or thoracic cancer (1 study; n=16) were included. The primary outcome was quadriceps muscle strength assessed immediately following a program of NMES. Secondary outcomes included: adherence to prescribed program, adverse events, muscle strength, endurance and mass with maximal and submaximal exercise capacity, breathlessness and aspects of health-related quality of life. NMES significantly improved quadriceps strength by a standardized mean difference of 0.9, equating to approximately 25 Newton meters, a unit of torque. Mean differences across various walking tests, favored NMES including 40 meters for the six-minute walk test, 69 meters for the incremental shuttle walk test and 160 meters for the endurance shuttle walk test. No serious adverse events were reported. Although the use of NMES showed improvement in leg muscle strength and ability to exercise, studies were limited by small patient populations, short-term follow-ups, and heterogeneity of inclusion criteria, place of service (home vs. inpatient), program characteristics and stimulation parameters. An update of this review in 2016 (Jones, et al.) included 18 studies (n=933). The overall conclusions remained the same. The quality of the evidence comparing NMES to a control was low for quadriceps muscle strength, moderate for occurrence of adverse events, and very low-to-low for all other secondary outcomes. Due to the limited data, the most beneficial type of NMES program for the

treatment of advanced disease could not be determined. Further research is needed to understand the role of NMES as a component of, and in relation to, existing rehabilitation approaches for these individuals.

Chronic Obstructive Pulmonary Disease: A 2018 randomized controlled trial (n=73) reported that home-based NMES as an add-on to pulmonary rehabilitation did not result in further improvements in subjects with severe to very severe COPD. Inclusion criteria were the following: aged ≥ 18 years; forced expiratory volume in one second $< 60\%$ predicted with a total lung capacity $> 80\%$ predicted; baseline modified Medical Research Council dyspnea scale ≥ 1 ; and optimized medical therapy. Exclusion criteria included: body mass index (BMI) < 18 or $> 35\text{kg/m}^2$; pregnancy or potential pregnancy; peripheral neuropathy; contraindication to cardiopulmonary exercise testing (CPET); progressive cancer; cardiac pacemaker; and implanted cardioverter-defibrillator. Subjects were randomized to pulmonary rehabilitation with and without NMES. There were within group significant increases in the distance walked during the 6-minute walk test (6MWT) ($p \leq 0.01$), peak oxygen consumption ($p=0.02$), maximal workload ($p < 0.01$), modified Medical Research Council dyspnea scale ($p < 0.01$) and Saint George's Respiratory Questionnaire total score ($p=0.01$), but there were no significant differences in the outcomes between the groups (Bonnieve, et al., 2018).

Hill et al. (2018) conducted a Cochrane review of sixteen randomized controlled trials (n=267) to determine the effects of NMES on subjects with chronic obstructive pulmonary disease (COPD). Seven studies investigated the effect of NMES versus usual care and nine assessed the effect of NMES plus conventional exercise training versus conventional exercise training alone. Six studies utilized sham stimulation in the control group. When applied in isolation, NMES produced an increase in peripheral muscle force and quadriceps endurance but the effect on thigh muscle size was unclear. There were increases in the six-minute walk distance (6MWD) and time to symptom limitation exercising at a submaximal intensity. There was a reduction in the severity of leg fatigue on completion of an exercise test. The increase in peak rate of oxygen uptake was of borderline significance. For NMES with conventional exercise training, there was an uncertain effect on peripheral muscle force and there were insufficient data to perform a meta-analysis on the effect on quadriceps endurance or thigh muscle size. There was an increase in 6MWD in favor of NMES combined with conventional exercise training. There was no risk difference for mortality or minor adverse events in participants who received NMES vs. the comparator. The quality of evidence was graded as low or very low. Studies were limited by the risk of bias, imprecision of the estimates, small number of studies and inconsistency between the studies. There is insufficient evidence to establish the clinical benefit of NMES in the treatment of COPD.

Dysphagia: Tan et al. (2013) conducted a systematic review and meta-analysis to compare the efficacy of NMES to traditional therapy (TT) in dysphagia rehabilitation. Three randomized controlled trials and four case series (n=291) met inclusion criteria. Outcomes were measured using the Functional Oral Intake Scale (FOIS), Swallow, Functional Scoring System (SFSS), American Speech-Language-Hearing Association National Outcome Measurement System (ASHA NOMS) Swallowing Level Scale, and M.D. Anderson Dysphagia Inventory (MDADI). Four studies compared NMES only to TT and three compared NMES with TT to TT alone. The Swallowing Function Scale of patients treated with NMES were significantly higher compared with patients treated with TT ($p=0.02$) but subgroup analysis according to etiology (i.e., stroke, cancer and Parkinson's disease) showed no significant differences between NMES and TT in post-stroke dysphagia. Limitations of the studies included the inclusion of four nonrandomized controlled trials, poor study designs, and heterogeneity of patient population and outcome measures. Due to the limitations, these outcomes need to be validated in well-designed randomized controlled trials with large patient populations and long-term follow-ups.

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.

Knee Indications: Toth et al. (2020) conducted a prospective, randomized, sham-controlled, blinded trial to determine whether neuromuscular electrical stimulation (NMES) started soon after anterior cruciate ligament (ACL) injury or reconstruction (ACLR) would preserve quadriceps muscle size and contractility. Patients (n=25) were included in the study if they had a body mass index of <35 kg/m², were < three weeks from a first time ACL injury, and scheduled to undergo reconstruction. Patients were excluded from participation if they had: a history of knee/lower extremity surgery; laxity of any knee ligament other than the injured ACL; symptoms or arthritis, an autoimmune or inflammatory disease, or diabetes; ≥ grade IIIb articular cartilage lesions to the tibiofemoral joint; or women who are or plan to become pregnant. The intervention group (n=14) received NMES assigned by unblinded study personnel with stratification for age, sex, and graft material. NMES began within three weeks of injury and continued through three weeks post-surgery in the home setting five days per week for 60 minutes per day. There was a 72 hour pause in the intervention during the surgical period. Sham NMES (n=11) delivered via simulated microelectrical neural stimulation administered at home five days per week for 60 minutes per day served as the comparator. All patients underwent ACLR rehabilitation. The primary outcome measured was skeletal muscle fiber size (i.e., via immunohistochemistry) and contractility (i.e., via maximal isometric force production (F_{max}), maximal isometric tension (T_{max}), maximum shortening velocity (V_{max}), and maximum power production (P_{max}) using isotonic load clamps). Whole muscle strength at six weeks served as a secondary outcome measure. Initial evaluation of the patients occurred twice; once upon enrollment and again one week pre-surgery and consisted of muscle strength and clinical and patient oriented assessments. Follow-up occurred at three weeks and six months post-surgery. At three weeks follow-up, post-surgery, bilateral, percutaneous biopsies were taken from the vastus lateralis muscles and computed tomography was performed. At six months post-surgery bilateral whole muscle strength and whole leg function by single leg hop were measured and clinical and patient oriented assessments were completed. Although atrophy was present in the injured leg in both treatment groups, a significant reduction was noted in the NMES group (p<0.001). A significant increase in overall muscle fiber contractility three weeks post ACLR was noted in the NMES group compared to the sham group (p<0.001). No differences were noted in whole quadriceps muscle size between the injured and non-injured legs at three weeks post-surgery, however, that ratio was significantly reduced at six months post-surgery in the NMES group (p<0.05). No differences were noted in muscle strength at six months post-surgery. No adverse events were reported. Author noted limitations included an unbalanced allocation of meniscal injury between treatment groups and patient attrition. Additional limitations include the small patient population, short-term follow-up, and risk of bias of intervention allocation. Additional high quality studies are needed to assess the value of NMES in this patient population. The study did not address health disparities.

Martimbianco et al. (2017) conducted a Cochrane review of randomized controlled trials to evaluate the benefits and harms of NMES for the treatment of patellofemoral pain syndrome, generally referred to as patellofemoral pain (PFP). Eight randomized controlled trials (n=345) met inclusion criteria. Subjects were age 24–43 years, follow-ups ranged from one to six months, and there was a wide duration of symptoms. Comparators included exercise, different types of NMES, NMES with exercise vs. exercise alone, patellar taping and/or ice. Studies varied widely in the characteristics of the NMES regimen, its application and associated co-interventions. There is insufficient evidence to support beneficial clinical outcomes from NMES when used for the treatment of PFP. There was a high risk of bias in the studies, conflicting outcomes, and “very low” quality of evidence.

Volpato et al. (2016) conducted a systematic review of randomized controlled trials to evaluate the effectiveness of NMES on adults who underwent rehabilitation following postoperative total knee arthroplasty. Four studies (n=376) met inclusion criteria. Primary outcome included function or disability evaluation. There was no statistically significant difference in knee function, pain and range of motion during the 12 month follow-up. Neuromuscular electrical stimulation was less effective than traditional rehabilitation in function, muscular strength and range of motion. Although postoperative treatment with NMES showed improvement in the femoral quadriceps function, due to the low quality evidence the clinical effectiveness of this intervention is unknown. No evidence indicated if NMES with physiotherapy provided benefits regarding the quality of life. There is insufficient

evidence to support neuromuscular stimulation for quadriceps strengthening with physical therapy before or after total knee replacement.

De Oliveira Melo et al. (2013) conducted a systematic review to identify the evidence for NMES for strengthening quadriceps muscles in elderly patients with knee osteoarthritis (OA). Inclusion criteria were randomized controlled trials comparing pre and post-intervention, elderly patients with clinical diagnosis of knee OA and outcome measurements of quadriceps muscle strength measured preferentially with an isokinetic dynamometer. Six randomized controlled trials (n=35–200) met inclusion criteria. Four studies included ≤ 50 patients. Study designs and outcome measures were heterogeneous and comparators varied. NMES parameters were poorly reported. The trials scored extremely low on the allocation concealment and blinding items. In most of the trials, the randomization methods were not described. Due to the poor methodology of the studies and poor description of the strength measurement methods, no or insufficient evidence was found to support NMES alone or combined with other modalities for the treatment of elderly patients with OA. Due to the study limitations, no meta-analysis was performed.

Giggins et al. (2012) conducted a systematic review and meta-analysis to assess the effectiveness of NMES for the treatment of knee osteoarthritis. Nine randomized controlled trials (n=395) and one controlled trial (n=14) were included. Outcome measures included self-reported disease-specific questionnaires and pain scales, strength measurements, knee range of motion, knee and thigh circumference and functional assessments. Two studies were considered of strong quality, four moderate and four of weak quality. Overall, there was inconsistent low level evidence that NMES significantly reduced pain and increased strength and function. Pooled analyses of six studies showed that NMES improved levels of self-reported pain and function, but not objective measures of function. The authors noted that the results should be interpreted with caution due to the heterogeneity of studies. Due to the conflicting data, definitive conclusions regarding the effectiveness of NMES for the treatment of knee osteoarthritis could not be made.

Stroke: 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 NMES in this patient population.

In a randomized controlled trial (n=60), Hsu et al. (2010) compared high-NMES and low-NMES to a control group (standard rehabilitation) for the treatment of upper-extremity function in acute stroke patients. The low NMES group received 30 minutes of stimulation per day and the high-NMES group received 60 minutes per day, five times per week, for four weeks. All patients received standard rehabilitation. Compared to the control group, the NMES groups showed significant improvement in the Fugl-Meyer Motor Assessment (p=0.003) and Action Research Arm Test scales (p=0.016) at week four and week 12. There were no significant differences between low- and high-NMES stimulation. No significant differences between the groups were reported on the motor activity log. Limitations of the study include the small patient population, short-term follow-up, and 12 patients lost to follow-up.

Professional Societies/Organizations:

In a 2017 clinical practice guideline on the treatment of low back pain, the Department of Veterans Affairs and the Department of Defense (VA/DoD) stated that there was no evidence found to recommend the use of electrical muscle stimulation for the diagnosis of low back pain.

Transcutaneous Electrical Nerve Stimulation (TENS)

A TENS device consists of an electronic stimulus generator that transmits pulses of various configurations through electrodes attached to the skin to stimulate the peripheral nerves for the purpose of pain management. 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. TENS has been used for a number of applications, including postoperative pain; acute and chronic pain, obstetrical pain, and pain associated with medical procedures.

U.S. Food and Drug Administration (FDA): TENS are approved by the FDA 510(k) process as a Class II device for the relief and management of chronic intractable pain. Examples of these devices include the Empi Active Transcutaneous Nerve Stimulator (Empi, Inc., Clear Lake, SD), TENS Stimulator AK-10M (ASTEK Technology Ltd, Tianan City, Taiwan), the StimPad™ TENS System (AEMED, Inc. West Palm Beach, FLA), JKH Stimulatory Plus (JKH USA, LLC, Diamond Bar, CA), the ReBuilder® (Micromed, Inc., Essex Junction, VT), TENS Stimulatory InTENSity 10 (Shenzhen Dongdixin Technology Co., Ltd., Shenzhen, CN), Nerivio Migra (Theranica Bio-Electronics Ltd, Netanya, Israel) the BiowaveHOME neuromodulation pain therapy device (Biowave Corporation, Norwalk CT), the Axon Therapy Device (NeuraLace Medical, Inc., San Diego, CA), and the TrueRelief Device (TrueRelief, Santa Monica, CA).

In 2014, the FDA approved the Cefaly Supraorbital Transcutaneous Neurostimulator (Cefaly-Technology, Herstal, Belgium) through the 510(k) de novo premarket review pathway, a regulatory pathway for generally low-to moderate-risk medical devices that are not substantially equivalent to an already legally marketed device. FDA classified the Cefaly as a Class II device indicated for the prophylactic treatment of episodic migraine in patients 18 years of age or older. FDA noted that this is the first TENS device approved for use prior to the onset of pain. In 2017 the Cefaly Acute and Cefaly Dual were FDA approved as 510(k) Class II TENS to treat headaches. The Cefaly Acute is “indicated for the acute treatment of migraine with or without aura in patients 18 years of age or older”. The Cefaly Dual is indicated for 1) the acute treatment of migraine with or without aura in patients 18 years of age or older and 2) the prophylactic treatment of episodic migraine in patients 18 years of age or older (FDA, 2017). The device is worn on the forehead for 20 minutes daily. It is proposed to externally stimulate the supraorbital and supratrochlear branches of the trigeminal nerve to normalize dysregulated pain pathways. These devices are also referred to as transcutaneous supraorbital neurostimulators (tSNS) or external trigeminal nerve stimulator (eTNS) (American Migraine Foundation, 2020; Lauritsen, et al., 2018).

In 2019, the FDA approved the Nerivio Migra trunk and limb electrical stimulator (Theranica Bio-Electronics Ltd, Netanya, Israel) through the 510(k) de novo premarket review pathway. FDA classified the Nerivio Migra device as a Class II device indicated for “acute treatment of migraine with or without aura in patients 18 years of age or older who do not have chronic migraine”. The device is self-administered by the user and worn on the upper arm for 45 minutes after the onset of migraine headache or aura. It is operated via software that is installed on a user’s personal mobile device. It is proposed to stimulate small peripheral nerves that, in turn, release neurotransmitters that inhibit the incoming messages of pain in the trigeminal cervical complex.

Literature Review - Acute Postoperative Pain The evidence in the peer-reviewed literature supports TENS for the treatment of pain in the acute post-operative period (i.e., within 30 days of surgery). Systematic reviews, meta-analysis and randomized controlled trials reported a reduction in pain and analgesic use in the treatment of acute post-operative pain and in some cases, shorter recovery times (Elboim-Gabyzon, et al., 2019; Li and Song, 2017; Zhu, et al., 2017; Sbruzzi, et al., 2012; Freynet and Falcoz, 2010; Bjordal, et al., 2003).

Literature Review - Other Indications: The evidence in the published peer-reviewed scientific literature has not established the effectiveness of TENS for the treatment of any other indications including, but not limited to: chronic low back pain; cervical pain; acute and chronic pain; acute and chronic headaches; migraines; abdominal pain; asthma; chemotherapy-induced pain; chronic leg ulcers; colonoscopy; drug withdrawal (e.g., opiate addiction); dysmenorrhea; fibromyalgia; fracture healing; hypertension; interstitial cystitis; knee osteoarthritis; mandibular disorders (e.g., neuromuscular orthodontics; temporomandibular joint [TMJ]); motion sickness; nausea and vomiting of pregnancy; postoperative nausea and vomiting; low back pain of pregnancy; pain associated with childbirth (i.e., labor); pelvic pain; post-traumatic acute pain; walking pain associated with peripheral artery disease; chronic anal fissure; rotator cuff tendinitis; stroke rehabilitation; suspected placental insufficiency; tinnitus; fecal incontinence; urinary incontinence; sickle cell disease; vestibulodynia; spasticity; and

unstable angina. Overall, systematic reviews, randomized controlled trials and case series have reported that there was no improvement with TENS for these indications or conclusions could not be made due to the poor methodology of the studies. Study limitations included small heterogeneous patient populations with short-term follow-ups, insufficient data or conflicting data, and heterogeneity of the application of TENS (e.g., physician applied vs. patient applied, location of electrodes). Evidence supporting TENS for these indications is lacking and TENS is not an established treatment modality. The clinical utility of TENS has not been established for all other indications.

Acute Pain: Johnson et al. (2015a) conducted a systematic review of randomized controlled trials to evaluate TENS as the sole treatment for acute pain (less than 12 weeks duration). Studies that met inclusion criteria compared TENS to placebo, no treatment, pharmacological interventions or non-pharmacological interventions. Nineteen studies (n=1346) met inclusion criteria. The types of acute pain included: procedural pain, (e.g., cervical laser treatment, venipuncture, screening flexible sigmoidoscopy) and non-procedural pain (e.g., postpartum uterine contractions, rib fractures). Data was pooled for pain intensity in studies comparing TENS to placebo, (n=6 trials), for subjects achieving $\geq 50\%$ pain reduction (n=4 trials), and pain intensity from noncomparative studies (n=5 trials). It was not possible to pool other data. There was some tentative evidence that TENS reduced pain intensity over placebo when TENS was administered alone. However, the reduction in pain was inconsistent across studies and there was insufficient number of patients to make a firm conclusion. Limitations of the studies included: high risk of bias, heterogeneity of patient populations, inadequate sample sizes in treatment arms and unsuccessful blinding of treatment interventions. The incomplete reporting of treatment made replication of many trials impossible. Adverse events included mild erythema and itching beneath the TENS pads and dislike of the sensations produced by the devices. The evidence does not support TENS for the treatment of acute pain.

Walsh et al. (2009) assessed the analgesic effectiveness of TENS in acute pain for adults (n=919) in a systematic review of 12 randomized controlled trials. The types of acute pain included procedural pain (e.g. cervical laser treatment, venipuncture, screening flexible sigmoidoscopy) and nonprocedural pain (e.g. postpartum uterine contractions, rib fractures). The authors were unable to make any definitive conclusions due to the insufficient extractable data.

Back Pain: Hayes (2018; reviewed 2019) conducted a technology assessment to evaluate the efficacy and safety of different forms of transcutaneous electrical nerve stimulation (TENS) compared with each other, with sham TENS, and with other minimally invasive nerve stimulation interventions for the treatment of adults with chronic low back pain (CLBP). Nine randomized controlled trials (RCTs) met the inclusion criteria. Interventions included: acupuncture-like TENS (AL-TENS), high-frequency TENS (HF-TENS), and low-frequency TENS (LF-TENS). Comparators were diadynamic current (DDC); high voltage electrical stimulation (HVES); interferential current (IFC); percutaneous electrical nerve stimulation (PENS); percutaneous neuromodulation therapy (PNT); and other TENS methods including sham. Outcome measures were pain, functional status, quality of life, sleep quality, physician rating of patient impairment, nonsteroidal anti-inflammatory (NSAID) and other analgesic use. Hayes described the body of evidence as moderate in size and low in overall quality. The available evidence did not support the use of TENS to relieve pain and/or improve pain. Three RCTs found that TENS was no more effective than sham and a fourth study reported mixed results depending on the outcome measure. Two RCTs found TENS to be inferior compared with PENS. One RCT found TENS to be inferior compared with PNT in some outcomes and no different in others. Another RCT found no significant differences between TENS and IFC, a second RCT found IFC to be superior; and a third study found TENS to be similar to HVES and superior to DDC. Different types of TENS were similar to each other in four studies. No serious complications were reported. Minor skin irritation at the electrode sites was the only TENS-related complication reported in the evaluated studies. Hayes concluded that there is no proven benefit of TENS in the treatment of chronic low back pain. No new studies were found in the 2019 Review.

Wu et al. (2018) conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) that compared the effectiveness of TENS to sham and other nerve stimulation therapies (NSTs) for the treatment of chronic back pain (CBP). Chronic pain was defined as pain lasting > 12 weeks. Twelve studies (n=700) met the inclusion criteria. RCTs were included if patients were age ≥ 18 years, treated for CBP, and the intervention compared TENS to sham, placebo, medication only or other types of nerve stimulation therapies (NSTs). Other NSTs included electroacupuncture (EA) (one study), percutaneous electrical nerve stimulation (PENS) and

percutaneous neuromodulation therapy (PNT). Studies were excluded if they did not provide numerical data regarding the degree of pain or disability. Letters, comments, editorials, and case reports were also excluded. The primary outcome was the difference in the mean change in pain from baseline to after the intervention. The secondary outcome was the difference between groups in improvement of functional disability. Nine TENS vs. sham/placebo studies reported pain scores before and after the intervention and were included in the meta-analysis. Patient populations ranged from 13–167 and follow-ups occurred at one week to three months. There was no significant difference in the improvement of functional disability in TENS vs. controls. For patients with a follow-up period of < 6 weeks, TENS was significantly more effective than sham in improving functional disability ($p < 0.001$). No significant difference in functional disability between the two groups was seen with a follow-up ≥ 6 weeks ($p = 0.707$). Five studies ($n = 19–102$) compared TENS to other NSTs. In patients with a follow-up period of < 6 weeks, other types of NSTs were significantly more effective than TENS in providing pain relief ($p = 0.021$). However, no significant difference in the pain relief was seen in patients with follow-up ≥ 6 weeks ($p = 0.326$). Only two studies provided disability data comparing scores before and after treatment and follow-ups were < 6 weeks. There was no significant difference in improvement between the two groups. Limitations of the analysis included the limited number of studies that met inclusion criteria, short-term follow-ups, and the small heterogeneous patient populations which limited the general applicability of the results. The results suggested that TENS does not improve symptoms of lower back pain, but may offer short-term improvement of functional disability. Additional RCTs comparing the efficacy of TENS and other established treatment modalities are needed to establish the clinical value of TENS for the treatment of this subpopulation.

Resende et al. (2018) conducted a systematic review and meta-analysis to evaluate the safety and effectiveness of transcutaneous electrical nerve stimulation (TENS) or interferential current (IFC) for the treatment of chronic low back pain (CLBP) ($n = 575$) and/or chronic neck pain (CNP) ($n = 80$). Nine randomized controlled trials met inclusion criteria and seven TENS studies with complete data sets were used for meta-analysis ($n = 655$). TENS was compared with sham TENS or standard of care. Studies were included if patients were age ≥ 18 years and had a diagnosis of non-specific CLBP and/or CNP. CLBP was defined as low back pain that had persisted for ≥ 3 months without radicular signs and was not caused by a primary conditions (e.g., cancer, multiple sclerosis, rheumatoid arthritis). CNP was defined as nonradicular pain located in the anatomical region of the neck that had persisted for ≥ 3 months and no specific cause had been identified (e.g., infection, neoplasms, metastasis, osteoporosis, rheumatoid arthritis, fractures or inflammatory processes). Studies were excluded if they reported subjects with acute or subacute pain or investigated subjects with medical diagnosis, signs or symptoms of radiculopathy, previous back surgery, pain conditions other than CLBP or CNP, mixed pain conditions and/or used a form of electrical stimulation other than TENS or IFC. The primary outcome measures included: pain intensity, visual analogue scale (VAS) and back function. Secondary outcomes were Short-Form Health Survey (SF-36), patient satisfaction survey and adverse events. Follow-ups ranged from immediately after to three months after treatment. Typically, treatment duration lasted 2–5 weeks, was performed 2–5 days per week, for 15–60 minutes. Only one trial evaluated subjects with chronic neck pain ($n = 80$) and one used TENS and IFC. Outcomes were conflicting. Four studies reported TENS was more effective than placebo/control for reducing pain intensity and four reported no significant difference in pain intensity between the groups. CLBP meta-analysis ($n = 148$) showed that TENS was significantly better in reducing pain than placebo/control ($p < 0.02$). TENS intervention was better than placebo/control during therapy ($p = 0.02$), but not immediately after therapy ($p = 0.08$) or 1–3 months following therapy ($p = 0.99$). Self-reported outcomes showed that TENS was no better than placebo for improving back function ($p = 0.68$). Limitations of the analysis includes the small number of studies with small patient populations, short-term treatment and follow-ups, and heterogeneity of treatment regimens, stimulation parameters and electrode placement. The authors noted that this systematic review provided inconclusive evidence of TENS benefits in the treatment of chronic low back pain.

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 week. 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 ($p < 0.001$). 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 ($p < 0.0001$) 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.

The Centers for Medicare and Medicaid (2012) conducted a systematic review of the literature to evaluate TENS for the treatment of chronic low back pain. Inclusion criteria included adults with chronic, persistent low back pain (with or without leg pain) for three months or more and used TENS for at least four weeks. Included clinical trials had a patient population of ten or more; well-defined comparators; and used all models, frequencies, and wave patterns of TENS. Studies that examined chronic low back pain in patients with pain related to malignancy, neurodegenerative diseases (e.g. multiple sclerosis) and well-defined rheumatic disorders (except for osteoarthritis) were excluded. Seven systematic reviews and five randomized controlled trials met the inclusion criteria. Relevant clinical practice guidelines were also considered. Following a review of the data, Medicare concluded that TENS did not produce a clinically meaningful reduction in pain, a clinically meaningful improvement in function or a clinically meaningful improvement in any other health outcomes. When compared to TENS, sham units provided equivalent analgesia. The authors also noted that the potential for significant bias in the studies included in this analysis limited their “confidence in the reported results of this body of literature”.

Buchmuller et al. (2012) conducted a 21-center, randomized controlled trial to evaluate the efficacy of TENS (n=117) compared to sham (n=119) in improving functional disability in patients with chronic low back pain (LBP), with or without radicular pain. Patients received treatment in four, one-hour daily sessions for three months. The primary outcome measure was improvement of functional status at six weeks based on the Roland–Morris Disability Questionnaire. Secondary outcome measures included functional status at three months, pain relief by weekly visual analogue scale (VAS) assessments, quality of life, use of analgesic and anti-inflammatory medication, satisfaction with the overall treatment strategy and compliance. Treatment was self-administered and recorded stimulation frequency and duration were checked at each study visit to verify compliance. Follow-ups occurred at 15 days, six weeks and three months. An improvement of at least 50% in lumbar pain between the first and last assessments was significantly greater in the TENS group (p=0.0003). The effect on pain intensity was particularly marked in the subgroup of patients with radicular pain. There were no significant differences between the groups in functional status at six weeks (p=0.351) or three months (p=0.816) or in any of the other outcome measures. Skin irritation was reported in 11 TENS patients and three sham patients. The authors noted that “the overall results of this study do not support the use of TENS in the treatment of patients with chronic LBP”. Limitations of the study include the short-term follow-up and heterogeneity of the patients.

Cancer Pain: 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.

Chronic Pain: Gibson et al. (2019) conducted a review of all Cochrane Reviews on the effectiveness of TENS for the treatment of chronic pain of any origin (e.g., rheumatoid arthritis, phantom stump pain, fibromyalgia, osteoarthritis). Studies evaluating headaches and migraines were excluded. All Reviews (n=9) of randomized controlled trials (RCTs) assessing the effectiveness of TENS versus sham; TENS versus usual care or no treatment/waiting list; TENS plus active intervention versus active intervention alone; comparisons between different types of TENS; or TENS delivered using different stimulation parameters were included. Primary outcomes included pain intensity and adverse effects. Secondary outcomes included: disability, health-related quality of life, analgesic medication use, and participant global impression of change. One review including five studies (n=207) reported a beneficial effect of TENS versus sham therapy at reducing pain intensity on a 0–10 scale (p<0.001). However, due to the significant methodological limitations the quality of the evidence was considered very low. Pooled analysis from a second study comparing TENS to sham and TENS to no intervention also reported a significant improvement with TENS. This analysis was also consider very low quality evidence due to significant methodological limitations and large between-trial heterogeneity. Due to the

methodological limitations and lack of useable data no meaningful conclusions could be made on the nature/incidence of adverse effects or the remaining secondary outcomes. Based on the poor quality of the evidence, including small patient populations, a determination on the benefits and harms of TENS for the treatment of chronic pain and its effect on disability, health-related quality of life, use of pain relieving medications, or global impression of change could not be made.

Colonoscopy: Amer-Cuenca et al. (2011) conducted a randomized controlled trial (n=90) to evaluate the effectiveness of TENS in controlling pain in unsedated patients undergoing screening colonoscopy. Patients were randomized to one of three groups: control group (n=30), active TENS (n=30), or placebo TENS (n=30). The control group received hospital standard protocol for unsedated colonoscopies without any kind of sedation or analgesia. Pain was assessed five minutes into the procedure and at the end of the procedure using a visual analogue scale (VAS) and a five-point Likert scale. The TENS group reported a $\geq 50\%$ reduction in the VAS scores compared to the placebo and control group ($p < 0.001$). There was also a significant reduction on the Likert scale scores in the TENS group compared to the placebo and control groups ($p = 0.009$). There were no significant differences between the groups in bloating sensation during the procedure and the duration of the procedure. Greater than 50% pain relief was achieved by 17 TENS patients, three placebo patients and six control patients ($p < 0.001$). Author-noted limitations of the study included: the active TENS group's experience of pain might have been affected by the potential distraction of continuously adapting stimulus intensity and the use of VAS as a measurement of pain. Another limitation is the small patient population.

Dementia: Cameron et al. (2003; updated 2005) conducted a systematic review on TENS for the treatment of dementia. Nine randomized controlled trials met inclusion criteria, and three were included in meta-analysis. A statistically significant improvement was reported immediately following therapy in: delayed recall of 8 words and motivation in one trial, each and face recognition in two trials and motivation in one trial. However, the authors concluded that there was insufficient data for definitive conclusions to be drawn.

Diabetic Neuropathy: 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.

Dysmenorrhea: In a systematic review of seven randomized controlled trials (n=164), Proctor et al. (2009) evaluated the effectiveness of low-frequency TENS (acupuncture-like TENS, 1–4 hertz [Hz]) and high-frequency TENS (conventional TENS, 50–120 Hz) (n=5) for the treatment of primary dysmenorrhea. Studies compared TENS to placebo, no treatment or medical treatment. Overall, high-frequency TENS was reported more effective than placebo TENS for relief of pain. There was no difference in pain relief with low-frequency TENS compared to placebo. There were conflicting results regarding whether high-frequency TENS was more effective than low-frequency TENS. Due to the small patient populations, various methods of the application of TENS, and the lack of precision in the comparisons, clear recommendations for clinical applications could not be made.

Fecal Incontinence: Edenfield et al. (2015) conducted a systematic review of the literature to assess the safety and effectiveness of cutaneous (TENS) and percutaneous posterior tibial nerve stimulation (PTNS) for the treatment of fecal incontinence. Regarding the use of cutaneous TENS, three randomized controlled trials and five case series met inclusion criteria. Outcomes included bowel diary information and generally reported improvement in fecal incontinence and bowel movement deferment time. Quality of life outcomes (coping, embarrassment, depression, general health) were conflicting. Some patients in sham groups reported improvement in symptoms. No serious adverse events were reported. Overall study quality was "poor" based on the study design. Some of the trials were pilot studies. Additional limitations of the studies included small patient populations (n=10-144) and short-term follow-ups (4-12 weeks) with maintenance sessions ranging from 1–40 months. Outcomes and treatment techniques were inconsistent. Well-designed randomized controlled trials with

large patient populations and long-term follow-up are needed to compare the effectiveness of TENS to conventional therapies.

Horrocks et al. (2014) conducted a systematic review to evaluate the safety and efficacy of posterior tibial nerve stimulation for the treatment of fecal incontinence. Five studies investigating cutaneous PTNS met inclusion criteria. Primary outcome measure was an improvement of at least 50% in the number of incontinent episodes. Secondary outcomes included reduction in weekly incontinent episodes, cure rates, improvement in incontinence scores and improvement in quality-of-life measurements. The proportion of patients who reported a reduction in fecal incontinence episode of at least 50% ranged from 0%–45% compared to baseline. In a randomized controlled trial, no significant difference was seen in TENS vs. sham and no patient had a 50% or greater reduction in weekly incontinence episodes. Overall, TENS stimulation of the posterior tibial nerve did not improve fecal incontinence.

Fibromyalgia: According to a 2020 article by Boomershine, fibromyalgia is the second most commonly encountered disorder by rheumatologists and is present in 3–5% of women and 0.5–1.6% of males in the United States. Additionally, fibromyalgia appears to affect African-American women more than white women, however “increased body pain and tenderness are associated with decreased socioeconomic status, so this may be an important influence on racial differences”.

Dailey et al. (2020) conducted a double-blind randomized controlled trial to determine if TENS use has a positive impact on movement-evoked pain and other secondary outcomes in women with fibromyalgia on a stable medication regimen. Female patients (n=301) aged 18–70 years were included in the trial if they: had a diagnosis of fibromyalgia, were on a stable medication regimen in the previous four weeks, and were projected to be on a stable medication regimen for the following two months. Patients were excluded from the trial if they: had a pain level < 4/10; had an inability to walk six minutes unassisted; used TENS in the past five years; had a pacemaker or metal implants in the spine; had a history of a neuropathic/ autoimmune disorder, spinal fusion, or epilepsy; had allergy to adhesive or nickel; were pregnant; or had a medical or psychiatric condition that would preclude participation. Patients were randomly assigned to receive either active TENS (n=103), placebo TENS (n=99), or no TENS at all (n=99). In the comparator placebo TENS group, patients received a TENS unit with attached electrodes that delivered stimulation for 45 seconds and then ramped down to no stimulation over the course of 15 seconds. All patients in either of the TENS groups were instructed to use TENS at least two hours per day every day during physical activity. All patients were screened for pain and fibromyalgia at visit one. Visit two occurred one week later at which time patients were assessed for pain again; randomized into treatment groups; administered a 30 minute treatment session; re-assessed for pain, function, and fatigue; and then given a TENS unit and instructions for home use for four weeks. Visit three repeated the treatment protocol from visit two however, after this visit all patients were given active TENS and then reassessed one month later. The primary outcome measured was movement-evoked pain assessed using a six minute walk and a five time sit to stand test. Fatigue, function, disease impact, quality of life, fear of movement and other psychological factors were secondary outcomes that were measured. Significant improvement was noted in movement-evoked pain in the active TENS group after four weeks of treatment compared to the placebo TENS group (p=0.008) and the no TENS group (p<0.0001). Resting pain was reduced significantly in the active TENS group after four weeks of treatment compared to the placebo TENS and no TENS groups (p<0.05). There were no significant differences noted between groups for rescue pain medication use after one month of treatment. The placebo TENS and no TENS groups experienced a significant reduction in movement-evoked and resting pain during the second phase of the trial in which all patients were administered active TENS (p<0.001) while the active TENS group continued to see further reductions in pain. Significant reductions in fatigue were observed in the active TENS group after four weeks of treatment compared to placebo TENS (p=0.001) and no TENS groups (p<0.0001). Patients in the active TENS group experienced significant reductions in disease impact and self-reported function compared to the no TENS group (p<0.001) but not compared to the placebo TENS group (p=0.074). There were no significant improvements noted between groups for performance-based function, physical activity, fear of movement, pain catastrophizing, self-efficacy, anxiety, quality of life, or depression. The most common adverse events reported (n=30 participants) were pain with TENS in all treatment groups and skin irritation at the site of electrode placement in the active TENS and placebo TENS groups. Author noted limitations of the study included: difficulty blinding patients to treatment allocation due to the presence of a perceptible stimulation with the active TENS device, non-compliance among the participants to fill out a symptom log, participant attrition, the fact that the study was performed in women only, and the short term follow-up. Additional limitations of the study

were the small patient population and an underrepresentation of non-White races (n=92% White) and Hispanic ethnicity (n=95% non-Hispanic) among the study participants. Due to the limitations of the study, conclusions about the safety and efficacy of TENS for fibromyalgia cannot be made and cannot be generalized across diverse patient populations.

Johnson et al. (2017) conducted a Cochrane review of randomized or quasi-randomized controlled (RCT) trials to assess the analgesic efficacy and adverse events of TENS for the treatment of fibromyalgia in adults. Primary outcomes were participant-reported pain relief from baseline $\geq 30\%$ or $\geq 50\%$ and Patient Global Impression of Change (PGIC). Eight RCTs (n=315) met inclusion criteria. Two studies compared TENS with placebo TENS (n=82). One study compared TENS with no treatment (n=43) and four studies compared TENS with other treatments including pharmacotherapy (n=74), electroacupuncture (n= 44), superficial warmth (n=32 participants) and hydrotherapy (n=10). Two studies compared TENS plus exercise with exercise alone (n=98). One study reported $\geq 30\%$ pain relief. No study measured participant-reported pain relief of 50% or greater or PGIC. Statistical pooling of outcomes was not possible because of the insufficient data and heterogeneous outcomes. No serious adverse events were reported. Due to the small patient populations, heterogeneity of study designs and low grade of evidence, the clinical benefit of TENS for the treatment of fibromyalgia could not be determined.

Labor: Bedwell et al. (2011) conducted a systematic review of randomized controlled trials comparing TENS to routine care or placebo devices for labor pain. Fourteen studies (n=1256) met inclusion criteria. TENS were applied to the back (n=11 studies), acupuncture points (n=2 studies) and in one study to the cranium. Primary outcome measures were pain intensity and patient satisfaction with pain relief. Secondary outcome measures included: duration of labor, cervical dilation on admission to hospital, augmentation of labor, other pain relief, assisted birth or caesarean section, side effects, and sense of control in labor. Outcomes for neonates included Apgar score (<7 at five minutes), cord pH (<7.1) and adverse events. Patients receiving TENS to acupuncture points were less likely to report severe pain. There were no significant differences in use of epidural analgesia or other types of analgesia between the groups, pain ratings and patient satisfaction. None of the studies reported information on Apgar scores or cord pH or women's sense of control in labor. There was no information that TENS affected any other outcomes on the mother or the baby. No adverse events were reported. The authors concluded that there was limited evidence that TENS reduced pain during labor but the "evidence is neither strong nor consistent". The use of TENS at home in early labor has not been evaluated. Author-noted limitations of the studies included: small patient populations, unbalanced study groups, heterogeneity of outcome measures, various type of TENS devices were used, TENS was offered alone or as an adjuvant therapy making it difficult to assess the true effect of TENS in some studies, and pain was measured in so many different ways it was not possible to pool results.

Mello et al. (2011) conducted a systematic review and meta-analysis to assess the effectiveness of TENS (n=529) compared to placebo or no TENS (n=547) for pain relief during labor including possible maternal and fetal complications. Nine randomized or quasi-randomized clinical trials (n=1076) with more than ten subjects met inclusion criteria. A meta-analysis of six studies demonstrated no evidence that TENS reduced the need for analgesia. There were no statistically significant differences between the groups in pain relief during labor. There was no evidence that TENS interfered in any of the outcomes except the mothers' desire to use TENS in future deliveries. The use of TENS had no impact on mother or child and no influence on labor. According to the results of this review, there was no evidence that TENS reduced the use of additional analgesia. The authors noted that no study carried out intention-to-treat analyses which may lead to overestimation of the treatment's clinical effect. Other noted limitations of the studies included a lack of uniformity in frequency or intensity of TENS, heterogeneity of the type of analgesia used, and the difficulty in measuring pain levels.

Migraine Headaches - Cefaly: There is insufficient evidence in the peer-reviewed literature to support TENS for the treatment of migraines, including the use of Cefaly devices. Studies investigating Cefaly are primarily observational in design and include small patient populations (n=23–90) with short-term follow-ups (e.g., two hours to four months) (Chou, et al., 2017; DiFiore, et al., 2017; Przeklasa-Muszyńska; Vikelis, et al., 2017; Miller, et al., 2016).

Tao et al. (2018) conducted a systematic review and meta-analysis of randomized controlled trials (four studies; n=161) to evaluate the effectiveness of TENS for the treatment of migraine headaches. The inclusion criteria were as follows: randomized controlled trials that compared TENS with sham, subjects age > 18 years, diagnosis

of migraine according to the International Classification of Headache Disorders (ICHD-II or ICHD-III beta version) and reported outcomes on migraine days, headache days, migraine attacks, pain intensity, painkiller intakes, adverse events and/or satisfaction. Exclusion criteria included: comparison with other therapies (e.g., medications, psychotherapy); application of invasive electrical nerve stimulation; and other types of trials such as cross-over designs, self-contrast trials and healthy controlled trials. The patient populations of the four studies ranged from 59–88 subjects and follow-ups occurred at 1–8 months. Pulsed TENS application was applied to supraorbital nerves (the branch of the trigeminal nerve), vagus nerve, occipital nerve and Taiyang (EX-HN 5) acupoints (trigeminal nerve indirectly) in various frequencies and amplitudes. Headache diaries were used to record pain control. The responder rate was significantly higher in TENS subjects compared to sham TENS subjects ($p < 0.001$). There was a significant reduction of the number of monthly headache days in TENS users ($p < 0.001$) and the use of pain medication ($p < 0.001$). TENS subjects reported a significantly higher level of satisfaction than sham patients. The most commonly reported adverse events were upper respiratory tract infections, facial pain and gastrointestinal symptoms which were considered mild to moderate and transient. Limitations of the analysis include: the limited number of studies, small patient populations, short-term follow-ups, and heterogeneity of treatment regimens (e.g., number of treatment sessions, stimulation parameters, stimulated nerve types). Due to the limitations of the studies and the risk of publication bias, the quality of the evidence was rated as low and the authors stated that no definitive conclusions could be made regarding the use of TENS for the treatment of migraines.

Schoenen et al. (2013) conducted a five-center randomized controlled trial ($n=67$) to assess the safety and efficacy of Cefaly in the Prevention of Migraine (PREMICE) study using Cefaly. Patients, age 18–65 years old, with migraines, with or without aura, experiencing at least two attacks per month were included in the study. After a one month run-in period, subjects were randomized to Cefaly or sham therapy for 90 days. Primary outcome measures included change in monthly migraine days between the run-in month and the third month of treatment and the percentage of “responders,” (i.e., at least 50% reduction of monthly migraine days). Subjects kept a diary of headache events and had a follow-up visit at day 45 and 90. In both groups, migraine days decreased by an average of 20% during month one. In months two and three the sham group did not maintain decreased migraines while the Cefaly group did. Between run-in and third month of treatment, the mean number of migraine days decreased significantly in the Cefaly group ($p=0.023$), but not in the sham group ($p=0.608$). The 50% responder rate was significantly greater in the study group ($p=0.023$). The number of monthly migraine attacks ($p=0.044$), monthly headache days ($p=0.041$) and monthly acute antimigraine drug intake ($p=0.007$) were significantly reduced in the study group but not in the sham group. There were no reported adverse events. Limitations of the study include self-reported outcomes, heterogeneity in patient demographics between the two groups (e.g., age, duration of migraines) and recruited patients were not the most disabled migraineurs. Published data from randomized controlled trials with large patient populations and long-term outcomes comparing TENS to conventional therapy are needed to establish the effectiveness of TENS/Cefaly for the treatment of migraines.

Migraine Headaches – Nerivio Migra: Yarnitsky et al. (2019) conducted a randomized, double-blind, sham-controlled, multicenter study to assess the efficacy and safety of a remote electrical neuromodulation (REN) device for the acute treatment of migraine. Adults ($n=252$), ages 18-75 years, were originally allocated to either active or sham group. A total of 45 patients did not start treatment within one hour of symptom onset or withdrew consent, leaving 207 patients. Patients were included if they had a history of 2-8 migraine headaches with or without aura per month, less than 12 headache days per month, and were on either no or stable migraine preventive medications in the last two months prior to recruitment. Exclusion criteria were: pregnancy, nursing, trying to conceive; pure menstrual migraine; implanted electrical device(s); treatment with Onabotulinumtoxin A in the prior month; nerve blocks in the preceding two weeks; current use of cannabis; uncontrolled epilepsy; received parenteral infusions for migraine in the preceding two weeks; other significant pain, medical or psychiatric illness that would confound the study assessments; inability to use a smartphone; and previous experience with REN in clinical trials for migraine. A smartphone-controlled wireless transcutaneous electrical nerve stimulation device (Nerivio Migra) was applied for 30-45 minutes on the upper arm within one hour of attack onset. Electrical stimulation was at a perceptible but non-painful intensity level. Sham stimulation served as the comparator. The primary outcome measure was the proportion of participants who achieved pain relief (improvement from severe/moderate pain to mild/none) at two hours post-treatment or improvement from mild pain to none at all. Most bothersome symptoms (MBS) including nausea, photophobia, and phonophobia and being pain-free at two hours were key secondary outcome measures. Migraine pain levels were recorded at

baseline, and at two, and 48 hours post-treatment. In the treatment group, 66/99 patients achieved statistically significant pain relief two hours post-treatment compared to 40/103 in the sham group ($p < 0.001$). More participants in the active group were completely pain-free at two hours post-treatment (37/99) compared with the sham group (19/103) ($p = 0.003$). The active treatment was significantly more effective (44/95) than sham for MBS relief (22/99) ($p < 0.001$) two hours post-treatment. Two hours following treatment the active treatment was also more effective (38/95) than sham (15/99) for combined pain and MBS relief ($p < 0.001$). There was no statistically significant difference between treatment groups for being completely MBS free (33/81 vs. 32/88) two hours post-treatment ($p = 0.55$). Significant sustained pain relief at 48 hours post-treatment was achieved in 34/87 patients in the active group and in 15/89 patients in the sham group ($p = 0.014$). Being pain free at 48 hours was achieved by more patients in the active group (18/87) compared to the sham group (7/89) ($p = 0.014$), which was statistically significant. Device-related adverse events included: warm sensation; temporary arm/hand numbness; redness; itching; tingling; muscle spasm; and pain in the arm, shoulders, or neck. An author noted limitation of the study was the low rate of severe baseline pain intensity and high rate of mild pain intensity (presumably due to the early treatment). Additional limitations of the study include: incomplete self-reported data and patient attrition.

Yarnitsky et al. (2017) conducted a randomized controlled trial to evaluate the efficacy of a remote TENS unit (Nerivio Migra) applied to the upper arm in reducing migraine pain. Patients ($n = 71$) between the ages of 22-72 years were evaluated (299 treatments) and were included if they experienced 2-8 attacks per month without preventive medications for at least two months prior to enrollment. Exclusion criteria included: presence of other significant pain problems (e.g., cancer pain, fibromyalgia, other head or facial disorders); severe cardiac or cerebrovascular disease; uncontrolled high blood pressure; implanted electrical or neurostimulation device; epilepsy; use of cannabis; chronic migraine; head or neck nerve block within the last two months; botox injections within the last six months; pregnant or planning pregnancy during the study period, or is in childbearing years and unwilling to use an accepted form of birth control; participation in another migraine clinical study; and lack of sufficient cognitive or motor skills needed to operate an android cell phone. The intervention consisted of a TENS device that was applied to the upper arm for 20 minutes, at pulse widths ranging from 50-ms - 200-ms soon after the onset of a migraine with or without aura. The device was controlled via a smartphone application and participants were instructed to refrain from medication use for two hours post treatment initiation. The comparator was sham consisting of a treatment protocol with no electrical stimulation delivered by the device. The primary outcome measures were the percentage of patients reporting a pain decrease of at least 50% as measured by the Numeric Pain Scale (NPS) at two hours posttreatment. Secondary outcome measures included: overall use of migraine medications during the study period, burden of treatment, and ease of device and application use. Pain responses were self-reported by the patients via the smartphone application at the onset of the migraine and at 10, 20, and 120 minutes after stimulation onset. At least 50% pain reduction was obtained for 64% of patients based on 200-ms, 150-ms, and 100-ms pulse width stimuli vs. 26% of sham-treated patients. For those patients initially rating their pain as severe or moderate, significant reduction to mild or no pain was reported by 58% (25/43) of participants for the 200-ms protocol and 24% (4/17) for placebo ($p = 0.02$). No adverse events related to the device and no side effects were reported. Limitations of the study include the small patient population, self-reported outcomes, and the fact that complete data was not reported by 30% of activations for 200, 150, and 100 pulse widths, 42% for activations for 50 pulse width, and 72% for placebo activations.

Neck Pain: Martimbianco et al. (2019) conducted a Cochrane review of randomized controlled trials (RCTs) to evaluate the effectiveness of transcutaneous electrical nerve stimulation (TENS) (alone or in association with other interventions) compared with sham and other clinical interventions for the treatment of chronic neck pain. Seven RCTs ($n = 651$) met inclusion criteria. Subjects had a mean age of 31.7–55.5 years with chronic neck pain lasting greater than 12 weeks. Most RCTs used a TENS current that created a tingling sensation without contraction in daily sessions lasting 20-60 minutes. The number of sessions ranged from 1-12 and the total duration of the treatment programs varied from 1-45 days. The control interventions consisted of sham TENS or another type of treatment. The primary outcomes were pain, disability and adverse events. The length of follow-up ranged from one week to six months. There was very low-certainty evidence from two trials about the effects of conventional TENS on pain when compared to sham TENS at short-term follow-up (up to 3 months after treatment). None of the included studies reported on disability or adverse events. Due to the heterogeneity in interventions and outcomes, meta-analyses did not take place. This review found very low-certainty evidence of a difference between TENS compared to sham TENS on reducing neck pain. At present, there is insufficient evidence regarding the use of TENS in patients with chronic neck pain.

Escortell-Mayor et al. (2011) conducted a 12-center randomized controlled trial to compare the effectiveness of TENS (n=43) to manual therapy (n=47) for the treatment of subacute or chronic mechanical neck disorders without neurological damage and followed for six months. Over half of the patients reported short-term effects following cessation of either therapy but at six months follow-up, success decreased in one-third of the patients. No significant differences were found between the groups in reduction of pain, decrease of disability or quality of life. No significant adverse events were reported.

Following a systematic review of randomized controlled trials regarding electrotherapy, including TENS, for neck pain, Kroeling et al. (2009) concluded that no definitive statements could be made regarding the efficacy and clinical usefulness of these modalities. Eleven TENS trials (n=7-30) met inclusion criteria including: TENS compared to placebo or another modality (i.e., ultrasound, manual therapy, electrical muscle stimulation); TENS plus another therapy (i.e., hot packs, infrared, exercises, neck collar and/or analgesic) compared to the other therapy alone; or different TENS regimens. The authors concluded that "very low quality" evidence showed that TENS might relieve pain better than placebo or electrical muscle stimulation but not as well as exercise and infrared and possibly as well as manual therapy and ultrasound.

Neuropathic Pain: Gibson, et al. (2017) conducted a Cochrane review of randomized controlled trials to determine the analgesic effectiveness of TENS versus sham TENS, TENS versus usual care, TENS versus no treatment and TENS plus usual care versus usual care alone for the management of neuropathic pain in adults. Fifteen studies met inclusion criteria (n=724). Duration of care ranged from four days to three months, There was sufficient data to conduct a pooled analysis for TENS compared to sham TENS (five studies). Insufficient data and large diversity in the control conditions prevented quantitative analysis for the remaining comparisons. Analysis of TENS versus sham TENS (n=207) showed a mean postintervention difference in effect size favoring TENS ($p < 0.00001$). However, the quality of evidence was rated very low. Data was lacking regarding the impact on quality of life. Six studies reported adverse events which were absent or minor and limited to 'skin irritation' at or around the site of electrode placement. Due to the very low quality of evidence, absence of data and the heterogeneity in TENS application times (15 minutes to one hour four times a day) and intensity of application conclusions could not be made regarding the benefit of TENS in the treatment of neuropathic pain in adults.

Osteoarthritis of the Knee: Hayes (2019; reviewed 2020) conducted a technology assessment to evaluate the safety and effectiveness of TENS for the treatment of knee osteoarthritis. Thirteen randomized controlled trials (RCTs) met the inclusion criteria consisting of the following: RCTs comparing TENS with sham/placebo, or other interventions (i.e., no TENS, exercise, medications, physiotherapy or other forms of electrical, ultrasound or laser therapies); patient populations ≥ 50 adults; investigated efficacy and safety of > 1 day of TENS treatment; included numerical data measuring pain and/or disability; and TENS was delivered as single modality or as part of multimodality if appropriate control was included to allow discrimination of TENS effect. Five studies comparing TENS versus sham, rated as low-quality evidence, concluded that TENS did not provide added benefits compared with sham TENS. One poor-quality RCT found that compared to sham TENS improved pain and function measures. Two fair-quality RCTs and two poor-quality RCTs found that TENS provided no additional benefit versus sham. Eleven studies provided inconsistent low-quality evidence regarding the relative effectiveness of TENS versus other interventions. Two poor-quality RCTs found TENS treatment to be more effective than other interventions in improving pain and other outcomes. Three poor-quality RCTs found no differences in outcomes between TENS and other interventions. One fair-quality RCT found mixed results for TENS versus other interventions, and two poor-quality RCTs favored other interventions versus TENS. A few cases of minor skin irritation were reported. No serious adverse events were noted. There is insufficient evidence to support TENS for the treatment of knee osteoarthritis. One new study was identified in the 2020 annual review consisting of a randomized controlled trial (n=148) comparing the efficacy of therapeutic ultrasound combined with TENS versus therapeutic ultrasound alone for pain relief and functional improvement in patients with symptomatic knee osteoarthritis. The authors concluded that adding transcutaneous electrical nerve stimulation to ultrasound demonstrated no additional beneficial effect over ultrasound alone in patients with symptomatic knee osteoarthritis.

Shimoura et al. (2019) conducted a single randomized controlled trial (RCT) with pre-post design to investigate the effect of transcutaneous electrical nerve stimulation (TENS) on knee pain and comprehensive physical function in preradiographic knee osteoarthritis (OA). Fifty patients with a knee pain Kellgren-Lawrence (K/L)

grade zero or one were randomly assigned to the TENS group (n=25) or the sham-TENS group (n=25). The inclusion criteria for the study were as follows: aged 50 years or older; K/L grades zero or one for one or both knees, evaluated using weight-bearing anteroposterior radiographs; and an average pain rating of 4–9 on a numeric rating scale (zero to ten points). Exclusion criteria were: symptomatic knee OA with K/L grade two or above; history of knee surgery; intra-articular injection within six months prior to enrollment; history of knee joint replacement or tibial osteotomy; undergoing physical therapy; any other major joint pain (e.g., back, hip, or ankle) that could limit functional ability; contraindications to the use of TENS; severe medical or nervous conditions; did not utilize stairs in daily living; and inability to walk without ambulatory assistive devices. All subjects wore the TENS device behind the patella of the symptomatic knee. After baseline measurement and a 30-minute rest period, the TENS devices in the TENS group were turned on. Those in the sham-TENS group were not connected. The primary outcome measure was assessment of pain using the visual analog scale (VAS) after the stair climb test, timed Up and Go (TUG) test, and the six-minute walk test (6MWT). Secondary outcomes included knee extensor strengths and the two-step test and stand-up test from the locomotive syndrome risk test. Follow-up assessment occurred after the 30-minute rest while wearing the TENS device in the on position for the intervention group and disconnected for the comparator group. TENS intervention significantly improved the walk distance and VAS score of the 6MWT (distance $p=0.015$; VAS $p=0.026$). No adverse events were noted with either groups. Author noted limitations of this study included the short-term follow up and possible selection bias due to the fact that the subjects obtained information regarding this study on a website. An additional limitation was the small patient population. Due to the limitations of the study, additional, high quality RCTs are needed to validate the outcomes of this trial.

Chen et al. (2016) conducted a systematic review of randomized controlled trials to evaluate the efficacy of TENS for the management of osteoarthritis of the knee. Eighteen trials (n=1260) met inclusion criteria and fourteen studies (n=639) were included in the meta-analysis. Study sample sizes ranged from 24–224 patients. Meta-analysis indicated that TENS significantly decreased pain ($p<0.00001$) compared with control groups. However, there was no significant difference in the Western Ontario and McMaster Universities Osteoarthritis Index ($p=0.09$) or the rate of all-cause discontinuation ($p=0.94$) between the TENS and control groups. There was no significant difference between the TENS and control groups in the pain-limited range of motion (ROM), total passive knee ROM, or “Timed Up-And-Go” test (time it takes to rise from sitting, walk to a designated line and return to seated position). TENS “might” significantly improve the maximum knee ROM on day 10 and during follow-up compared with the control group. Author-noted limitations of this analysis included: possible selection biases as only articles in English were included; small sample sizes prevented definitive conclusions from being drawn; substantial heterogeneity in study methodologies, outcome measures, and the presentation of data; short-term follow-ups; and the low quality of the studies. Finally, the authors explained that although the pooled estimate of the effects of TENS on pain relief was significant, it was below the 3-point reduction considered to indicate a clinically meaningful change. Therefore strong conclusion regarding the impact of TENS on pain relief for knee osteoarthritis could not be made.

Palmer et al. (2014) conducted a randomized controlled trial (n=224) to evaluate the effectiveness of TENS for the treatment of osteoarthritis (OA) of the knee. Exclusion criteria included comorbidities preventing participation in the knee group, contraindications to TENS or previous use of TENS. Patients, \geq age 18 years, with OA or suspected OA were randomized to one of three groups: TENS and knee group (n=73), sham TENS and knee group (n=74), or knee group alone (n=77). The knee group participated in a six-week group education and exercise program. The primary outcome was the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) function subscale. Secondary outcomes included WOMAC pain, stiffness, and total scores; extensor muscle torque; global assessment of change; exercise adherence; and exercise self-efficacy. All groups improved over time and the improvements were maintained at the 24-weeks follow-up. There were no significant difference between the outcomes in all three groups ($p>0.05$). The addition of TENS did not improve outcomes.

Phantom Pain and Stump 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.

Rotator Cuff Tendinopathy: Desmuelles et al. (2016) conducted a systematic review of randomized controlled trials to assess the efficacy of TENS for the treatment of rotator cuff tendinopathy in adults. Six studies met inclusion criteria. One placebo-controlled trial reported that a single TENS session provided immediate pain reduction for patients with rotator cuff tendinopathy but provided no short, medium or long-term follow-ups. Two trials compared TENS with ultrasound therapy and outcomes were conflicting regarding pain reduction and shoulder range of motion. Corticosteroid injections were reported superior to TENS for pain reduction in the short term, but the differences were not clinically significant. Other studies that compared TENS to heat or pulsed radiofrequency concluded that TENS was not superior to these modalities. Due to the limited number of studies and the overall high risk of bias of the studies, no conclusions could be drawn on the efficacy of TENS for the treatment of rotator cuff tendinopathy.

Sickle Cell Disease (SCD): Pal et al. (2020) conducted a Cochrane review of randomized controlled trials and quasi randomized controlled trials to determine the effectiveness of TENS vs. sham TENS for managing pain in people with SCD who experienced pain crises and/or chronic pain. One double-blind cross-over RCT met inclusion criteria (n=22). The trial was concluded after 60 treatment episodes (30 treatment episodes of each treatment group). Cross-over treatment design was unclear. The review reported a high risk of bias regarding random sequence generation and allocation concealment and an unclear risk regarding the blinding of subjects and personnel. The included trial did not report pain relief at two to four weeks post intervention. There were no differences in outcomes between the TENS and the sham groups. Additionally, analgesic usage did not show any difference between groups. Given the low quality of evidence, small patient population, high risk for bias, and the unclear cross-over treatment design, it is uncertain whether TENS improves overall satisfaction as compared to sham TENS. There is a need for well-designed, adequately-powered, RCTs to evaluate the role of TENS in managing SCD pain.

Spasticity: Fernandez-Tenorio et al. (2019) conducted a systematic review of randomized controlled trials (RCTs) to determine whether TENS is more effective than sham or alternative treatments for spasticity or any of its associated symptoms (spasms, clonus, etc.) when applied to patients with neurological disorders. Ten RCTs met inclusion criteria for patients with cerebrovascular accidents (n=207), multiple sclerosis (n=84), and spinal cord lesions (n=39). Additional inclusion criteria included: trials with at least one intervention group receiving TENS with surface electrodes, regardless of the area of application and stimulation parameters; current intensity was low enough not to cause muscle contraction; studies included variables quantifying spasticity or any of its associated symptoms (Ashworth Scale, H-reflex test, Penn Spasm Frequency Scale, clonus, Resistance To Passive Movement [REPAS] scale, etc.); and studies included a group receiving sham stimulation or an alternative treatment for spasticity. Exclusion criteria included: articles not applying TENS alone to any of the study groups and articles not specifying the pulse frequency, width, or intensity used. The RCTs used TENS described by the patient as a tolerable tingling sensation. The number of sessions in the studies ranged from 1-20. Most treatments ranged from 15-90 minutes with one treatment lasting eight hours. Comparators used were: baclofen, no treatment, sham, and cryotherapy. The primary outcome assessed was spasticity from a clinical viewpoint using the Ashworth Scale or the Modified Ashworth Scale, either in isolation for one or several joints or as a part of the Composite Spasticity Scale (CSS). Secondary outcomes included: strength in spastic patients, reflex amplitude and latency, functional disability, and functional independence. Follow up assessments occurred immediately after the intervention was applied. TENS was found to be superior to the sham treatment in three of the five studies using the CSS. Other studies using the Ashworth Scale or its modified version reported that TENS had similar or more beneficial effects than baclofen. In another study, CSS scores decreased faster in patients treated with TENS than in controls. Three studies have evaluated the effects of TENS on strength in spastic patients and the results for intra- and intergroup comparisons were controversial. No studies directly

demonstrated that TENS increased the strength of plantar flexor or dorsiflexor muscles significantly more than sham. No adverse events were reported. Limitations of the studies include: heterogeneity of the treatment regimen, small patient populations, and short term follow up. There is insufficient evidence to support TENS for the treatment of spasticity in patients with neurological disorders.

Stroke: Lin et al. (2018) conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) to evaluate the effectiveness of TENS in stroke patients. Seven studies met inclusion criteria (n=214) with the number of subjects per study ranging from 12–20 and mean time post-stroke ranging from 9.2 days to five years. The control for five studies was placebo TENS, one study used placebo without stimulation and one study used physiotherapy. The primary outcome was the modified Ashworth scale (MAS). Secondary outcomes included dynamic balance as evaluated by Timed Up and Go (TUG) test (time required for a patient to stand up from a 46-cm high chair, walk three meters, and return to the chair) and static balance with eyes open and closed. Three RCTs reported that TENS significantly reduced spasticity ($p=0.0006$). Compared with a control group, TENS did not alter dynamic balance. TENS significantly improved static balance with eyes opened ($p<0.0001$) and closed ($p<0.00001$), and walking speed ($p=0.03$). Limitations of the analysis includes the small patient populations, limited number of included studies, post-stroke time range (several days to several years) and the heterogeneity of the intensity, frequency of stimuli, and frequency of application of TENS. Randomized controlled trials with large patient populations and homogenous treatment regimens and follow-ups are needed to validate the significant findings of this analysis.

Ng and Hui-Chan et al. (2009) conducted a randomized controlled trial (n=109) to determine if TENS would improve functional walking performance (i.e., gait velocity, walking endurance and functional mobility) in hemiparetic stroke patients with spastic plantar flexors. In addition to a control group (n=29), patients were assigned to one of three intervention groups: TENS only (n=28), TENS plus exercise (n=27) or placebo stimulation plus exercise (n=25). Each patient self-administered 20 sessions, five days per week for four weeks. Each group received 60 minutes of TENS and the exercise groups received an additional 60 minutes of exercise following TENS or placebo stimulation. Final follow-up occurred four weeks after the treatment ended. At the final follow-up compared to all other groups, significant improvements were seen in the TENS plus exercise group in gait velocity ($p<0.001$) and reduction in timed up and go scores ($P<0.01$). The TENS plus exercise group covered significantly more distance in the 6-minute walk test (6MWT) ($p<0.01$) compared to the control group and the TENS only group. Additional studies with larger patient populations and long-term follow-up are indicated to validate the results of this study. The generalizability of this study is limited to stroke patients with moderate to severe spasticity in the ankle plantar flexors. The frequency, duration, and intensity of combined rehabilitation programs have not been established.

Yan et al. (2009) conducted a randomized controlled trial (n=62) to investigate whether TENS, when applied to acupuncture points in patients after acute stroke, decreased spasticity and/or increased muscle strength and was more effective than placebo stimulation and standard rehabilitation. Patients were randomized to TENS, placebo-TENS, or standard rehabilitation. Stimulation was applied to four acupuncture points in the affected lower leg for 60 minutes, five days a week for three weeks. Compared to placebo or rehabilitation, TENS significantly increased the number of patients with normal tone and ankle dorsiflexor strength and decreased the co-contraction ratio ($p<0.05$). Overall, the TENS patient walked two to four days earlier than the other patients, but the difference was not significant between the three groups. Limitations of the study include the small patient population and short-term follow-up.

Urinary Incontinence and Infections: Monga et al. (2012) conducted a systematic review to evaluate electrical stimulation therapies (i.e., TENS, sacral nerve stimulation, percutaneous posterior tibial nerve stimulation) for the treatment of lower urinary tract infections (LUTI). A total of 73 studies including randomized controlled trials (RCTs), case series and retrospective reviews met inclusion criteria. Thirteen studies (n=377), including three RCTs, three comparative studies and seven case series investigated outcomes using TENS. The studies included treatment of pediatric populations, detrusor instability, overactive bladder syndrome, various LUTIs, and irritative voiding dysfunction. Comparators included placebo stimulation, medical therapy, percutaneous neuromodulation, biofeedback or no treatment. The authors concluded that it was not possible to make any meaningful generalizations related to outcomes for the TENS studies due to the significant heterogeneity of the mode of therapy delivery, definition of patient subgroups, and outcome measures.

Vestibulodynia: Murina et al. (2008) assessed the efficacy of TENS in the treatment of 40 women with vestibulodynia. The women were randomized to either TENS or sham and received treatment twice a week for 20 sessions. At the three month follow-up, visual analogue scale scores and short-form McGill-Melzack Pain Questionnaire scores improved significantly ($p=0.004$, $p=0.001$, respectively) in the TENS group compared to the sham group. Three of 15 women in the TENS group relapsed three months following the end of the study. No adverse events were reported. Limitations of the study include the small patient population and short-term follow-up.

Professional Societies/Organizations: The American College of Physicians 2017 guidelines on noninvasive treatments for acute, subacute and chronic low back pain stated that there was insufficient evidence to determine the effectiveness of TENS for the treatment of low back pain.

Following a systematic review of non-pharmacological treatment modalities for dementia, the Department of Veterans Affairs Health Services Research and Development Services (VA/DOD) (2011) stated that three randomized controlled trials found no significant effects on sleep disturbance or behavioral symptoms following treatment and six-weeks thereafter. Possible benefits of TENS for the treatment of dementia could not be made.

The VA/DOD (2019) practice guideline on the management of stroke rehabilitation stated that the benefits of using TENS outweigh the harms and could provide improved function over standard of care. Based upon the very low level of evidence and the potential for benefit, a “weak for” recommendation was given for using TENS as an adjunctive treatment to improve upper and lower extremity motor function.

The Department of Veterans Affairs and Department of Defense (VA/DoD) stated in a 2020 clinical practice guideline on the management of headache that a recommendation either for or against the use of supraorbital electrical stimulation for the treatment of headache could not be given due to insufficient evidence.

In a 2020 clinical practice guideline on the management of hip and knee osteoarthritis, the Department of Veterans Affairs and Department of Defense (VA/DoD) stated that a recommendation could not be given for or against the use of transcutaneous electrical nerve stimulation for the treatment of osteoarthritis of the knee because there is insufficient evidence.

The Department of Veterans Affairs and Department of Defense (VA/DoD) stated in a 2017 clinical practice guideline on the diagnosis and treatment of low back pain that the evidence is inconclusive on the use of transcutaneous electrical nerve stimulation (TENS) for the treatment of low back pain. The guidelines notes that the data did not find significant differences in patient outcomes with the use of TENS.

In practice guidelines for chronic pain management, the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine (2010) recommended TENS as part of a multimodal approach to pain management for the treatment of patients with chronic pain (e.g., back pain, neck pain, phantom limb pain). A meta-analysis of randomized trials comparing TENS to sham for back pain reported greater relief for assessment periods of one hour to one month. Observational studies reported that TENS improved pain scores for a variety of conditions for 3–6 months.

In a 2010 (reaffirmed 2018) technology assessment on the efficacy of TENS in the treatment of pain in neurologic disorders, the American Academy of Neurology (AAN) stated that based on the available evidence, TENS is not recommended for the treatment of low-back pain. There are conflicting reports on TENS compared to sham-TENS but the stronger evidence established TENS as ineffective for back pain. Based on two studies comparing TENS to sham-TENS ($n=19$ and 31) and one study comparing high-frequency muscle stimulation to TENS ($n=41$), AAN stated that TENS is “probably effective” in reducing diabetic peripheral neuropathy pain.

In a joint clinical practice guideline on the diagnosis and treatment of low back pain, the American College of Physicians and the American Pain Society point out that TENS is not a recommended treatment option for low back pain as the evidence is of low quality with variable results (Chou, et al., 2007).

The 2013 American Academy of Orthopedic Surgeons (AAOS) guidelines for treatment of osteoarthritis of the knee stated that evidence from a single low quality study or conflicting findings does not enable AAOS to make

recommendations for or against the use of physical agents, including electrotherapeutic modalities (e.g., TENS). The evidence was mixed regarding efficacy and the outcomes in the limited number of studies were conflicting.

The American College of Rheumatology's (ACR) 2019 recommendation on the treatment of osteoarthritis of the hand, hip, and knee, "strongly" recommended against the use of TENS stating that the available literature is limited to low quality studies with small patient populations and heterogeneous design. (Kolasinski, et al., 2020).

Conductive Garments

Conductive garments are fabric electrodes placed between an electrical stimulator and a patient's skin for the delivery of electrical stimulation. They are an established alternative to standard electrodes and aid in the treatment of patients with chronic pain who have large areas or a large numbers of sites to be stimulated or the frequency is such that it is not feasible to use conventional electrodes, tapes or lead wires. The electrodes may also be indicated when sites requiring stimulation are not accessible by the patient with conventional electrodes, tapes or lead wires (i.e., back) and/or when medical conditions (e.g., skin problems) preclude the use of conventional electrodes, tapes or lead wires.

U.S. Food and Drug Administration (FDA): AG Garments (San Diego, CA) conductive electrodes are Class II, 510(k) approved by the FDA "as reusable (by a single patient), cutaneous, flexible, conductive garment/fabric electrodes for interface between electrical stimulators and a patient's skin for the delivery of electrical stimulation" (FDA, 2002). Additional examples of conductive garments are the Dr-Ho's Foot Pad Electrode (Guangzhou GLOMED Biological Technology CO., LTD, Guangdong, China) and the Wrap Accessory Electrodes (Hi-Dow International Inc., Maryland Heights, MO).

Other Electrical Stimulation Therapies

Auricular Electroacupuncture

Auricular electroacupuncture, auricular electrostimulation or electrical auriculotherapy, is electrical stimulation of auricular acupuncture points. Auricular therapy (AT) is most commonly based on the theory that the outer ear has a somatotopic map and each part of the auricle corresponds to a specific part of the human body or organ. By stimulating ear acupoints, AT is proposed to produce a positive impact by rebalancing the central nervous system and treat a specific malfunctioning organ or systemic illness by applying a TENS unit to the correlating part of the external ear. Electrical auriculotherapy has been suggested for use for smoking cessation, substance abuse, obesity, adrenal disorders, acute and chronic pain control, headaches, arthritis, vertigo, high blood pressure, inflammation, musculoskeletal disorders, relaxation, sciatica, stress, depression and swelling (Schukro, et al., 2013).

U.S. Food and Drug Administration (FDA): Devices used for electro acupuncture are 510(k) approved by the FDA as a Class II device using product classification code BWK. Examples of these devices are the ACULIFE/Model IDOC-0I (Inno-Health Technology, Co., Ltd. Taiwan, Republic of China), E-pulse model UH 900 (AMM Marketing LLC, Coral Springs FLA) and Stivax System (Biegler GmbH, Bonita Springs, FLA) which were approved as predicate devices for the PStim™ (NeuroScience Therapy Corp). In 2021, the AXUS ES-5 Electro-Acupuncture Device was granted 510(k) approval using the ACULIFE device as the predicate. The devices are approved "for use in the practice of acupuncture by qualified practitioners of acupuncture as determined by the states".

Literature Review: There is insufficient evidence in the published peer-reviewed scientific literature to support the effectiveness of auricular electroacupuncture. A limited number of randomized controlled trials have included small patient populations (n=14–44) with a limited number of sessions (e.g., one) and short-term follow-ups (e.g., three months). Outcomes are conflicting and no significant differences for some outcome measures (e.g., postoperative laparoscopic pain; heart rate, blood pressure, overall quality of life) have been reported. Studies were conducted to evaluate various conditions and indications including: hypertension, decrease the need for anesthesia; treatment for cervical pain, postsurgical gynecological pain and rheumatoid arthritis; chronic kidney disease, measure vagal activity in men; treatment of cancer pain, and for the treatment of depression (Kim, et al., 2016; Yeh, et al., 2015; Hein, et al., 2013; Holzer, et al., 2011; Tsang, et al., 2011; La Marca, et al., 2009; Sator-Katzenschlager, et al., 2003; Greif, et al., 2002; Ruela et al., 2018).

Zhao et al. (2015) conducted a systematic review of randomized controlled trials (RCTs) to assess the safety and efficacy of auricular therapy (AT) for the management of chronic pain. Subjects were age > 18 years with any chronic pain syndrome (pain for > 3 months). Trials compared AT (auricular acupuncture, auricular acupressure or auricular electro-stimulation, etc.) to one or more of the following: sham AT, waiting-list, standard medical treatment or no treatment. Five studies included auricular electrostimulation for the treatment of low back pain, rheumatoid arthritis, neck pain and miscellaneous chronic pain. Subgroup meta-analysis (four studies; n=131) showed a significant improvement in pain ($p=0.01$) with auricular electrostimulation compared to the control group interventions. Limitations of the studies included: small, heterogeneous patient populations, heterogeneous acupoints and treatment regimens, short-term treatment sessions, and short-term follow up. Due to the significant clinical heterogeneity and methodological flaws identified in the analyzed trials, there is insufficient evidence to support auricular electrostimulation for the treatment of chronic pain management.

A systematic review including 43 randomized and nonrandomized controlled trials (Tan, et al., 2014) reported that adverse events from the use of auricular therapy included: skin irritation; local discomfort and pain; and minor infection. The events were transient, mild and tolerable. No serious adverse events had been reported.

Hayes (2012; reviewed 2014) conducted a search of the literature and reported on seven randomized controlled trials evaluating the safety and efficacy of PStim. Four studies that investigated acute peri- and postoperative pain reported conflicting results. The studies used PStim for pain from tooth extraction, laparoscopy, intraoperative oocyte retrieval and tonsillectomy. Compared to sham, three studies reported no improvement in pain or use of analgesic medication. Two additional studies reported an improvement with PStim for the treatment of chronic cervical pain and low back pain. According to Hayes, the overall quality of the evidence was low due to the limited number of studies and small patient populations. Only subjective outcome measures were used and the majority of studies did not report functional outcomes or physical or psychosocial quality-of-life measures. No severe, long-term adverse events have been reported. Additional well-designed studies are needed to establish long-term effects and treatment regimens. The 2014 Hayes annual review found no new published studies.

Yeh et al. (2014) conducted a systematic review and meta-analysis of randomized controlled trials to assess the efficacy of auricular therapy compared to sham therapy. A total of 22 randomized controlled trials met inclusion criteria and 13 were used for meta-analysis. Auricular acupressure, auricular acupuncture and electroacupuncture were evaluated. Included studies had to compare auriculotherapy to sham and/or standard medical care with wait-list control and use a validated pain outcome measurement (e.g., Visual Analog Scale for Pain [VAS Pain], Numeric Rating Scale for Pain [NRS Pain], or McGill Pain Questionnaire. In the two studies using electroacupuncture stimulation (EAS), EAS was found to be nonsignificant for pain reduction compared to sham or control group.

Sator-Katzenschlager et al. (2004) conducted a randomized controlled trial to compare the results of auricular electroacupuncture (EA) (n=31) to conventional auricular acupuncture (CA) (n=30) for the treatment of chronic low back pain. Common low back pain of muscular origin was noted in 36 subjects and 25 additional patients had skeletal changes. Treatment was administered once a week for six weeks and needles were withdrawn 48 hours after insertion. Follow-up occurred at three months. During the study period and at three months follow-up, patients completed the McGill questionnaire. The Visual Analog Scale was used to assess psychological well-being, activity level, quality of sleep, and pain intensity. Analgesic drug use was also documented. Compared to the CA group, the EA group reported a significant improvement in pain relief ($p<0.001$), psychological well-being, activity, sleep and analgesic consumption ($p<0.001$). More patients in the CA group returned to work ($p=0.0032$). There were no reported adverse side effects. An author-noted limitation of the study included the lack of a placebo-controlled group. Additional limitations include the small patient population and short-term follow-up.

Moura et al. (2019) conducted a systematic review and a meta-analysis of randomized controlled trials (RCTs) to investigate the action of auricular acupuncture for chronic back pain in adults. The analysis included identifying the most commonly used outcomes for assessing this condition, the protocol used for applying the intervention, and the efficacy of the therapy on pain intensity. A total of 22 studies were included in the review. Ages of the individuals ranged from 18-90 years. Subjects 18 years or older with chronic pain (three months or more) in either the cervical, thoracic, and/or lumbar spine were included. Studies that did not provide the full abstract online and studies with pregnant women were excluded. The intervention consisted of auricular acupuncture

(e.g., needle puncture, pressure, electrical stimulation, magnetic stimulation). Three studies evaluated auricular acupuncture with electric stimulus (n=94). The comparators for these three studies included auricular acupuncture with electric stimulus on points that did not correspond to the affected areas and auricular acupuncture without electric stimulus (n=47). The primary outcome was pain intensity. Secondary outcome measures included: analgesic consumption, lumbar spine flexibility, psychological well-being, activity level, sleep quality, and treatment satisfaction. The auricular electro acupuncture was left in place for two days, every week, for six weeks for two of the studies and was applied one time for 30 seconds to each of six application points in the third study. Follow up varied and occurred immediately post intervention or weekly based upon the treatment regimen. The meta-analysis showed that auricular acupuncture was effective in reducing pain intensity scores compared to the control ($p=0.038$); however, the data did not reflect that the outcomes were statistically significant. There were no adverse events reported. Author noted limitations included lack of information for the measurement and mismatches in the randomization and masking process. Additional limitations include the heterogeneity of the intervention protocol, the small patient population, and the short-term follow-up. Additional, high quality studies are needed to validate the findings of this review.

Sibbritt et al. (2018) conducted a systematic review and meta-analysis of 59 randomized controlled trials (RCTs) to identify and summarize the evidence of acupuncture interventions for those people with lifestyle risk factors for stroke, including alcohol-dependence, smoking dependence, hypertension, and obesity. Eight studies evaluated auricular electro-acupuncture as the intervention including one study for alcohol dependence (n=59), four studies for smoking dependence (n=430), and three studies for obesity (n=166). RCTs focusing on the efficacy and safety of acupuncture for the aforementioned lifestyle risk factors were included. RCT protocols, observational studies, quasi-pseudo RCTs, cross-over RCTs, studies focusing on complications of stroke risk factors, conference abstracts, and contemporary acupuncture such as trigger points and dry needling were excluded. The auricular electro-acupuncture interventions for each of the three lifestyle risk factors had a high degree of heterogeneity for the treatment program frequency, duration, and intensity (e.g., 20 minute sessions for two weeks, 30 minute sessions weekly for 24 weeks). Comparators for the studies included: individual counseling, group therapy, sham, and nonspecific acupuncture group. The primary outcomes were body weight (BW), body mass index (BMI), and waist circumference (WC) for obesity-focused RCTs; alcohol craving, completion rate of treatment, and withdrawal symptoms for alcohol-dependence RCTs; and withdrawal symptoms, daily cigarette consumption, and abstinence rate for smoking-dependence RCTs. Heterogeneity existed in the follow-up time frame between the various studies ranging from four weeks to six months based upon the intervention and in several studies was not documented at all. Meta-analysis was not conducted on the alcohol-dependence study due to heterogeneity on interventions and outcome measures. Sub-group meta-analysis for smoking dependence did not show a significant improvement in smoking withdrawal symptoms ($p=0.12$), short term smoking cessation rate ($p=0.44$), or long term smoking cessation rate ($p=0.82$). Although sub-group meta-analysis for obesity did not show a significant improvement in body mass index ($p=0.81$) statistically significant improvement was reported for waist circumference ($p<0.001$). Adverse events included: drowsiness, transient bleeding on needle removal, and pain for the alcohol dependence studies; soreness, itch, and pain of ears for the smoking dependence studies; and skin irritation for the obesity studies. Author noted limitations included the heterogeneity of the interventions. Additional limitations of the study include: the presence of add-on strategies in the treatment group (e.g., conventional treatment, medication usage), patient attrition during follow up, small sample sizes of the individual studies, failure to blind patients and personnel, and incomplete outcome data reporting. This review found no convincing evidence to support the effects of acupuncture interventions for improving lifestyle risk factors for stroke.

Bioelectric Nerve Block (Electroceutical Therapy)

Bioelectric therapy, also known as electromedicine, noninvasive neuron-blockade devices, electroceutical neuron-blockade devices and bioelectric treatment systems, is proposed as a treatment for acute and chronic pain (e.g., back pain, diabetic pain, joint pain, fibromyalgia, headache, and reflex sympathetic dystrophy). Electroceutical treatments use much higher electrical frequencies than TENS units (ranging from one to 20,000 Hz compared to 0.5 to 100 Hz used in TENS).

U.S. Food and Drug Administration (FDA): An example of a device used for bioelectric therapy is the Matrix PRO ElecDT (Matrix Electromedical, Inc., Las Vegas, NV) which was 510(k) approved by the FDA as an interferential current therapy device.

Literature Review: There is insufficient evidence in the published peer-reviewed scientific studies to support the safety and effectiveness of bioelectric therapy. Well-designed, randomized controlled clinical studies are needed to determine the clinical utility of electroceutical therapy in the treatment of patients with acute or chronic pain.

Combination Therapy

Combination therapy is delivered with devices that are capable of providing more than one electrical stimulation modality such as transcutaneous electrical stimulation along with interferential current therapy and galvanic direct current stimulation by changing the electrical stimulation parameters on the device. They are proposed for a number of indications including but not limited to chronic intractable pain, post-surgical pain, muscle re-education, and thrombosis prevention.

U.S. Food and Drug Administration (FDA): The Neufit Neubie device originally received FDA approval through the 510(k) process in 2001 as a Class II medical device and is known under several proprietary names including: AP439, HILL IFC Interferential Unit, Neubie, and Neuro-M Trainer Model A. It is capable of providing transcutaneous electrical nerve stimulation (TENS), interferential current therapy (IFT), and galvanic direct current continuous stimulation. It uses direct current (DC) as opposed to traditional TENS units that use alternating current (AC). The Flex-MT+ received FDA approval in 2014 through the 510(k) process as a Class II medical device. It is capable of providing TENS and electrical muscle stimulation therapy.

Both devices are indicated for:

- Chronic intractable, acute post traumatic, and acute post-surgical pain
- Muscle spasm relaxation.
- Venous thrombosis prevention
- Increase of circulation
- Prevention or retardation of disuse atrophy
- Muscle re-education
- Maintaining or increasing range of motion

Literature Review: There is a paucity of published literature to support the use of combination devices. As such, conclusions about the safety and efficacy of the use of combination units cannot be made.

Cranial Electrical Stimulation

Cranial electrical stimulation (CES), also called electrotherapy, electrotherapeutic sleep, electrosleep, electric cerebral stimulation, cranial transcutaneous electrical nerve stimulation, cerebral electrotherapy, transcranial electrotherapy, transcranial electrical stimulation (tES), transcranial direct electrical stimulation (tDCS), transcerebral electrotherapy, neuroelectric therapy, and craniofacial electrostimulation, delivers low level electrical stimulation (i.e., microcurrent) to the brain through electrodes that are attached to the ear lobes or behind the ears. It has been proposed that CES's direct effect on the brain's limbic system, hypothalamus, reticular activation system, and/or the autonomic nervous system can control the symptoms of various conditions. CES has been proposed for the treatment of anxiety, depression, insomnia, substance abuse, fibromyalgia, Alzheimer's, attention-deficit/hyperactivity disorder (ADHD), asthma, bipolar depression, obstructive sleep apnea, spastic colitis, tension headaches, cluster headaches, migraines, hypertension, hot flashes, tinnitus, preoperative relaxation, aphasia and functional ability following stroke, chemotherapy symptoms in cancer patients, burn patients, multiple sclerosis, and other pain-related disorders (Liu, et al., 2019; Woodson, et al., 2016; Mao, et al., 2015; McClure et al., 2015; Barclay and Barclay, 2014; Kavirajan et al., 2014, Rose, et al., 2009). This therapy is not to be confused with transcranial magnetic stimulation or vagus nerve stimulation.

U.S. Food and Drug Administration (FDA): CES devices are approved under the FDA 510(k) class III process for the treatment of insomnia, depression, or anxiety. Examples of these devices include the Cranial Electrical Nerve Stimulator (Johari Digital Healthcare Ltd., Fall CITY, WA), Alpha-Stim® (Electromedical Products, Inc., Hawthorne, CA), LISS Cranial Stimulator and Fisher-Wallace Cranial Stimulator (Medical Consultants Intl. Ltd., Glen Rock, NJ), and the Cervella Cranial Electrotherapy Stimulator (Innovative Neurological Devices LLC, Carmel, IN). Some devices are approved for use by the patient at home.

Literature Review: The evidence in the published peer-reviewed literature does not support the effectiveness of CES for any indication. Studies consist of randomized trials with small patient populations, short-term follow-ups, and conflicting outcomes.

Alzheimers: Rose et al. (2009) conducted a randomized controlled trial to compare the short-term effects of CES (Alpha-Stim) (n=19) to sham stimulation (n=19) on sleep disturbance, depressive symptoms, and subjective appraisal in individuals who were the primary caregivers for spouses with Alzheimer's disease. Subjects used CES 60 minutes per day for four weeks and completed a daily log. At the end of four weeks, there were no significant differences in overall sleep disturbances, sleep quality, or sleep onset latency scores. The CES group did report a nine-minute decrease in sleep onset latency compared to a one minute increase in the sham group. There were no significant differences between the groups in depressive symptoms or in burden, mastery, impact or satisfaction of the care giving situation.

Anxiety and Depression:

Borrione et al. (2018) conducted a systematic review of randomized controlled trials investigating transcranial direct current stimulation (tDCS) for the treatment of the acute phase of major depressive disorder. Fourteen randomized clinical trials (n=898) met the inclusion criteria. Double-blind, randomized, sham-controlled trials investigating tDCS with primary clinical and therapeutic outcomes in depression scale scores were included. Studies investigating bipolar depression as per Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria, "major depressive episode" in unipolar and bipolar depression were also included. Studies with duplicated data, involving other psychiatric disorders (e.g., schizophrenia, obsessive-compulsive disorder) or other types of noninvasive brain stimulation (e.g., repetitive transcranial magnetic stimulation, electroconvulsive therapy) were excluded. Most studies were pilot studies and reported mixed outcomes but outcomes were primarily negative. Some studies reported positive effects with sham therapy. Limitations of the studies included the heterogeneous, small patient populations (n=9–245; mean 64.1) that included unipolar, bipolar and secondary depression patients with and without antidepressant therapy. Substantial variation was seen in the sham and the tDCS approaches including electrode placement, stimulation parameters, and number of treatment sessions. Patient selection criteria and tDCS treatment parameters have not been established. The current role of tDCS in the treatment of depression has not been established.

In a systematic review of the literature, a Hayes Health Technology Assessment (2017; reviewed 2020) identified eleven randomized controlled trials, randomized comparative studies or randomized crossover trials (n=22–245) that met inclusion criteria and evaluated transcranial direct current stimulation (tDCS) for the treatment of chronic and/or severe depression. Adults underwent therapy primarily for unipolar depression that was not secondary to other disorders or conditions such as stroke, epilepsy, cancer, recent childbirth, or substance abuse. Four studies included patients who had treatment-resistant depression and two studies enrolled patients who had bipolar disorder. In the studies that found tDCS beneficial, patients typically had mild depression after completion of treatment. Some studies had no follow-up and those that did were for one month or less. Comparators included sham therapy, antidepressant medication, and/or cognitive control training. Hayes reported that although it was a large body of evidence, the quality of the studies was low. Studies were limited by small patient populations, inconsistencies in findings, heterogeneity of treatment regimens, high dropout rates, small number of treatment sessions, crossover design with no washout period, and limited or no follow-up to assess the duration of antidepressant effects. Large, well-designed randomized controlled trials are needed to determine the optimal treatment parameters and to evaluate the long-term safety and effectiveness of tDCS. The 2020 Hayes annual review identified six new relevant publications that did not change the Hayes conclusion.

Barclay and Barclay (2014) conducted a randomized controlled trial (n=115) to evaluate the effectiveness of CES for the treatment of anxiety disorders and comorbid depression. Subjects were age 18–65 years and met the DSM-IV criteria for anxiety disorder. Subjects with comorbid depression (n=23) had a primary diagnosis of anxiety disorder and some were on antidepressants during the trial. The device used for electrical stimulation was the Alpha-Stim 100 (Electromedical Products International, Inc., Mineral Wells, TX). Outcomes were measured using the Hamilton Rating Scale for Anxiety (HAM-A) and the Hamilton Depression Rating Scale₁₇ (HAM-D₁₇). Follow-ups occurred at one, three and five weeks. A ≥50% reduction in these measures was considered response to treatment. The CES group had significantly lower HAM-A anxiety scores (p<0.001) and HAM-D₁₇ depression scores (p<0.001) following CES compared to the sham group. In the CES group, 83% of subjects had a decrease of ≥50% in anxiety and 82% had a decrease of ≥50% in depression scores. No adverse

events were reported. Limitations of the study include the small patient population, small number of patients with anxiety disorder and depression, and the short-term follow-up.

Kavirajan et al. (2014) conducted a Cochrane systematic review of randomized controlled trials evaluating CES vs. sham CES for the treatment of acute depression. No studies met inclusion criteria. There is insufficient evidence to support CES for the treatment of acute depression.

Cerebral Palsy: Hamilton et al. (2018) conducted a systematic review and meta-analysis to investigate the effects of transcranial direct-current stimulation (tDCS) on motor function for children with cerebral palsy. Nine randomized controlled trials (n=178) met the inclusion criteria. Included studies investigated tDCS as a stand-alone treatment or as an adjunctive therapy. The treatment effect was measured in terms of function (e.g., balance, gait, or upper limb); impairments (spasticity, muscle length, muscle strength); or physiological changes (e.g., electroencephalographic recordings or magnetic resonance imaging data). Subjects, aged 4–18 years, had Gross Motor Function Classification System (GMFCS) scores between I–IV, with the majority being classified as II (46%) or III (42%). Data from seven studies were included in seven separate meta-analyses looking at the immediate and follow-up effects of tDCS on mobility, dynamic and static balance, and gait. The remaining two studies did not include suitable summary statistics. One study (n=24) reported statistically significant reductions in center of pressure (COP) ($p<0.0001$). One study (n=20) reported an improvement with tDCS in virtual reality and gait training when combined with anteroposterior eyes open (APEO), anteroposterior eyes closed (APEC), and medio-lateral eyes closed (MLEC) ($p<0.001$), but not in medio-lateral eyes open (MLEO). A study with six subjects reported statistically significant results in anteroposterior ($p<0.008$) and medio-lateral ($p<0.01$) directions, with eyes closed (EC), but not with eyes open (EO). The effects of 20 minutes of mobility training combined with virtual reality and tDCS (n=12) reported statistically significant results across all areas when measured on the ground (not on foam) compared with control (APEO $p<0.001$, APEC $p<0.05$, MLEO $p<0.001$, MLEC <0.001). tDCS (n=11) was statistically significant and superior to the control in the management of dystonia ($p<0.01$). There was no statistically significant improvement on mobility ($p=0.28$), dynamic balance ($p=0.22$), or static balance ($p=0.63$) with tDCS. There was no benefit of tDCS compared with the control condition for step length ($p=0.87$). No serious adverse events were reported. Limitations of the analysis included the limited number of studies with heterogeneous small patient populations (n=6–46) and short-term follow-ups or no follow-ups, making it impossible to determine the overall longevity of the benefit from a single session of tDCS. The authors concluded that additional research is needed before tDCS therapy can be endorsed for this patient population.

Chronic Pain: O'Connell et al. (2018) conducted a Cochrane review of randomized and quasi-randomized controlled trials to evaluate electrical stimulation of the brain for the treatment of chronic pain. The review included five studies (n=270) using cranial electrotherapy stimulation (CES). No significant differences were found between CES and sham for pain intensity or disability. One study (n=36) comparing CES with sham reported a positive effect for quality of life at short-term follow-up. Meta-analysis of 27 studies (n=747) investigating transcranial direct cranial stimulation showed a short-term positive effect on quality of life but no evidence that tDCS improved disability. Due to the low quality of the evidence, firm conclusions could not be made regarding the clinical benefit of cranial electrical stimulation.

Fibromyalgia: Taylor et al. (2013) conducted a randomized controlled trial (n=46) to investigate the effectiveness of microcurrent CES on the pain and symptoms of fibromyalgia. Three groups included active CES (n=17), sham device (n=14) and usual care alone (n=15). All subjects remained on their usual care regimen, including medications. Follow up occurred for eight-weeks. Subjects using CES reported a significantly greater decrease in average pain ($p=0.23$), fatigue ($p=0.71$), sleep disturbance ($p=0.001$) and functional status compared to the other two groups. Limitations of the study include the small patient population, short-term follow-up, self-monitoring and reporting of outcomes, loss to follow-up (n=5), and the study included mainly females (n=43) and cannot be generalized to males.

Multiple Conditions: Shekelle et al. (2018) conducted a systematic review to assess the safety and efficacy of cranial electrical stimulation (CES) for the treatment of chronic pain conditions, depression, anxiety and insomnia. A total of 26 randomized controlled trials met inclusion criteria. The studies included patients with painful conditions (n=14 studies), depression (n=3 studies), depression and anxiety (n=5 studies), insomnia (n=2 studies), anxiety and insomnia (n=1 study) and anxiety (n=1 study). Painful conditions included fibromyalgia, headache, pain with spinal cord injury, neuromusculoskeletal pain and degenerative joint disease. A variety of

devices were used. Patient populations were ≤ 30 in 21 studies. Comparators included sham, usual care, relaxation and/or another form of CES. Follow-ups ranged from one treatment to 24 days. The studies were considered of low quality due to the small patient populations; short-term follow-up; heterogeneity of treatment regimens and outcome measures; and inconsistent results.

Parkinson's Disease: Elsner et al. (2016) conducted a Cochrane systematic review to assess the effectiveness of transcranial direct current stimulation (tDCS) in improving motor and non-motor symptoms in people with idiopathic Parkinson's disease (IPD). Six randomized controlled trials met inclusion criteria. Two studies ($n=45$) investigated the effects of tDCS compared to sham tDCS on impairment as measured by the Unified Parkinson's Disease Rating Scale (UPDRS). There was no evidence that tDCS resulted in a change in the global UPDRS score. There was evidence of an effect on UPDRS part III motor subsection score at the end of the intervention phase. One study with 25 participants measured the reduction in off and on time with dyskinesia, but there was no evidence of an effect. Two studies ($n=41$) measured gait speed and found no significant difference with tDCS. There was no evidence that tDCS improved quality of life. There is insufficient evidence to determine the effects of tDCS for reducing off time (when the symptoms are not controlled by medication) and on time with dyskinesia (time that symptoms are controlled but the person still experiences involuntary muscle movements), and for improving health-related quality of life, disability, and impairment in patients with IPD. Evidence of very low quality indicated no difference in dropout rate and adverse events between tDCS and control groups. There is insufficient evidence to support tDCS for the treatment of IPD.

Spinal Cord Injury: Tan et al. (2011) conducted a multi-site randomized controlled trial ($n=111$) to evaluate the effectiveness of the Alpha-STIM CES in patients with spinal cord injury (SCI) and chronic neuropathic pain at or below the level of injury. Of the 111 enrolled patients, 46 patients were randomized to CES at a sub-threshold level of 100 μA (microamperes) and 56 to sham CES. Patients were trained on the use of the device either in person or via mail and telephone, instructed to apply therapy at home for 21 days and to monitor and record the intensity of pain before and after each treatment. Coordinators contacted the patients via phone on a weekly basis. At the end of 21 days, patients completed a packet of post-intervention questionnaires. Some questionnaires were completed via telephone. At the end of the 21-day study period, patients in the sham group were allowed to use active CES for three weeks at a current setting of the patient's choice (100–500 μA). Following the 21 days of active CES, patients were also given the option of using CES for up to six months on an as needed basis and were paid to complete the questionnaires. During the three week blinded phase, the active and sham groups did not differ significantly on average daily pain ratings before ($p>0.60$) or after treatment ($p>0.90$). However, the active group had a significantly greater average decrease in pain from before to after the daily treatments compared to the sham group ($p<0.05$). More pain relief was reported by the participants during the open-label phase. In the 40 sham patients who crossed over to CES, a significant reduction in pain was reported ($p<0.001$). Although an improvement was shown in pain after a session, the improvement did not last until the next day. Less than 14% of patients in either group achieved a 30% or more reduction in pain. The most commonly reported side effects were pulsing, tingling, stinging, itching, and/or a small electric feeling produced by the ear clips. Author noted limitations included: the baseline differences between active and sham groups on several of the outcome measures made group differences in change scores difficult to interpret; loss to follow-up at three (<55%) and six months (>70%); and all of the outcome measures were obtained by self-report.

Stroke: Elsner et al. (2019) conducted a Cochrane systematic review to assess the effectiveness of tDCS for improving aphasia in stroke patients. A total of 21 randomized controlled trials (RCTs) and randomized controlled cross-over trials comparing tDCS versus control were included. The primary outcome measure was functional communication and the secondary outcome measure was accuracy in naming nouns at the end of the intervention. Outcomes reported no evidence of an effect ($p=0.37$) of tDCS on functional communication (three studies; $n=112$). There was evidence of an effect ($p=0.0005$) on accuracy in naming nouns (11 studies; $n=298$) and at follow-up ($p=0.006$) (two studies; $n=80$). The quality of evidence was rated as low to moderate. There was no evidence of an effect regarding accuracy in naming verbs post intervention (three studies; $n=21$). No studies investigating the effect of tDCS on cognition in people with aphasia after stroke were found nor were serious adverse events reported. Further methodologically rigorous RCTs with large patient populations are needed to determine the effectiveness of tDCS for the treatment of aphasia in stroke patients.

Professional Societies/Organizations:

In a 2019 clinical practice guideline on the management of insomnia and obstructive sleep apnea, the Department of Veterans Affairs and Department of Defense (VA/DoD) gave a “weak against” recommendation for the use of cranial electrical stimulation for the treatment of chronic insomnia disorder. This recommendation was given as a result of the low level body of evidence that exists due to small sample size, uncertainty about participants’ diagnoses, and a short follow-up period.

The Department of Veterans Affairs and Department of Defense (VA/DoD) stated in a 2020 clinical practice guideline on the management of headache that a recommendation either for or against the use of transcranial direct current stimulation for the treatment of headache could not be given due to insufficient evidence.

Electrical Sympathetic Stimulation Therapy

Electrical sympathetic stimulation therapy is a form of electrical stimulation of the peripheral nerves by applying eight electrodes bilaterally to the lower legs, feet, arms and hands. The therapy targets the autonomic nervous system and treats systematically as opposed to locally and is proposed for the treatment of chronic, intractable pain. Multiple beat frequencies are generated between 0-1000 Hz. Treatments are typically one hour in duration and may be administered in a physician’s office or at home.

U.S. Food and Drug Administration (FDA): Sympathetic therapy devices are approved by the FDA 510(k) process. Two such devices are the Dynatron STS and the Dynatron STS RX, a home device (Dynatronics Corp., Salt Lake city, UT). The devices are indicated for “symptomatic relief of chronic intractable pain and/or management of post-traumatic or post-surgical pain” (FDA, 2001).

Literature Review: The evidence in the published peer-reviewed scientific literature does not support the safety and effectiveness of sympathetic therapy. Studies are primarily in the form of case series and retrospective reviews with small patient populations and short-term follow-ups (Guido, 2002).

Electro Therapeutic Point Stimulation (ETPSSM)

ETPS neuromechanical therapy or neuropathic acupuncture involves the detection and treatment of chronic intractable neuromyofascial pain using the TENS US Unit (Acumed Medical Supplies, LTD, Stanford, CT). The transcutaneous device detects treatment points on the skin and applies brief, concentrated electrical microstimulation in short bursts. Traditional TENS units apply alternating current compared to the direct current applied by ETPS. Depending on how the device is programmed, the therapy is also proposed to decrease circulation and assist in resolution of swelling and pain or to increase circulation to enhance immune response and neural regeneration. The treatments can be self-administered by the patient at home (Hocking, 2002).

U.S. Food and Drug Administration (FDA): The TENS US Unit is approved by the FDA as the TENS Pro 900 (Acumed Medical Supplies, LTD, Stanford, CT) for the treatment of chronic intractable pain. The device was approved as a 510(k) Class II device.

Literature Review: There is insufficient evidence in the published peer-reviewed scientific literature to support the safety and effectiveness of ETPS. The available studies are primarily in the form of case reports and case series with small patient population and short-term follow-ups.

Functional Electrical Stimulation (FES)

FES or functional neuromuscular stimulation (FNS) attempts to replace stimuli from destroyed nerve pathways to assist neurologically impaired patients (e.g., spinal cord injury, stroke) with functional movement and to suppress spasticity. FES is a high-intensity (25–100 milliamps), short duration therapy that may be delivered for 20 minutes to one hour, several times a week, for months. For the device to be effective, the peripheral nerve must be intact.

FES is proposed for multiple indications, including:

- To assist ambulation in paraplegics (e.g., Parastep[®] I System, Sigmedics, Inc., Fairborn, OH). Parastep is a microcomputer controlled walker proposed to aid standing, walking, balance and stability in individuals with a spinal cord injury for whom gait training and standing are indicated. Using surface

electrodes, the device delivers electrical current to peripheral nerves in the lower extremities. Parastep is a proposed alternative to traditional orthotics and bracing;

- As a means of stationary exercise to prevent or reduce muscle atrophy in upper and lower extremities (e.g., ERGYS 2; Therapeutic Alliance, Inc., Fairborn, OH). The ERGYS 2 provides cycling activity proposed to improve muscle strength and circulation in the lower extremities;
- To improve ambulation in patients with gait disorders such as drop foot, hemiplegia due to stroke, cerebral injury, or incomplete spinal cord injury (e.g., Walkaide™ stimulator; Neuromotion, Edmonton, Alberta, Canada; NESS L300 Foot Drop System, Bioness Inc., Valencia, CA). WalkAide is a device that attaches to the leg just below the knee and is proposed to counteract foot drop and improve mobility during walking by stimulating the peroneal nerve. The Ness L300 is a similar device that also attaches below the knee, provides nerve stimulation and is proposed to assist the individual with foot drop to walk with increased balance and speed. The Ness L300 Plus builds on the L300 Foot Drop System by adding a thigh cuff. The thigh cuff is proposed to add control over bending and straightening the knee. The Bioness L300 Go System was FDA approved in March 2018 as a Class II device “intended to provide ankle dorsiflexion in adult and pediatric individuals with foot drop and/or to assist knee flexion or extension in adult individuals with muscle weakness related to upper motor neuron disease/injury (e.g. stroke, damage to pathways to the spinal cord). The L300 Go System electrically stimulates muscles in the affected leg to provide ankle dorsiflexion of the foot and/or knee flexion or extension; thus, it also may improve the individual’s gait”. The L100 Go System, which has a modified cuff design that does not alter the intended use of the device, was FDA approved in March 2020 as a Class II device using the L300 Go System as a predicate.
- To provide range of motion and function in patients with upper limb paralysis or hemiplegia (NESS H200 hand rehabilitation system [previously known as the Handmaster], Bioness Inc., Valencia, CA). NESS H200 is for use by an individual with hand paralysis. The device attaches to the lower forearm and is proposed to activate various muscle groups, enhancing grip and allowing opening and closing of the hand.
- As a modality for acute and chronic conditions with impaired respiratory function. It is hypothesized that abdominal FES may increase abdominal muscle mass and tone, placing the diaphragm in a more efficient position for respiration (McCaughey, et al., 2016).

The current evidence does not support FES for these indications.

U.S. Food and Drug Administration (FDA): FES devices, such as the Parastep, that have been proposed for restoring ambulation to paraplegics are regulated by the FDA’s premarket approval (PMA) process.

Functional electrical stimulators that are used to provide stationary exercise for paraplegics, to correct gait disorders, or to provide range of motion and function are approved by the FDA 510(k) process as Class II devices. The RT300 FES cycle ergometer (Restorative Therapies, Inc., Baltimore, MD) is approved as a powered muscle stimulator for “general rehabilitation for relaxation of muscle spasms, prevention or retardation of disuse atrophy, increasing local blood circulation and maintaining or increasing range of motion” (FDA, 2009). The WalkAide System is FDA approved as an external functional neuromuscular stimulator to electrically stimulate the muscles involved in dorsiflexion of the ankle in patients with damage to upper motor neurons. Other Restorative FES devices include the RT300 Leg, RT300 Leg and Arm, RT300 Arm, RT300 for children.

Literature review

Cerebral Palsy: Moll et al. (2017) conducted a systematic review to assess the effect of FES of the ankle dorsiflexors in children and adolescents with spastic cerebral palsy (CP) during walking. Outcomes were classified according to the International Classification of Functioning Disability and Health (ICF). Fourteen randomized and non-randomized controlled trials and single subject design studies were used for analysis. There was limited evidence showing a decrease in self-reported frequency of toe-drag ($p=0.02$) and falls ($p=0.022$). There was evidence that FES increased ankle dorsiflexion angle and strength and improved selective motor control, balance, and gait kinematics but decreased or unchanged walking speed. None of the studies addressed the effect of FES at the activity and participation level. Reported adverse events included skin problems and poor tolerance of stimulation. Limitations of the studies included the small patient populations ($n=1-32$); short-term follow-ups (1-12 weeks); various methods used to measure outcomes (gait analysis, questionnaires, clinical measurements/scales) and the heterogeneity of FES (e.g. electrical field, timing). The

authors concluded that there were insufficient data supporting functional gain by FES on activity and participation level. FES may have a role as an alternative to orthoses in children with spastic CP. Based on the current evidence no guidelines could be provided for treatment intensity, simulator setting and types of electrodes. Additional studies are needed to support the use of FES in this subpopulation.

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.

Gait Disorders: 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. 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; Stein, et al., 2010; Barrett, et al., 2009; Postans, et al., 2004).

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.

In a randomized controlled trial (n=74), Field-Fote and Roach (2011) evaluated whether there was a difference in walking speed and distance using four locomotor training regimens for patients with chronic spinal cord injuries. The regimens included treadmill-based training with manual assistance (TM) (n=19), treadmill-based training with bilateral electrical stimulation (TS) (Digitimer DS7AH, Digitimer Ltd, Welwyn Garden City, Herts, UK) (n=22), overground training with electrical stimulation (OG) (n=18) (WalkAide™), and treadmill-based training with locomotor robot (LR) (Lokomat Robotic Gait Orthosis, Zurich, Switzerland) (n=15). Training was administered five days per week for 12 weeks. There was a statistically significant improvement in walking speed (p<0.001) in the TM, TS and OG groups and overall time effect on training (p<0.0001). There was a significant improvement in walking distance in the TS and OG groups. Distance gain was greater for OG. Post hoc testing indicated the increase in "time X group" interaction in the OG group was significantly greater than the other groups (p≤0.01). Effect sizes for speed (d=0.43) and distance (d=0.28) were largest with OG. Effect sizes for speed were the same for TM and TS (d=0.28). There was no effect from LR. The Lower Extremity Motor Scores increased 8%–13%, with no significant between group differences. Ten patients were available for an average 20.3 month follow-up (4 OG and 6 in the other groups). These subjects had declined an average of 0.06 meter per second

(m/s) in walking speed since completion of training, but were still an average 0.08 m/s faster than before training. Author-noted limitations of the study included: they did not know if the training dosage was optimal for improving walking speed and distance; the focus was on walking rather than other aspects of walking (e.g., producing optimal kinematics); and most of the subjects used a wheelchair as their primary means of mobility so the amount of change qualified as meaningful change may be different from subjects who use other means of mobility; "the training parameters used in the robotic gait orthosis approach were configured to impose a kinematically appropriate gait pattern and stepping proceeded regardless of whether participants contributed effort;" and only ten people returned for longer follow-ups. Other limitations of the study include the small patient population, short-term follow-up, patients lost to follow-up, and the OG group had the largest number of patients who were less impaired.

Heart Failure: Smart et al. (2013) conducted a systematic review and meta-analysis of randomized controlled trials to evaluate FES (devices not given) in the treatment of heart failure. Ten studies met inclusion criteria (n=301) which included 158 FES patients, 85 aerobic cycle exercise training and 58 sedentary controls or sham FES. Five studies compared FES to cycle exercise training, two studies compared FES to a sedentary control group and three studies compared active FES to sham FES. Training sessions varied from three to seven sessions per week, FES frequencies varied from 10–50 Hz, off and on intervals ranged from 2–50 seconds, and studies ranged from 5–10 weeks duration. Most studies used FES of the quadriceps and gastrocnemius muscles or hamstrings in the home and exercise training intensity ranged from 50%–80%. FES produced inferior improvements in peak oxygen consumption (VO_2) compared to cycling ($p=0.04$) but superior improvements compared to sedentary or sham FES ($p<0.00001$). There was no significant difference in change in six minute walk distance (6MWD) between cycling and FES, but following FES 6MWD was significantly greater than sedentary care or sham FES ($p=0.0002$). There was no significant difference in change in quality of life between cycling and FES, but FES elicited significantly larger improvements in the standardized quality of life score than sedentary or FES sham treatment ($p<0.00001$). The data suggested that in patients with heart failure, FES was inferior to exercise training, but resulted in larger benefits in peak VO_2 , 6MWD and quality of life compared to placebo. Increasing the number of FES hours improved peak VO_2 . Author-noted limitations of this review included: studies were small, of "mediocre methodological quality" and of short duration; and analyses of hard end points (e.g., mortality and episodes of hospitalization) were not possible due to insufficient numbers of events. According to the authors, although FES may be a possible modality for heart failure patients who are unable to exercise, the benefits may be smaller than those obtained from conventional exercise training.

Sbruzzi et al. (2010) conducted a systematic review and meta-analysis of randomized controlled trials to evaluate FES (devices not given) for the treatment of patients with chronic heart failure (CHF). The aim of the study was to review the effect of treatment with FES compared to conventional aerobic exercise training (CA) or control group. FES has been proposed as an alternative for patients unable to engage in conventional exercise therapy to improve functional capacity and prognosis of this population. Seven studies (n=224) met inclusion criteria. FES was applied to muscles in both legs for 30–60 minutes per day for 5–10 weeks. FES was compared to conventional aerobic exercise (CA) (n= 5 studies) or to a control group, no FES (n=2 studies). FES resulted in a small gain in peak oxygen consumption (VO_2) and an increase in peak VO_2 of 2.78 milliliters of oxygen per kilogram (ml/kg) per minute, distance of the 6-minute walk test and muscle strength. However, the differences in muscle strength and distance of the 6-minute walk test were not significant. There was insufficient data to conduct a meta-analysis. Limitations of the review included the poor methodology of the studies, small patient populations and short-term follow-up.

Multiple Sclerosis: Miller et al. (2017) conducted a systematic review and meta-analysis to evaluate the efficacy of FES on gait for people with multiple sclerosis (MS) who had foot drop. Included studies reported on a minimum of one measure of gait speed using either short or long walking tests with and without the device, at a minimum of one time point. Gait speed was described in meters per second and measured by walking over a short (e.g., 10m, 25ft) or a longer distance (e.g., 2- or 6-min walk). A total of 20 articles/19 studies (n=490) met inclusion criteria. Studies were primarily observational in design including retrospective and patient populations ranged from 2–39 subjects. Almost half of the studies investigated the single-channel Odstock Dropped Foot Stimulator (ODFS). Other studies used dual- or single-channel ODFS, Walkaid, or NESS L300. The only RCT compared a single-channel ODFS with an exercise program. A randomized crossover trial compared a single-channel ODFS followed by a dual-channel ODFS with weekly physiotherapy. Analysis of pooled data found a statistically significant initial ($p=0.016$) and ongoing ($p=0.003$) orthotic effect of FES on gait speed in short

walking performance, increasing gait speed by 0.05 and 0.08m/s, respectively. No therapeutic effect was found. A change of 0.05m/s in walking speed was considered clinically significant. FES produced small, nonsignificant initial and ongoing orthotic and therapeutic effects on gait speed in long walking performance tests. Limitations of the studies included: small, heterogeneous patient populations with various types of MS; various inclusion and exclusion criteria or absence of criteria; heterogeneity of outcome measures; lack of blinding; conflicting outcomes; probably of performance bias; variation in the walking tests used both in terms of distance, pace and method of collection. Due to the limitations and poor quality of the studies, firm conclusions could not be made regarding the clinical benefit of FES in this patient population.

Hayes (2015; reviewed 2017) conducted a systematic review of the literature on FES for the treatment of foot drop in individuals with multiple sclerosis. In the technology assessment, Hayes reported that “low-quality” evidence from eight studies suggested that FES increased walking speed, improved gait quality, reduced falls and improved activities of daily living and quality of life. However, outcomes were inconsistent and it was unclear if the reported improvements were clinically meaningful in real-life settings. There was no evidence that the use of a FES device helped this subpopulation reach normal walking speed. None of the studies evaluated whether FES enabled patients to walk up and down stairs, walk on uneven ground, or perform side steps, or whether its use improved confidence while performing these various activities. The majority of the studies used the Odstock ODFS devices (IMedical LTD, Wiltshire, UK). Studies were primarily non-comparative and limited by small patient populations, short-term follow-ups and reporting of indirect outcomes. Patient selection criteria, extent of treatment benefit in real-life settings, and long-term efficacy have not been established. Patients were primarily adults with secondary progressive MS. Therefore, the use of FES in adult patients with foot drop due to MS other than secondary progressive MS and for the use of FES devices other than the ODFS is unproven.

Muscle Atrophy in Upper and Lower Extremities: Randomized controlled trials using various FES devices have evaluated FES cycling (MOTOmed®, RECK GmbH, Betzenweiler, Germany) compared to passive cycling (n=35) (Ambrosini, et al., 2011); FES (H200 device) combined with self-directed exercise vs. exercise alone (n=23) (Weber, et al., 2010); FES cycling (device not given) with standard rehabilitation vs. rehabilitation alone (n=20) (Ferrante, et al., 2008); and with arm and hand rehabilitation comparing FES (Compex Motion, Compex SA, Switzerland) to conventional therapy (n=23) (Mangold, et al., 2009). Some studies reported no significant differences with FES. Due to the small patient populations, short-term follow-ups (e.g., 4–12 weeks) and conflicting results, the effectiveness of FES for the treatment of stroke patients has not been established.

Respiratory Function: McCaughey et al. (2016) conducted a systematic review and meta-analysis to evaluate the efficacy of abdominal FES when used to improve respiratory function in acute and chronic conditions following spinal cord injury. A total of 14 studies (n=141) met inclusion criteria. Ten studies investigated acute conditions and four investigated chronic conditions. Acute studies compared respiratory function before and during abdominal FES applying a self-control study design. Chronic studies measured the chronic effect of abdominal FES training. These studies applied a self-control (randomized crossover) study design or a randomized controlled trial approach. Acute effect of abdominal FES caused a significant (p=0.000) acute improvement in cough peak flow (n=54), gastric and esophageal pressure (p=0.000) (n=42) and maximum expiratory pressure (p=0.018) (n=20) but not in forced exhaled volume (p=0.357) (n=33), vital capacity (p=0.585) (n=32) and peak expiratory flow (p=0.870) (n=56). Chronic effect saw a significant increase in forced vital capacity in three studies (p=0.043) while one study reported no significant difference. No significant difference (p=0.134) was reported in pooled data for maximum expiratory pressure. Small patient populations and heterogeneity across studies reduced the power of the meta-analysis. Other limitations of the studies included; heterogeneity in electrode position with a range of positions used to stimulate either or both of the rectus abdominis and external oblique muscles; conflicting outcomes; and lack of a standardized protocol (e.g., range of stimulation devices, stimulation parameters, electrode positions). Additional randomized control trials with large patient populations that follow a standardized protocol are required to fully quantify the efficacy of abdominal FES.

Spinal Cord Injury: In a Directory Report (2017; reviewed 2019), Hayes evaluated FES for rehabilitation in patients with spinal cord injury (SCI). Nine randomized controlled trials and six pretest/posttest studies were included. Patient populations included adults and children (n=9–70) and follow-ups ranged from zero to 40 months. FES was used for therapeutic (e.g., RT300 FES cycle, Ergys2) or functional applications (e.g., Ness H200, WalkAide; NESS L300, Parastep) in patients with SCI. Comparators included standard care (e.g., physical

therapy, occupational therapy) and exercise with and without FES. Outcomes measures included: walking ability, hand function, muscle strength, muscle atrophy, bone loss, cardiovascular and respiratory outcomes, quality of life (QOL), and health complications. The clinical goals of the studies varied (e.g., cardiac conditioning, correct foot drop, ambulation, hand grasp). Hayes concluded the following:

- For FES in adult patients with complete motor spinal cord injury the overall low-quality body of evidence suggested that FES appeared to improve health outcomes in adult patients but there remains uncertainty regarding the long-term effectiveness and safety of FES, as well as optimal treatment parameters.
- For FES in children and adolescents with complete motor SCI there was an overall very-low-quality body of evidence with inconsistent results. There was insufficient evidence to allow any conclusions regarding safety and efficacy in this population.
- For FES in adult patients with incomplete SCI, the low-quality body of evidence reported inconsistent outcomes suggesting that FES appeared to improve some health outcomes in adult patients with incomplete motor SCI. Long-term effectiveness and safety of FES, as well as optimal treatment parameters are unknown.
- For FES in children and adolescents with incomplete SCI there was a lack of evidence and the safety and efficacy of FES is unknown.

The 2019 review identified one new relevant study that did not change the original conclusions of this report.

Studies investigating FES using Parastep were published in 2000 or before and are primarily case series with small patient populations and short-term follow-ups. Brissot et al. (2000) investigated the motor performances of Parastep in 15 thoracic-spine injured patients (T3-T11). Patients had to have a stable neurologic and orthopedic status and be at least six months status-post injury and/or restorative surgery. Two patients did not complete the required training. Follow-up occurred at 40 ± 11 months. After a mean 20 sessions, the patients achieved independent ambulation with a mean walking distance of 52.8 ± 69 meters (m), and a mean speed of 0.156 ± 0.14 m/second. At the final follow-up five patients were using the Parastep regularly and all patients used it for physical fitness and not for functional ambulation. According to the authors the high ratio of energy cost of the use of the device may have explained its limited use in daily activity. The authors also noted that the Parastep approach had 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.

Stroke Rehabilitation: Prenton et al. (2018) conducted a systematic review and meta-analysis of randomized controlled trials to assess the effectiveness of FES compared to ankle-foot orthoses (AFO) in individuals with foot drop associated with a central nervous system disorder. Six studies included stroke patients, one study evaluated cerebral palsy subjects and the other study did not specify diagnosis. Seven studies (n=464) met inclusion criteria. Patient populations ranged from 14–197 and follow-ups occurred at 4–36 weeks. Three trials used customized AFOs that were made or modified for the subject. Two of the trials used a variety of different types of AFOs and in one trial off-the-shelf orthoses were used. Four studies recruited subjects who did not already use an AFO while the other trials included current AFO users. All trials recruited new users of FES. One trial used an implantable FES system. The remaining trials used surface systems from three different manufacturers. Four trials allowed use within the home/community setting and three provided devices used only under supervision. Meta-analysis of final-assessment walking speed data from six trials (n=437) showed that FES and AFO had equivalent positive overall therapeutic effects ($p=0.46$). The same held true for stroke victims ($p=0.54$) and after 4–6 weeks' use ($p=0.49$). Due to lack of data, sub-group analysis of walking speed was not possible at 12–13 weeks. The meta-analysis showed that FES and AFO were statistically proven to have the same therapeutic effect on walking speed in foot drop in stroke and cerebral palsy subjects (one study). Limitations of the study include the heterogeneous, small patient populations short-term follow-ups; possible selection bias; heterogeneity of AFOs used (customized, off the shelf, type not specified); failure to report FES set-up parameters or AFO mechanical properties; variation in secondary outcome measures (e.g., electromyography, kinematics and Fugl-Meyer Assessment) and how data was reported. Additional randomized controlled trials with large patient populations, long-term follow-up and homogeneous study designs are needed to support the outcomes of this meta-analysis.

Eraifej et al. (2017) conducted a systematic review and meta-analysis of randomized controlled trials (n=20 studies; 431 subjects) to evaluate the effectiveness of post-stroke upper limb FES on activities of daily living

(ADL) and motor outcomes. Subjects were age > 18 years diagnosed with hemorrhagic/ischemic stroke. The study group received upper limb FES plus standard care (n=238) vs. standard care only (n=193). Maximum group size was 28 subjects and nine studies included less than ten subjects. Standard care included: physiotherapy, occupational therapy, task-based activities or other exercise based interventions, orthoses, botulinum toxin, mirror therapy and/or sham FES. Primary outcome measures were those measures which directly assessed ADLs. Secondary outcomes included measures that assessed performance of a task that was not classified as an activity of daily living (e.g., grasping and moving a cube). Tertiary outcomes were any other measure of motor outcome: muscle tone, force generation, distance reached and range of active movement. Ten studies were eligible for meta-analysis. Six studies (n=67) reported no significant benefit of FES on ADLs. Three studies where FES was initiated within an average of two months following stroke showed significant benefit of FES on ADL (n=32). No significant improvement was shown in three studies (n=35) when FES was initiated more than one year after stroke. Meta-analysis performed on objective ADL measures (not self-reported) found no significant benefit of FES. Meta-analysis of Fugl-Meyer Assessment (FMA), the most commonly reported measurement instrument, showed a statistically significant benefit of FES. Analyses on the severity of stroke and stimulation parameters were not possible due to methodological variability. Author-noted limitations of this analysis included: the small patient populations, heterogeneity of the treatment of the control groups, heterogeneity of the instruments used for outcome measures, lack of subject blinding, and high risk of bias. Due to the "very low" quality of evidence of the studies, firm conclusions could not be made regarding the effectiveness of upper limb FES following a stroke.

Vafadar et al. (2015) conducted a systematic review and meta-analysis to evaluate the effect of FES when used as an adjunctive therapy to conventional and/or occupational therapy for shoulder subluxation, pain, and upper arm motor function in stroke patients (ischemic or hemorrhagic). Ten randomized and quasi-randomized controlled trials (n=214) met inclusion criteria. The results of the meta-analyses showed a significant difference ($p < 0.00001$) in the prevention or treatment of shoulder subluxation only when FES was applied early after stroke (less than six months). The effects were mostly observed during the treatment period and not after the follow-up period. However, the studies were primarily rated as fair quality and were limited by small patient populations; short-term follow-ups; and heterogeneity of treatment regimens (number, length and frequency of sessions) and various types of conventional therapies used. No effects were found on pain or motor function outcomes. Additional well-designed long-term, comparative studies are needed to support FES for the treatment of shoulder subluxation in this subpopulation and to identify patient selection criteria.

Kafri and Laufer (2015) conducted a systematic review of the literature to assess the effects of lower leg FES in patients following a stroke. Sixteen randomized and nonrandomized trials met inclusion criteria. Therapeutic effects were mainly measured in individuals in the chronic post-stroke phase (>3–6 months). Overall, findings indicated increases in gait speed. Some studies reported positive effects in walking independence, walking distance, muscle strength and voluntary range of motion. However, it was unclear whether these effects were due primarily to FES or whether they could have been achieved by any means that enabled functional movement. The training studies presented conflicting results regarding the superiority of training with FES relative to control training without FES. When FES was used as an alternative for assistive devices, no superior therapeutic effects were reported with the FES compared to ankle foot orthosis (AFO). The therapeutic effect of FES on balance did not demonstrate any clear patterns. Although positive benefits were reported with FES when compared to matched treatments without FES, the results were inconsistent. Therefore, no definite conclusions could be drawn regarding superiority of FES. Consistent findings indicated that when FES was used as an alternative to an assistive device it had no superior therapeutic effects over AFO. The therapeutic effects achieved by habitual FES intervention did not typically eliminate the need to use the FES as an assistive device during walking. Limitations of the studies included inconsistent and wide ranging outcome measures, varying exposures to FES, and various FES parameters used. From the data, it is not clear which individuals will benefit from FES and what baseline characteristics predict better therapeutic outcomes. Additional well-designed, controlled studies are needed to support the use of FES.

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.

Bethoux et al. (2014) conducted a multicenter randomized controlled trial (n=495) to compare outcomes using FES and ankle-foot orthoses (AFO) in patients who were at least six months post stroke (average 6.9 years). Primary outcome measures were the 10-Meter Walk Test (10MWT), a composite of the Mobility, Activities of Daily Living/Instrumental Activities of Daily Living, and Social Participation subscores on the Stroke Impact Scale (SIS). Secondary outcomes included: 6-Minute Walk Test, GaitRite Functional Ambulation Profile (FAP), Modified Emory Functional Ambulation Profile (mEFAP), Berg Balance Scale (BBS), Timed Up and Go, individual SIS domains, and Stroke-Specific Quality of Life measures. Follow-ups occurred for six months. Although both groups showed statistically significant improvement in outcomes, there were no between-group statistically significant differences. There were no significant improvements with the use of FES compared to AFOs. Author-noted limitations of the studies included: subjects were not stratified by gait speed; compliance with the use of the device and any changes in spasticity medications were not tracked; and the study designs did not allow analysis of the magnitude of post-device fitting improvement regarding ambulation ability, balance, and quality of life. Another limitation is the number of patients lost to follow-up (n=96).

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 \geq 6 months). Seven studies (n=231; 12-53 subjects per study) met inclusion criteria. Sufficient data for pooled analysis was only available for the 6-minute walk test (6MWT) and a significant treatment effect was shown for FES (p=0.013). There was no significant effect on 6MWT distance (p=0.10). A subanalysis determined that there was no significant treatment effect of FES on the performance of the 6MWT. Most studies reported significant gains from baseline within their group. Limitations of the studies included variation in FES delivery (i.e., surface vs. intramuscular stimulation) and heterogeneity of the muscles that were stimulated, intensity and type of stimulation, outcome measures and comparators. Outcomes varied and were conflicting. Additional studies are needed to assess the effectiveness of FES in this patient population.

Professional Societies/Organizations:

The American Heart Association's (AHA)/American Stroke Association (ASA) scientific statement on rehabilitation of the stroke patient (2010) stated that there is evidence to support FES/NMES as an adjuvant therapy within the first six months following a stroke. AHA/ASA also stated that the effects of electrical stimulation on the maintenance of functional gains are variable and evidence for wrist and finger rehabilitation over usual care did not show enhanced improvement with FES.

H-Wave Electrical Stimulation

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 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. H-wave devices are available for self-administered home therapy.

U.S. Food and Drug Administration (FDA): The H-WAVE[®] Muscle Stimulator (Electronic Waveform Laboratory, Inc., Huntington Beach, CA) is FDA 510(k) approved is a class II device.

Literature Review: There is insufficient evidence in the published peer reviewed scientific literature to support the safety and effectiveness of the H-Wave electrical stimulators.

Hayes evidence analysis research brief on H-Wave therapy for the treatment of low back pain (2018a) and lower extremity pain (2018b) concluded that there was insufficient evidence to assess the safety and effectiveness of H-wave therapy for these indications. For low back pain, five abstracts were retrieved including retrospective reviews, a meta-analysis, and review articles. Regarding lower extremity pain, six abstracts were retrieved including one randomized sham-controlled trial (n=23); two retrospective reviews, one meta-analysis (Blum et al., 2008) and one review article.

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.

High Voltage Galvanic Stimulation (HVG)

Galvanic stimulation is characterized by high voltage pulsed stimulation and is proposed primarily for local edema reduction through muscle pumping and polarity effect. Edema is comprised of negatively charged plasma proteins, which leak into the interstitial space. The theory of galvanic stimulation 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. The high voltage and direct current used in HVG differentiates it from the low voltage and alternating current used in TENS or NMES. Besides reducing edema, HVG is also proposed for wound healing and numerous other conditions (Medi-Stem, 2014).

U.S. Food and Drug Administration (FDA): HVG stimulators are FDA approved as a 510(k) Class II device. An example of these devices is the CS3102 High Voltage Galvanic Stimulator (Control Solutions, Inc., Northbrook, IL).

Literature Review: The few studies that were identified in the literature that addressed HVG were primarily randomized clinical trials and case comparisons published prior to 1997 with small patient populations and short-term follow-up. Patient selection criteria were lacking. There is insufficient evidence in the published peer reviewed scientific literature to support the safety and efficacy of HVG stimulation.

Interferential Therapy (IFT)

IFT, also known as interferential stimulation (IFS), is a treatment modality that is proposed to relieve musculoskeletal pain and increase healing in soft tissue injuries and bone fractures. Two medium-frequency, pulsed currents are delivered via electrodes placed on the skin over the targeted area producing a low-frequency current (1–200Hz). IFT delivers a crisscross current at 4000–4150 pulses per second resulting in deeper muscle penetration. These features are proposed to provide more effective pain control compared to TENS. 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. IFT has been proposed to have a similar effect to TENS in controlling pain and improving function over time. However, studies comparing IFT to TENS are lacking and the methodological quality of current studies is heterogenic in several area (e.g., kilohertz frequency, pulse duration, electrode size and placement, and intensity) (Almeida, et al., 2018).

U.S. Food and Drug Administration (FDA): Interferential stimulator instruments are approved as 510(k) Class II devices. Examples of FDA-approved devices include the RSJ, RS JC, RS-4i Plus Sequential Stimulator (RS Medical, Vancouver, WA), IF 8000 (Biomotion, Madison, AL), Flex-IT™ (EMSI, Alexander, VA).

Literature Review: The evidence in the published peer reviewed scientific literature does not support the safety and effectiveness of IFT for the treatment of multiple conditions including: constipation, enuresis, urinary

incontinence, pain associated with musculoskeletal disorders or injuries, osteoarthritis, dyspepsia, swallowing disorders, stimulation of soft tissue healing, subacromial impingement syndrome (SAIS), and stimulation of bone fracture healing. Studies 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 with conflicting results. Some studies reported no significant difference in outcomes with IFT (Nazligul, et al., 2018; Yik, et al., 2018; Zivkovic, et al., 2017; Kajbafzadeh, et al., 2015; Facci, et al., 2011; Fuentes, et al., 2010; Demirturk, et al., 2008). Randomized controlled trials with large patient populations and long-term follow-ups comparing IFT to established treatment options are lacking.

Chronic Low Back Pain: Facci et al. (2011) conducted a randomized controlled trial (n=150) to compare the analgesic effectiveness of TENS and IFC for the treatment of nonspecific chronic low back pain. Patients were randomized to TENS (group 1; n=50), IFC (group 2; n=50) and controls (group 3; n=50). The active therapy groups were treated for a total of ten, 30-minute sessions while the control group received no therapy. Patients were followed for up to two weeks. Outcome measures included visual analog scale (VAS), Brazilian version of the McGill Pain Questionnaire classified according to the number of words chosen (NWC), Pain Rating Index (PRI), Pain Intensity Index (PPI) and Roland-Morris Disability Questionnaire (RMDQ). There was a significant difference in pain reduction in group 1 vs. group 3 ($p<0.01$) and group 2 vs. group 3 ($p<0.01$). Recurrence of pain occurred in 4% of groups 1 and 2 and 38% of group 3. Following treatment, the mean PPI, PRI and NWC were significantly improved ($p<0.01$) in groups 1 and 3, but the differences were the same for groups 1 and 2. There was no significant difference in duration of analgesia between TENS and IFC ($p<0.77$). There was a significant improvement in RMDQ score in groups 1 and 2 compared to group 3 ($p<0.01$), but was significantly improved in all three groups ($p<0.01$). A total of 84% of the patients in group 1, 75% in group 2 and 34% in group 3 stopped using non-steroidal anti-inflammatory drugs (NSAIDs) and analgesic drugs after the treatment. Limitations of the study include the small patient population, patients lost to follow-up (n=13), short-term follow-up and lack of use of therapeutic exercises. The authors noted that studies needed to be conducted to determine what type of equipment is most appropriate for long-term pain relief.

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: whether the analgesic effect of 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.

Osteoarthritis: Gundog et al. (2012) conducted a randomized controlled trial (n=60) to compare the effectiveness of IFC to sham IFC (n=15) for the treatment of osteoarthritis. Active IFC was delivered at 40 Hz (n=15), 100 Hz (n=15) or 180 Hz (n=15), taking into account patient's age and sex. Treatments were given for twenty minutes each, five times a week, for three weeks. Patients were allowed to use paracetamol during the study. The primary outcome was pain intensity measured by the Western Ontario and McMaster University Osteoarthritis Index (WOMAC). Secondary outcomes included range of motion (ROM) of both knees, time to walk a distance of 15-meters, and the amount of soft-tissue swelling and synovial effusion. Pain at rest, pain on movement, and disability were measured by the Visual Analog Scale. There was a significant improvement in all patients in all outcomes compared to baseline ($p<0.05$, each) except for ranges of motions. The mean percentage decreases in all outcomes were significantly greater in the active IFC group compared to sham ($p<0.05$, each). Improvement in WOMAC stiffness subscale was only reported in the IFC group ($p<0.05$). Intake of paracetamol was significantly higher in the sham group ($p<0.05$). The effectiveness of the different amplitude-modulated frequency (AMF) of active IFC was not significantly different between the groups. Author-noted limitations of the study included: the small patient population; difficulty finding patients to include in the study who

had not experienced any electrotherapy before the study and who were approved to participate in a singular treatment regimen for three weeks; and short-term follow-up.

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.

Urinary Incontinence: In a randomized controlled trial, Demirturk et al. (2008) compared IFT (n=20) to Kegel exercises using a biofeedback device (n=20) for the treatment of urinary stress incontinence in women. Treatments lasted 15 minutes per session, three times a week, for 15 sessions. Outcome criteria included pelvic floor muscle strength, one-hour pad test and quality of life questionnaire. Following treatment, all parameters improved significantly ($p < 0.5$ each) in each group. There were no significant differences in outcomes between the two groups. No adverse events were reported. Limitations of the study include the small patient population and short-term follow-up.

Professional Societies/Organizations: The American College of Physicians 2017 guidelines on noninvasive treatments for acute, subacute and chronic low back pain stated that there was insufficient evidence to determine the effectiveness of interferential therapy for the treatment of low back pain.

Microcurrent Electrical Nerve Stimulation (MENS)

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., 1000 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, 2020).

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, 2020).

U.S. Food and Drug Administration (FDA): The FDA categorizes microcurrent devices as TENS devices intended for pain relief. The device is used to apply an electrical current to electrodes on a patient's skin to treat pain. Precision Microcurrent (Precision Microcurrent, Inc., Newberg, OR) is 510(k) FDA approved as a class II device equivalent to predicate TENS devices.

Literature Review:

There is insufficient evidence in the published peer-reviewed scientific literature to support the safety and effectiveness of MENS including FSM. Studies included 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).

A Hayes Health Technology Assessment (2018; reviewed 2019) investigating microcurrent electrical therapy (MET) for the treatment of musculoskeletal pain concluded that there is insufficient evidence to assess the efficacy of MET for the treatment of pain associated with lateral epicondylitis. Substantial uncertainty remains regarding whether MET provides reduction in pain compared with usual care. There is insufficient evidence to assess the efficacy of MET for the treatment of pain associated with lower back disorders, Achilles tendinopathy, temporomandibular joint (TMJ) disorders, or bruxism. The Brief included two studies that evaluated MET for the treatment of lateral epicondylitis, and one study each that evaluated MET for the treatment of pain associated with low back pain, Achilles tendinopathy, TMJ disorders, and bruxism. Study designs included: four poor-quality RCTs, one poor-quality crossover RCT and one poor-quality prospective cohort study. Patient populations ranged from 10–60 and follow-ups ranged from end of treatment to 50 weeks. Hayes rated the overall body of evidence as very-low-quality for the use of MET for the treatment of these conditions. The 2019 Hayes annual review identified one new study that did not change the Hayes conclusion.

Pelvic Floor Electrical Stimulation (PFES): Although the exact mechanism is not fully understood, it is postulated that electrical stimulation of the bladder floor activates the pudendal nerve, causing contraction of smooth, striated urethral muscles and striated pelvic floor muscles. The electrical stimulation is transmitted via vaginal or anal electrodes intending to improve urethral closure and strengthen the pelvic floor muscles.

U.S. Food and Drug Administration (FDA): All devices with surface electrodes used for bladder stimulation are Class II devices. Examples of FDA 510(k) approved, nonimplantable electrical stimulators include the Detrusan® 500 (Innovamed USA, Inc., Lehigh Acres, FL), the Pathway™ CTS 2000 (Prometheus Group, Duxbury, MA), and the ApexMV (InControl Medical, LLC, Brookfield, WI).

Literature Review: There is insufficient evidence in the published peer-reviewed scientific literature to support electrical bladder stimulation for the treatment of urinary incontinence. Hayes (2016; reviewed 2020) conducted a systematic review of the literature to evaluate PFES for the treatment of urinary incontinence. The Health Technology Assessment included 11 randomized controlled trials (RCTs) that investigated PFES in women with stress urinary incontinence (SUI) or urge urinary incontinence (UUI); one RCT that evaluated the effectiveness of PFES in adult women with SUI, UUI, or mixed urinary incontinence (MUI); and three RCTs that evaluated PFES in men with SUI following radical retropubic prostatectomy (RRP). No RCTs were found that evaluated PFES for the treatment of UI in men who had not undergone prostatectomy for prostate cancer. Comparators included: no active treatment, sham stimulation, or pelvic muscle exercise or training. Hayes concluded that the moderate amount of evidence suggesting benefit from PFES for the treatment of SUI in women was of low quality. A limited amount of low-quality evidence suggested that PFES may benefit some women with UUI although results were conflicting. Likewise, a limited amount of low-quality evidence also suggested that PFES may improve some outcomes of men with post-RRP SUI. The addition of PFES to standard treatment did not add any benefit. Limitations of the studies included the heterogeneity of stimulation parameters, including stimulus frequency, intensity or amplitude, pulse duration, duty cycle (contraction/relaxation), length of treatment sessions, number of sessions per week, and number of weeks of treatment. The stimulus frequency and pulse duration were typically chosen based on the predominant type of urinary incontinence. Meaningful comparisons between studies were difficult because of the significant heterogeneity and inconsistent or conflicting results. The long-term effectiveness of PFES is not known and most patients who responded to treatment required maintenance stimulation to sustain any improvement that was seen. The 2020 annual review included two new studies that did not change Hayes' initial conclusion.

Jerez-Roig et al. (2013) conducted a systematic review of randomized (n=24) and non-randomized controlled trials (n=3) to evaluate the effectiveness of ES in the treatment of women with urinary incontinence (UI) and overactive bladder syndrome (OAB). The review focused on maximal ES in outpatient and home-based settings as well as, local application of non-implanted transcutaneous electrodes in the pelvic area. Inclusion criteria were women over age 18 years with stress urinary incontinence (SUI), urge urinary incontinence (UUI), mixed urinary incontinence (MUI) and/or overactive bladder (OAB) treated with ES. Outcomes were conflicting with some studies reporting that ES was effective while others reported ES was no more effective than controls. Evidence reported that pelvic floor muscle training was more effective, less effective or not superior to ES for SUI. Four studies reported that vaginal cones were equally effective to ES. Some studies reported ES was well tolerated but others reported adverse events including pain, discomfort, hypersensitivity, irritation, tingling in the thigh, hemorrhage, fecal incontinence, diarrhea, bladder spasms, and vaginal or urinary infection. There was no evidence of which approach (outpatient or home) was more effective. No studies compared different ES treatment regimens therefore; it is unknown as to which parameters are most effective. Due to the heterogeneity of the ES treatment parameters, patient populations and outcome measures, it is difficult to clarify the effectiveness of ES for these indications.

Berghmans et al. (2013) conducted a Cochrane review of randomized and quasi-randomized controlled trials to evaluate the effectiveness of electrical stimulation (ES) with non-implanted devices for men with stress, urgency or mixed urinary incontinence. Comparators included no treatment, placebo treatment, or any other solo therapy. The authors also compared ES in combination with other intervention compared to the other intervention alone and the effectiveness of one method of ES compared to another method. Six randomized controlled trial met inclusion criteria. Of the 544 men included in the trial, 305 received ES compared to control or other treatment (n=239). There was some evidence that electrical stimulation (ES) had a short-term effect in reducing

incontinence compared with sham treatment but the effects were not maintained at the six-month follow-up. When pelvic floor muscle training (PFMT) with ES was compared to PFMT alone or with biofeedback, there was no statistically significant difference in urinary incontinence and there were more adverse events with combined therapy. It was not possible to determine in one method of ES was better than another.

Zhu et al. (2012) conducted a systematic review and meta-analysis of randomized controlled trials to evaluate the role of PFES for the treatment of urinary incontinence (UI) following radical prostatectomy. Four studies (n=210) met inclusion criteria. Two trials compared pelvic floor muscle training (PFMT) with and without PFES, one compared PFMT to extracorporeal magnetic innervation (exMI) plus PFES and the last study compared PFMT to biofeedback plus PFES. Study durations generally ranged from 6–12 months. Pooled analysis did not show that PFES improved UI better than PFMT ($p=0.12$) nor was there a relative benefit in men treated with PFMT plus PFES in achieving continence ($p=0.73$). In conclusion, the pooled data suggested no benefit from PFES in the recovery of UI after radical prostatectomy, in the early or late phase of recovery. Author-noted limitations included: most of the studies were of uncertain quality lacking description of randomization concealment and blinding techniques, variability among treatment regimens and outcome measures; treatment regimens and training were not standardized; and heterogeneous patient populations.

Goode et al. (2011) conducted a three-center randomized controlled trial (n=208) to determine if the addition of PFES to behavioral therapy (behavioral plus) enhanced the effectiveness of behavioral therapy in reducing persistent (1–17 years) post-prostatectomy incontinence. Patients were stratified by site, incontinence type (i.e., stress, urgency or mixed) and severity (i.e. < 5, 5–10, > 10 episodes per week), and randomized to eight weeks of behavioral therapy (i.e., pelvic floor muscle training and bladder control strategies); behavioral therapy plus in-office, dual channel electromyograph biofeedback and daily home pelvic floor electrical stimulation at 20–100 Hz (behavior plus); or delayed treatment (control group). The primary outcome measure was percent reduction in number of incontinence episodes at eight weeks as measured by a seven-day bladder diary. Follow-up occurred for one year after active treatment. Mean incontinence episodes decreased significantly from 28 to 13 per week following behavioral therapy and from 26 to 12 per week following behavior plus therapy ($p=0.001$, each). Both reductions were significantly greater than the reduction from 25 to 21 in the control group. However, there was no significant difference in incontinence reduction between the two treatment groups ($p=0.69$). Improvements were maintained at 12 months in both treatment groups but the difference between the groups was not significant ($p=0.32$). The addition of biofeedback and PFES did not result in greater effectiveness of incontinence reduction. A limitation of the study noted by the authors was that the study was unblinded. Another limitation is the short-term follow-up.

In a Cochrane review of conservative management for post-prostatectomy urinary incontinence, Anderson et al. (2015) reported that analysis of other conservative interventions such as transcutaneous electrical nerve stimulation and anal electrical stimulation, or combinations of these interventions were inconclusive. Fifty randomized and quasi-randomized controlled trials met the inclusion criteria, forty-five trials included men after radical prostatectomy (RP), four trials after transurethral resection of the prostate (TURP) and one trial included one man with benign disease but was classed as a radical prostatectomy. There were too few data to determine treatment effects on incontinence after TURP. The findings should continue to be treated with caution, as most studies were of poor to moderate quality.

Percutaneous Electrical Nerve Stimulation (PENS) and Percutaneous Neuromodulation Therapy (PNT):

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. As with TENS, small wires are attached to a battery-powered electrical stimulator. However, with PENS needle electrodes deliver current closer to the nerves or the muscles beneath the skin, in an effort to make the nerves less sensitive to pain. Typically PENS is used on patients who fail pain relief from TENS. PENS therapy is likely to be used first in a health care or physical therapy setting, but can also be used at home.

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 typically consists of two to three, 30-minute sessions per week, for two to six weeks.

U.S. Food and Drug Administration (FDA): The Vertis PNT System (Vertis Neuroscience Inc., Seattle, WA) was granted marketing approval by the FDA via the 510(k) process. PNT “is indicated for the symptomatic relief and management of chronic or intractable pain and/or as an adjunctive treatment in the management of post-surgical pain and post-trauma pain” (FDA, 2002). The Vertis PNT Control Unit with a cervical electrode and cable also received 510(k) approval.

The FDA approved the NSS-2 Bridge device as a Denovo Class II percutaneous nerve stimulator for substance use disorders. This device was used as a predicate for a PENS device called the IB-Stim (Innovative Health Solutions, Inc., Versailles, IN) which is intended to be used in patients 11-18 years of age with functional abdominal pain associated with irritable bowel syndrome (FDA, 2019). Prior to branding, the IB-Stim device was known as “Neuro-Stim”.

Literature Review: 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.

Back Pain: In a health technology assessment, Hayes (2017; reviewed 2019) 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. The 2019 review reported one new relevant study which did not change Hayes’s initial conclusion regarding the outcomes and quality of evidence.

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 (CGAE) or to 4) control-PENS plus CGAE. 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 CGAE 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%.

Knee Pain: 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 (p=0.0071). At one week follow-up, the live group reported significantly less medication use (p<0.0001) than the sham group.

Functional Gastrointestinal Disorders: Kovacic et al. (2017) conducted a randomized controlled trial (RCT) to evaluate the efficacy of percutaneous electrical nerve field stimulation (PENFS) using the Neuro-Stim device in adolescents with abdominal pain related to functional gastrointestinal disorders (e.g., irritable bowel syndrome, functional dyspepsia). There were 104 patients aged 11-18 years old who underwent either PENS with an active device (n=60) or sham (n=55); however, 11 patients were lost to follow up, leaving a total of 93 patients analyzed at long term follow up. Adolescents who met Rome III criteria for abdominal pain-related functional

gastrointestinal disorders and had an average abdominal pain rating of three or higher and a minimum of two pain days per week were included. Patients who had less than one week of data and those with organic disease were excluded. Patients were also excluded if they had a history of: seizures, developmental delay, or had an implanted electrical device. The intervention, Neuro-Stim device, delivered electrical stimulation two hours on and two hours off for five days per week for four weeks. The comparator was sham (no electrical charge). The primary outcome measure was change or improvement in abdominal pain scores using the Pain Frequency-Severity-Duration (PFSD) scale. Secondary outcomes were global symptoms improvement (global wellbeing scale), functioning (Functional Disability Inventory), and anxiety (State-Trait Anxiety Inventory for Children). Follow-up occurred every seven days for three weeks and again at 8-12 weeks following therapy. Results showed that patients in the active PENS group had a statistically significant greater reduction in worst pain compared to the sham group after three weeks of treatment ($p < 0.0001$) and was sustained for an average of 9.2 weeks. Additionally, median pain scores were reduced by 11.48 points after three weeks of treatment. Ten patients reported side effects including: ear discomfort ($n=3$ in the active group; $n=3$ in the sham group), adhesive allergy ($n=1$ in the active group; 2 in the sham group), and syncope due to needle phobia ($n=1$ in the sham group). The study is limited by the small patient population, patient attrition, and short term follow-up.

Krasaelap et al (2020) conducted a randomized double-blind trial to analyze the effects of PENFS, using the Neuro-Stim device, on abdominal pain, global wellbeing, and functioning in adolescent irritable bowel syndrome (IBS). Patients (11-18 years) were included if they met criteria for IBS (based on the Rome III version of the Questionnaire on Pediatric Gastrointestinal Symptoms), had an average abdominal pain intensity of \geq three (on an 11-point numeric rating scale), and experienced abdominal pain \geq two times per week for \geq two months. Patients were excluded if they were on medications or had chronic conditions that can cause gastrointestinal symptoms. The intervention consisted of PENFS ($n=27$) five days per week for four weeks. The comparator was sham PENFS ($n=23$). The primary outcome measure was the number of patients with a reduction of 30% or more in worst abdominal pain severity after three weeks. Secondary outcome measures were reduction in composite abdominal pain severity score, reduction in usual abdominal pain severity, and improvement in global symptom based on a symptom response scale after three weeks. Follow-up consisted of questionnaires completed by the patients at baseline; after the first, second, and third weeks of therapy; and at eight to twelve weeks after the completion of therapy. Patients also completed a daily diary during the fourth week. A 30% decrease of worst abdominal pain was observed in a statistically significant number of patients who received PENFS vs. sham stimulation ($p=0.024$). A statistically significant reduction in composite pain median score in the PENFS treatment group vs. the sham group ($p=0.026$), statistically significant reduction in usual pain median score in the PENFS group vs. sham ($p=0.029$), and a statistically significant improvement in global symptoms in the PENFS group vs. sham ($p \leq 0.001$) were all observed. These effects were not sustained at eight to twelve weeks after the completion of therapy. Allergy to the adhesive used to apply the device was the only reported adverse event. Author noted limitations of the study include the small sample size, short term follow up, and incomplete data extraction. Additional larger and longer-term follow-up studies are needed to assess the effects of PENFS on abdominal pain, global wellbeing, and functioning in adolescent irritable bowel syndrome (IBS).

Percutaneous nerve field stimulator (PNFS) for Substance Use Disorders

A recently FDA approved PNFS device is the NSS-2 Bridge (Innovative Health Solutions Inc., Indianapolis, IN). The Bridge is a battery-powered percutaneous nerve field stimulator (PNFS) proposed to be used as an aid to reduce the symptoms of opioid withdrawal. The device contains a battery-powered chip that emits electrical pulses to stimulate branches of cranial nerves V, VII, IX, X and the occipital nerves. Patients can use the device for up to five days during acute symptoms (e.g., sweating, gastrointestinal upset, agitation, insomnia and joint pain) that may be experienced during the physical withdrawal phase. NSS-2 was originally created to alleviate soreness and chronic pain. The NSS-2 Bridge is worn behind the ear and requires a prescription (Hayes, 2017; Innovative Health, 2018).

U.S. Food and Drug Administration: The FDA approved the NSS-2 Bridge device as a Denovo Class II percutaneous nerve stimulator for substance use disorders. FDA identifies this generic type of device as a “percutaneous nerve stimulator for substance use disorders. A percutaneous nerve stimulator for substance use disorders is a device that stimulates nerves percutaneously to aid in the reduction of withdrawal symptoms associated with substance use disorders” (FDA, 2017).

Literature Review: Published studies investigating the safety and effectiveness of the NSS-2 Bridge are primarily in the form of retrospective reviews with small patient populations (n=73) (Miranda and Taca, 2018). There is currently insufficient evidence to support the use of this device for any indication including the treatment of chronic pain and opioid withdrawal.

Threshold/Therapeutic Electrical Stimulation (TES)

TES is the application of a low level current (2–10 milliamps) to the muscles in the body. It is typically applied at home while the patient is sleeping, for 8–12 hours per night, for up to six nights a week, for years. Researchers have proposed the use of TES for decreasing neuromuscular spasms that result from involuntary muscle contractions in patients with motor disorders (e.g., cerebral palsy, spina bifida). Proposed outcomes of TES include: improved muscle strength, decreased spasticity, increased joint mobility, and improved bowel and bladder dysfunction. It is also proposed as a treatment option for scoliosis and urinary incontinence (Nakagawa, et al., 2010).

U.S. Food and Drug Administration (FDA): TES devices are approved as 510(k) FDA Class II devices. The NT2000-TES (Bio-Medical Research LTD, Laurel, MD) is an example of an approved device.

Literature Review: The exact mechanism by which threshold electrical stimulation (TES) might improve motor function in children with cerebral palsy or other motor disorders is unclear. Study results are conflicting regarding the potential benefit of TES. There is insufficient published peer-reviewed scientific literature to support TES in the treatment of cerebral palsy or other motor disorders.

NG et al. (2016) conducted a Cochrane review of randomized controlled trials to assess the safety and effectiveness of TES to improve bowel function and constipation symptoms in children. Any type of TES, administered at home or in a clinical setting, compared to no treatment, sham TES, other forms of nerve stimulation or any other pharmaceutical or non-pharmaceutical measures used to treat constipation in children were considered for inclusion. One study (n=46) met inclusion criteria. There was a high risk of bias, indirectness and imprecision in the study. There is insufficient evidence to assess the effectiveness of TES on bowel movements, colonic transit, soiling symptoms and quality of life in children.

Negm et al. (2013) conducted a systematic review of randomized controlled trials to determine if low frequency (≤ 100 Hz) TES by pulsed electrical stimulation (PES) or by pulsed electromagnetic field (PEMF) compared to PEMF/PES sham is an effective treatment for osteoarthritis. Seven studies (n=459) met inclusion criteria. Follow-ups ranged from 2–26 weeks and the frequency of PEMF/PES varied from 5–100 Hz. Overall, the evidence suggested that PEMF/PES seemed to improve function but did not significantly decrease pain. However, the studies were of low quality, had a high risk of bias and included small patient populations. Due to heterogeneity of outcome measures, pulsed subsensory threshold electrical stimulation types and treatment regimens, well-designed randomized controlled trials with large patient populations and long-term follow-ups are needed to determine the effectiveness of PEMF/PES for this osteoarthritis.

Kerr et al. (2006) conducted a randomized, placebo-controlled trial to assess the efficacy of NMES and TES in strengthening quadriceps muscles of both legs in 60 children with cerebral palsy (CP) with diplegia. The children were randomized into one of three groups: NMES (n=18), TES (n=20), or placebo (n=22). Outcome measures included peak torque of the left and right quadriceps muscles, gross motor function, and impact of disability. They were assessed at baseline, at a six week follow-up visit, and at the end of treatment (16 weeks). No statistically significant difference was noted for NMES or TES versus placebo for strength or function. Statistically significant differences were noted between NMES and TES versus placebo for impact of disability at the end of treatment, but only between TES and placebo at the six week follow-up. The authors noted that further evidence is required to establish the role of NMES and TES as an adjunct therapy, to define patient populations that would benefit from NMES and TES and to determine the appropriate dosing parameters.

Dali et al. (2002) conducted a randomized controlled trial to determine whether a group of stable children with CP (i.e., 36 males, 21 females; mean age 10; age range 5–18) would improve their motor skills after 12 months of TES. Two-thirds received active and one-third received inactive stimulators. Tests were videotaped and assessed blindly to record qualitative changes that might not be reflected in performance measurements. Range of motion, degree of spasticity, and muscle growth measured by computed tomography (CT) were evaluated.

Fifty-seven of 82 outpatients who were able to walk at least with a walker completed all 12 months of treatment (hemiplegia [n=25]; diplegia [n=32]). There was no significant difference between active and placebo treatment in any of the study groups. Visual and subjective assessments favored TES, whereas objective indices showed the opposite trend. The authors concluded that TES in these CP patients did not have any significant clinical effect during the test period and that additional studies are needed to establish whether or not TES causes improvement in children with other movement disorders than the children with hemiplegia and diplegia in this study.

Transcutaneous Electrical Acupoint Stimulation

Transcutaneous electrical acupoint stimulation (TEAS), also called electrical acustimulation, and transdermal neuromodulation, involves placing cutaneous electrodes on the skin to deliver an electrical pulse to designated acupoints depending on the condition or indication for TEAS. The median nerve is an acupuncture site (Neiguan point P6) proposed to be associated with nausea and vomiting. Some TEAS devices have a watch-type appearance and are worn on the wrist. These devices have been proposed for the relief of nausea and vomiting associated with pregnancy, surgery, chemotherapy and motion sickness. Neurowave Medical Technologies™ (Chicago, IL) offers several of these devices. Nometex™ is proposed for the relief of chemotherapy induced nausea and vomiting, PrimaBella™ for nausea and vomiting associated with pregnancy, Reletex™ for post-operative nausea and vomiting (PONV), and GNV for general nausea and vomiting from motion sickness. Reliefband (Reliefband Technologies LLC, Philadelphia, PA) is proposed for relief of motion sickness, morning sickness and nausea due to chemotherapy. This device is available over the counter.

TEAS is also being proposed for use in other conditions such as control of diabetes, glaucoma and muscle spasticity following brain injury, pain-relieving effects before and after surgical abortion. However, there is insufficient evidence to support TEAS for these indications. Studies involved small patient populations, short treatment periods and short-term follow-up. In some cases reported benefits were not sustained. Treatment regimens, optimal acupoint locations, long-term efficacy and patient selection criteria have not been defined (Feng, et al., 2016; Yeh, et al., 2015; Zhiyuan, et al., 2015; Zhao, et al., 2015).

U.S. Food and Drug Administration (FDA): The original FDA approval for these devices was for various models of the ReliefBand NST (Woodside Biomedical, Inc., Lake Forest, CA). Approved indications included the treatment of nausea and vomiting due to motion sickness, chemotherapy, pregnancy and therapy related to acquired immune deficiency syndrome (AIDS) (FDA, 1998). A year later, ReliefBand was approved as an adjunct for postoperative nausea and vomiting. In 2007, the product rights for ReliefBand were purchased by Neurowave Medical Technologies (FDA, 2002).

Literature Review

There is insufficient evidence in the published peer-reviewed scientific literature to support the safety and efficacy of transcutaneous electrical acupoint stimulation (TEAS) for any indication. Studies primarily include small patient populations, short-term follow-ups or no follow-up and conflicting outcomes. Some studies reported that there was no benefit gained from the use of these devices or no lasting benefit when compared to placebo or standard of care. Patient selection criteria and treatment regimens have not been established. Overall, significant reductions in the use of antiemetics and occurrence of vomiting/retching have not been reported with electrical acustimulation.

Cancer: Chao et al. (2009) conducted a systematic review to evaluate acupoint stimulation for the management of adverse events in breast cancer. Twenty-six articles addressing acupoint stimulation for various conditions related to anticancer therapies including vasomotor syndrome, chemotherapy-induced nausea and vomiting, lymphedema, post-operation pain, aromatase inhibitors-related joint pain and leucopenia met inclusion criteria. Two randomized controlled trials (RCT) (n=64–67) and one case series (n=27) evaluated electrical acustimulation for the treatment of vomiting. When compared to standard care, one study reported a significant improvement in emesis with acustimulation ($p < 0.001$) at five days but not at day nine. The other RCT reported no significant difference with acustimulation compared to placebo.

In a 2007 systematic review, Tipton et al. reviewed strategies for the treatment of chemotherapy-induced nausea and vomiting and concluded that the effectiveness of acustimulation using a wristband device had not been established. One systematic review reported that no benefit was found with the use of the band. Two

randomized controlled trials reported positive but inconclusive results, and two reported that there were no significant differences in the outcomes.

To evaluate the effectiveness of stimulation of P6 for the treatment of chemo-therapy induced nausea and vomiting, Roscoe et al. (2003) randomized 739 patients to either an acupressure band, an acustimulation band (ReliefBand), or no band (control). Patients were chemotherapy naïve and about to begin a cancer treatment regimen. Appropriate pharmacotherapy for symptoms were given as indicated. Compared to no band, patients in the acupressure group had significantly less nausea on the day of treatment ($p < 0.05$), but this reduction was not maintained days 2–5. The acupressure group took fewer antiemetic pills ($p < 0.05$) than the no band group. Men in the acustimulation group reported less vomiting ($p < 0.05$) and less severe nausea ($p \leq 0.05$). No differences were reported in the amount of antiemetic medication taken or in delayed nausea in the acustimulation group. In women ($n=645$), there were no significant differences in all outcomes among the three groups and no significant differences between each treatment group and the control group. Women in the acupressure group experienced less severe nausea overall and in the delayed phase compared to the women in the acustimulation group ($p < 0.05$). Women in the acustimulation group reported more nausea on day three. Expected efficacy of the bands resulted in higher scores in the acupressure group but not in the acustimulation group. The authors noted that the expected benefits appeared at least in part to be a placebo/expectance effect. The results of this study do not support the efficacy of acustimulation and the differences in the outcomes in men and women were unexplained.

Postoperative Nausea and Vomiting: Chen et al. (2020) conducted a meta-analysis of 14 randomized controlled trials (RCTs) ($n=1653$) to evaluate the effectiveness of transcutaneous electrical acupoint stimulation (TEAS) for preventing postoperative nausea and vomiting (PONV) after general anesthesia. The studies included a total of 835 patients in the study group and 818 subjects in the sham group. Individual sample sizes of the various studies ranged from 50-361 patients. Ages of the patients ranged from 18-70 years. Studies were included if: the study was an RCT, the intervention was TEAS, and the placebo was sham TEAS. Case reports, crossover studies, letters, editorials, review articles, animal experiments, and studies involving data that couldn't be extracted or was lacking adequate data were excluded. The intervention consisted of TEAS on the target acupoints delivered through electrode tabs. Variances were noted in the treatment protocol including the time point of the application of the intervention (e.g., 30 minutes before anesthesia; four, eight, and 12 hours postoperatively and three times on the next two days after surgery; and 30-60 minutes before induction until the end of surgery). Sham TEAS served as the comparator. The primary outcome measures included: incidence of PONV, postoperative nausea (PON), and postoperative vomiting (POV). Secondary outcome measures included: the need for antiemetic rescue and the incidence of postoperative adverse effects referred to general anesthesia. Follow-up occurred within 24 hours after surgery. Seven RCTs demonstrated that patients in the TEAS group had a lower incidence of PONV compared to the control group ($p < 0.0001$), seven RCTs demonstrated a lower incidence of PON ($p < 0.0001$), and seven RCTs demonstrated a lower incidence of POV ($p < 0.0001$). Additionally, four RCTs found that the TEAS group had less numbers of patients needing antiemetic rescue ($p=0.0005$), four RCTs reported the incidence of dizziness was lower ($p < 0.0001$), and three RCTs found that the incidence of pruritis was lower ($p=0.02$). There were no adverse events discussed in the review. The authors stated that the findings should be interpreted with caution due to the limitations of the studies and noted that 12 out of the 14 studies were conducted in China, which may impact the reliability of the results. The limitations of the study included: small patient populations ($p < 100$) for numerous studies, short-term follow-up (24 hours after surgery), and heterogeneity of the interventions, acupoints, frequency, and use of postoperative opioids. Additional, homogeneous RCTs are needed to validate the outcomes of this analysis and the long term effects of TEAS in this subpopulation.

Sun et al. (2019) conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) to explore whether non-needle acupoint stimulation (electrical stimulation and acupressure) could have an effect on preventing post-operative nausea and vomiting after breast surgery. A total of 14 RCTs met inclusion criteria ($n=1009$). The individual sample sizes ranged from 50-112 subjects. Studies evaluating electrical stimulation or acupressure as a therapeutic intervention for preventing postoperative nausea and vomiting after breast surgery utilizing general anesthesia in female patients were included. Studies used sham and/or active control procedures. Surgery other than that performed on the breast; RCTs using antiemetic, laser acupuncture, traditional acupuncture, and massage as controls; RCTs using traditional acupuncture as the primary intervention in the treatment group; and trials that failed to offer proper data were excluded. The interventions

consisted of transcutaneous electrical acupoint stimulation (n=12 studies) and acupressure (n=2 studies) for more than 30 minutes intraoperatively. Comparators included sham stimulation (n=6 studies), stimulation in sham acupoint (n=3 studies), routine nursing care (n=4 studies) and auricular acupoints stimulation (n=1 study). The primary outcome measured was the frequency of post-operative nausea/vomiting at selected time intervals. A secondary outcome was the use of an antiemetic. Follow up assessments occurred post operatively at six hours, 12 hours, 24 hours, and 48 hours. Overall, there were no statistically significant differences in the individual outcomes. Nausea could be reduced by acupoint stimulation in the early phase after breast surgery (0-12 hours). However, acupoint stimulation had no reducing effect on vomiting at the same time. Two studies (n=77) reported adverse events which included wrist and hand side effects such as redness, swelling, tenderness, and paresthesias attributed to the wristbands. Author noted limitations of the various selected studies included: an unclear risk of selection bias, performance bias, detection bias, attrition bias, and reporting bias. Heterogeneity existed in the type of surgery, duration of surgery, controls, and anesthesia. There was also a lack of description of allocation concealment, blinding of participants, and outcome assessors. An additional limitation was noted in the post-operative time at which the outcomes were measured. Due to the limitations of the studies, additional, homogeneous RCTs are needed to validate the outcomes of this analysis.

A 2015 Cochrane systematic review (Lee, et al., 2015) of randomized controlled trials evaluated the effectiveness of PC6 acupoint stimulation for the treatment of postoperative nausea and vomiting (PONV) compared to sham or drug therapy or PC6 plus drug therapy vs. drug therapy alone. A total of 59 studies (n=7667 including 727 children) met inclusion criteria. Compared to sham PC6 acupoint significantly reduced nausea, vomiting and the need for rescue antiemetics. However, due to the heterogeneity of the trials (e.g., variation in treatment regimen and outcomes) and study limitations, the quality of evidence was rated as low. PC6 acupoint stimulation was compared to six different types of antiemetic drugs (metoclopramide, cyclizine, prochlorperazine, droperidol, ondansetron and dexamethasone). There was no significant difference between PC6 stimulation and antiemetic drugs. Based on "very low" quality of evidence, PC6 acupoint stimulation plus antiemetic therapy vs antiemetic drugs alone reduced the incidence of vomiting and need for rescue antiemetics but not for nausea. Fourteen trials reported minimal and transient side effects (e.g. skin irritation, blistering, redness and pain) of PC6 stimulation. Twenty-five trials were considered at high risk of bias. The authors concluded that there was moderate-quality evidence showing no difference between PC6 acupoint stimulation and antiemetic drugs to prevent PONV and that PC6 stimulation vs. antiemetic trials were "futile in showing a significant difference". The evidence supporting the use of combination therapy with PC6 acupoint stimulation and antiemetic drugs was inconclusive.

Pregnancy: Matthews et al. (2015) conducted a Cochrane systematic review of randomized controlled trials to assess the safety and efficacy of interventions for the treatment of nausea, vomiting and retching during the first 20 weeks of gestation. Interventions included acupressure, acustimulation, acupuncture, ginger, vitamin B6 and several antiemetic drugs. Forty-one trials (n=5449) met inclusion criteria. Only one study (n=230) evaluated acustimulation and usable data was not reported.

Helmreich et al. (2006) conducted a meta-analysis to evaluate the effectiveness of acustimulation on the prevention of nausea and vomiting in pregnant women. Eight randomized controlled trials and six cross over controlled trials met inclusion criteria (n=1655). Only two studies used electrical acustimulation, Rosen et al. 2003 discussed below and a crossover trial with 25 patients. There was insufficient evidence to support electrical acustimulation for the treatment of nausea and vomiting in pregnancy.

Professional Societies: In a 2018 practice bulletin, the American College of Obstetricians and Gynecologists (ACOG) stated that acupressure, acupuncture, or electrical nerve stimulation (acustimulation) at the P6 or Neiguan point on the inside of the wrist has been studied for the treatment of nausea and vomiting during pregnancy and results were conflicting. Although most studies reported a benefit many had significant methodologic flaws and two of the largest, best designed studies showed no benefit compared to sham. Two other systematic reviews reported some limited benefit with P6 acupressure but no benefit in P6 acupuncture or nerve stimulation.

Transcutaneous Electrical Joint Stimulation

Transcutaneous electrical joint stimulation has been proposed as an alternative treatment for osteoarthritis and rheumatoid arthritis. The devices are noninvasive and deliver low-amplitude pulsed electrical stimulation (PES).

Proponents theorize that PES can facilitate bone formation and cartilage repair and alter inflammatory cell function to reduce the pain and symptoms associated with osteoarthritis (OA) of the knee and rheumatoid arthritis (RA) of the hand. These devices differ from traditional transcutaneous electrical nerve stimulation (TENS) units in that the TENS units deliver electrical pulses that theoretically block pain or reduce the perception of pain, not repair the underlying cause of the pain. There is insufficient evidence to demonstrate that transcutaneous electrical joint stimulation is effective and facilitates bone formation and cartilage repair.

U.S. Food and Drug Administration (FDA)

FDA initially approved the BioniCare Bio-1000 System as a substantially equivalent 510(k) Class II predicate device to the transcutaneous electrical nerve stimulator (TENS). The BioniCare System is approved for use as an adjunctive therapy in reducing the level of pain and symptoms associated with osteoarthritis of the knee and for overall improvement of the knee as assessed by the physician's global evaluation. In 2005, the device was approved as an adjunctive therapy to reduce the level of pain and stiffness associated with rheumatoid arthritis of the hand. The J-Stim1000 (Pain Management Technologies, Akron, OH), was also approved as an adjunctive therapy in reducing the level of pain and symptoms associated with OA of the knee and RA of the hand.

Literature Review

The evidence in the published peer reviewed scientific literature does not support the efficacy of transcutaneous electrical joint stimulation devices for any indication. The limited numbers of studies are primarily in the form of randomized controlled trials and case series with small patient populations and short-term follow-ups. There was no significant difference in the outcomes compared to placebo (Hungerford, et al., 2013; Fary et al., 2011; Farr, et al., 2006; Mont, et al., 2006).

Garland et al. (2007) conducted a randomized, double-blind, controlled study to evaluate the clinical effectiveness of the BioniCare Bio-1000 in patients (n=58) with knee OA. Primary outcome measures included: (1) the percent change from baseline on a 0–100 visual analog scale (VAS) measuring patient global evaluation of arthritis symptoms in the treated knee, (2) the percent change from baseline of pain and other symptoms, and (3) the percent change from baseline on the Western Ontario and McMaster Universities (WOMAC) pain, stiffness, and function subscales. Patients were randomly assigned an active (n=39) or placebo (n=19) device in a 2:1 ratio. All differences in each of the five categories favored the active group over the placebo group. Devices were used for 4–6 hours per day at home and follow-up occurred at three months. According to the study, based on the percentage of patients in each treatment group who experienced 50% or greater improvement in each primary outcome, three of five primary outcome measures showed a statistically significant difference. The exceptions were WOMAC stiffness (p=0.08) and function (p=0.14). Limitations of the study include the small sample size, short-term follow-up and self-reported outcomes.

Transcutaneous Electrical Modulation Pain Reprocessing (TEMPR)

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).

U.S. Food and Drug Administration (FDA): The Scrambler St 5 TENS Device (Competitive Technologies, Inc., Fairfield, CT) was approved by the FDA 510(k) process in 2009 and classified as a multi-channel TENS that allows simultaneous treatment of a number of pain sites. It is indicated for "symptomatic relief of chronic,

intractable pain, post-surgical and post-traumatic acute pain". The Scrambler Therapy MC-5A Device and the Scrambler Therapy Technology ST-5A Device (Delta international Service & Logistics S.r.l.) were approved by the FDA 510(k) process in 2015 and 2020 respectively for the same indication.

Literature Review: 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., 2010~~; Smith, et al., 2020; Sabato, et al., 2005; Marineo, et al., 2003).

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.

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.

Systematic Reviews of Multiple Devices/Therapies

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 ≥ 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.

Stewart et al. (2017) conducted a Cochrane review of randomized or quasi-randomized controlled trials investigating electrical stimulation (ES) with non-implanted devices compared with any other treatment for stress urinary incontinence (SUI) in women. A total of 56 studies (n=3781) met inclusion criteria. Subjects were adult women with SUI or stress-predominant mixed urinary incontinence (MUI).

Results included the following:

- For subjective cure of SUI, moderate-quality evidence reported that ES was probably better than no active treatment. Similar results for cure or improvement of SUI were reported, but the quality of evidence was lower.
- Due to the low quality of evidence, it could not be determined if there was a difference between ES and sham treatment in terms of subjective cure. For subjective cure or improvement, ES may be better than sham treatment.
- The effect estimate was 660/1000 women cured/improved with ES compared to 382/1000 with no active treatment; and for sham treatment, 402/1000 women cured/improved with ES compared to 198/1000 with sham treatment.
- Low-quality evidence suggested that there may be no difference in cure or improvement for ES versus PFMT, PFMT plus ES versus PFMT alone or ES versus vaginal cones.
- Electrical stimulation probably improved incontinence-specific quality of life (QoL) compared to no treatment (moderate quality evidence) but there may be little or no difference between electrical stimulation and PFMT (low quality evidence).
- It was uncertain whether adding electrical stimulation to PFMT made any difference in terms of quality of life, compared with PFMT alone (very low quality evidence).
- There may be little or no difference between electrical stimulation and vaginal cones in improving incontinence-specific QoL (low quality evidence).
- The impact of electrical stimulation on subjective cure/improvement and incontinence-specific QoL, compared with vaginal cones, PFMT plus vaginal cones, or drugs therapy, was uncertain (very low quality evidence).
- In terms of subjective cure/improvement and incontinence-specific QoL, the available evidence comparing ES versus drug therapy or PFMT plus vaginal cones was very low quality and inconclusive.
- Comparisons of different types of ES to each other and of ES plus surgery to surgery were inconclusive in terms of subjective cure/improvement and incontinence-specific QoL (very low-quality evidence).

A total nine of the women treated with ES in the trials reported an adverse effect. A total of 25% of the studies were assessed at high risk of bias. The authors concluded that there was insufficient evidence to compare the risk of adverse effects in women treated with ES compared to any other treatment. Due to the low quality of the unreliable evidence, no firm conclusions could be made regarding the effectiveness of ES compared to active or sham treatment nor was it possible to determine whether ES was similar to PFMT or other active treatments.

The Agency for Healthcare Research and Quality (AHRQ) (2016) conducted a comparative effectiveness review on noninvasive treatments for acute or subacute low back pain. A total of 156 studies were included. Most trials enrolled patients with pain symptoms of at least moderate intensity (e.g., >5 on a 0- to 10-point numeric rating scale for pain). Effects on function were generally smaller than effects on pain; in some cases, there were positive effects on pain but no effects on function, and fewer studies measured function than pain. Benefits were mostly measured at short-term follow-up. Pharmacotherapy and physical modalities including TENS, PENS and interferential therapy (IFT) were reviewed. The studies evaluating TENS vs. sham for acute and subacute pain and function were too limited to permit reliable conclusions regarding effectiveness. A systematic review found no differences between TENS vs. sham in pain intensity (n=4 trials) or function at short-term follow-up (n=2 trials). Likewise, a systematic review found no differences between TENS vs. acupuncture for short- (n=4 trials) or long-term (n=2 trials) chronic LBP. Seven trials investigating PENS vs. sham, PENS plus exercise vs. exercise

alone, and PENS vs. other interventions for chronic LBP met inclusion criteria. The evidence was insufficient to determine the effectiveness of PENS due to methodological limitations and inconsistencies in the studies. Four studies investigated IFT vs. another intervention for subacute to chronic LBP but the evidence was inconclusive due to the poor methodology. There is insufficient evidence to support the effectiveness of TENS, PENS and IFT for the treatment of acute or chronic LBP.

Cherian et al. (2016) conducted a systematic review and meta-analysis of non-operative treatment modalities proposed for osteoarthritis of the knee. The treatment modalities included transcutaneous electrical nerve stimulation (TENS) and neuromuscular electrical stimulation (NMES). Seven randomized controlled trials and case series (n=107) evaluated the use of TENS. Follow-ups ranged from 2–4 weeks (mean, eight weeks). There was a significant improvement in pain from pre- to post-treatment with TENS ($p < 0.001$). However, the studies included small patient populations and short-term follow-ups. Six randomized controlled trials and case series (n=148) evaluated the use of NMES. Follow-ups ranged from 4–16 weeks (mean 11 weeks). A significant overall pain reduction ($p = 0.001$) was reported. However, the heterogeneity among NMES studies was substantially significant ($p < 0.0001$). Another limitations of the studies was a lack of consistency in implementation (e.g., length of time used; electrode positions, frequency of use). Additional further longer-term follow-up studies are needed to assess the effects of TENS and NMES on quality of life, functional outcome and patient satisfaction as adjuncts to other modalities, as well as for their potential to reduce the need for total knee arthroplasty. Based on the current evidence TENS and NMES cannot be recommended for the treatment of osteoarthritis of the knee.

Page et al (2016) conducted a Cochrane systematic review of randomized and quasi-randomized controlled trials to assess the effectiveness of electrotherapy modalities for the treatment of rotator cuff disease. Forty-seven trials (n=2388) met inclusion criteria. Transcutaneous electrical nerve stimulation (TENS) (n=8 studies) and microcurrent electrical stimulation (MENS) (n=1 study) were among the modalities investigated. There was no high quality evidence to support the use of TENS. Due to the lack of data, it could not be determined if TENS was clinically beneficial compared to placebo, hot packs, glucocorticoid injection, or extracorporeal shockwave treatment. Studies included small patient populations, short-term treatment and/or follow-up and overall high risk of bias due to lack of blinding. One study (n=40) compared MENS with placebo three times a week for six weeks. Subjects receiving MENS reported significantly less overall pain. However, Page et al. did not consider the differences to be clinically significant. No serious adverse events were reported with TENS. Adverse events for MENS were not reported in the included study. There is insufficient evidence to support TENS and MENS for the treatment of rotator cuff disease.

Zeng et al. (2015) conducted a systematic review (n=27 studies) and meta-analysis (n=20 studies) to investigate electrical stimulation for the treatment of knee osteoarthritis pain. Studies included high-frequency transcutaneous electrical nerve stimulation (h-TENS) (50–100 Hz), low-frequency transcutaneous electrical nerve stimulation (l-TENS) (2–10 Hz), neuromuscular electrical stimulation (NMES), interferential current (IFC), pulsed electrical stimulation (PES), and noninvasive interactive neurostimulation (NIN). IFC was significantly more effective than control group and NMES in pain relief. However, the authors noted that the heterogeneity of the studies and the small patient populations could be a potential threat to the validity of results. Other limitations of the studies included variation in treatment regimens, heterogeneity of doses of stimulation, low level of methodological quality, and there was no assessment of change in status of function of the knee. There were no significant improvements with the other electrical stimulation modalities. There is insufficient evidence to support these electrical stimulation modalities for the treatment of knee pain due to osteoarthritis.

Lu et al. (2015) conducted a systematic review of the literature to evaluate electrical stimulation therapy for the treatment of constipation in children, ages 3–18 years. Two randomized controlled trials (n=26 and 33) and four case series (n=11–39) met inclusion criteria. TENS and interferential current were evaluated. Statistically significant improvements after electrical stimulation therapy were recorded in one to four outcome measures in each of the studies. However, the improvements were modest and of uncertain clinical significance. No improvement in pain was reported in the two studies that recorded abdominal pain. The studies were limited by the small patient populations, short-term therapy sessions, short-term follow-ups, reporting and selection bias, incomplete data and heterogeneity of therapy regimens (duration, frequency, length of sessions). Various outcome measures were used. There is insufficient evidence to support electrical stimulation for the treatment of constipation in children.

Moreno-Durate et al. (2014) conducted a systematic review to evaluate the safety and efficacy of electrical and magnetic stimulation for the treatment of chronic pain following spinal cord injuries (SCI). Electrical stimulation devices included: transcranial direct current stimulation (tDCS) (n=3 studies; 108 subjects); cranial electrotherapy stimulation (CES) (n=2 studies; 143 subjects); and TENS (n= 1 study; 24 subjects). Included studies used quantitative scales to measure pain, reported pain outcomes before and after treatment and described the SCI population. Six studies were randomized controlled trials. Primary outcome included mean pain scores at baseline, post-intervention and follow-up scores. Conclusions could not be made due to the poor quality of the studies. No significant adverse events were reported. Limitations of the studies included: variability in study design (e.g., parameters of stimulation, clinical characteristics); heterogeneity of type and definition of pain; short-term follow-up and heterogeneity of outcomes.

Use Outside of the US

Electrical stimulation therapy and devices are available outside of the United States by multiple distributors. For example, the Cefaly device has received the CE (Conformité Européenne) mark for distribution in Europe, a Canadian License Listing, and registration with the Australian Register of Therapeutic Goods. The Bioness L300 Foot Drop System is CE-marked for the European Union, and used in rehabilitation centers worldwide. The WalkAide device was granted CE Marking in 2006 and the Odstock FES (IMedical LTD, Wiltshire, UK) devices have also been granted CE Marking. The Odstock Dropped Foot Stimulator (ODFS) Pace received a Class IIa medical device CE mark in November 2008. The certification was amended in April 2012 to add the ODFS Pace XL device which is a wireless device (NICE, 2016; Hayes, 2016).

In a guideline on the assessment and management of chronic pain, the National Institute for Health and Clinical Excellence (NICE) (2021) does not recommend offering TENS for chronic primary pain (i.e., pain with no clear underlying cause) because “limited evidence for TENS showed no clinically important difference compared with sham TENS and usual care across several outcomes at less than 3 months, and no longer-term evidence was identified. The committee noted these technologies have been around for some time so it is unlikely that new research would be undertaken. These treatments are being used by some in the NHS without evidence of benefit, so the committee agreed that TENS, ultrasound and interferential therapy should not be offered for chronic primary pain. Resources should be re-allocated to areas with more evidence of clinical and cost effectiveness.”

In a 2019 guideline on the management of urinary incontinence, the National Institute for Health and Clinical Excellence (NICE) (United Kingdom) stated that electrical stimulation should be considered as a means to motivate and promote adherence to therapy for women who cannot contract the pelvic floor muscles but should not be used to treat women with overactive bladder or in combination with pelvic floor training. The guideline also states that transcutaneous electrical nerve stimulation to the sacral nerve should not be offered for treatment of overactive bladder. Pelvic floor muscle training is effective for about half of women with stress urinary incontinence.

The National Institute for Health and Clinical Excellence (NICE) (United Kingdom) stated in a 2018 interventional procedures guidance document that transcutaneous neuromuscular electrical stimulation for oropharyngeal dysphagia should only be used in the context of research since the evidence is limited in quality and quantity.

The National Institute for Health and Clinical Excellence (NICE) (United Kingdom) (2016, updated 2020) stated that TENS, PENS, and interferential therapy should not be offered for the treatment of low back pain with or without sciatica. The guideline included the assessment and management of low back pain and sciatica in people aged 16 years and over. Studies included small patient populations, short-term follow-up, lack of a comparator, and high risk of bias.

In a 2016 interventional procedure guidance (IPG), the National Institute for Health and Clinical Excellence (NICE) (United Kingdom) stated that transcutaneous electrical stimulation of the supraorbital nerve for treating and preventing migraines raises no safety issues, but the evidence on efficacy is limited and the procedure should only be used with special arrangements for clinical governance, consent and audit or research.

In a guidance document for stroke rehabilitation, the National Institute for Health and Clinical Excellence (NICE) (United Kingdom) (2013) stated that electrical stimulation (ES) for patients with stroke should not be routinely

offered for hand and arm rehabilitation. They did however, state that a trial of ES could be considered for patients who had evidence of muscle contraction but could not move their arm against resistance. The trial should be guided by a qualified rehabilitation specialist in the context of a comprehensive program and should only be continued if progress toward “clear functional goals” is demonstrated.

In a 2009 guidance document on FES for foot drop of central neurological origin, the National Institute for Health and Clinical Excellence (NICE) (United Kingdom) stated that the evidence on safety and efficacy “appears adequate to support” the use of FES for foot drop in terms of improving gait, but the efficacy as it relates to quality of life and activities of daily living needs to be further investigated.

The 2014 quick reference guide on the prevention and treatment of pressure ulcers endorsed by the National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel and Pan Pacific Pressure Injury Alliance, stated that electrical stimulation (ES) can be considered for the use of prevention of pressure ulcers in at risk body parts in individuals with spinal cord injury, but the evidence is indirect and the Societies do not make a specific recommendation for it use. A recommendation is given for ES to facilitate healing in recalcitrant stage II-IV pressure ulcers.

In a 2013 (revised 2019) national clinical guideline on the management of chronic pain, the Scottish Intercollegiate Guidelines Network (SIGN) stated that the use of transcutaneous electrical nerve stimulation (TENS) on patients with chronic pain resulted in a positive analgesic and therefore, TENS should be considered for treatment in this population.

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	Electrical Stimulation (ES) and Electromagnetic Therapy for the Treatment of Wounds (270.1)	07/01/2004
NCD	National	Neuromuscular Electrical Stimulaton (NMES) (160.12)	10/02/2006
NCD	National	Non-Implantable Pelvic Floor Electrical Stimulator (230.8)	06/19/2006
NCD	National	Transcutaneous Electrical Nerve Stimulation (TENS) for Chronic Low Back Pain (CLBP) (160.27)	01/07/2013
NCD	National	Supplies Used in the Delivery of Transcutaneous Electrical Nerve Stimulation (TENS) and Neuromuscular Electrical Stimulation (NMES) (160.13)	07/14/1988
NCD	National	Electrotherapy for Treatment of Facial Nerve Paralysis (Bell’s Palsy) (160.15)	The effective date has not been posted.
NCD	National	Assessing Patient’s Suitability for Electrical Nerve Stimulation Therapy (160.7.1)	06/19/2006
NCD	National	Transcutaneous Electrical Nerve Stimulation (TENS) for Acute Post-Operative Pain (10.2)	01/07/13
NCA	National	Transcutaneous Electrical Nerve Stimulation for Chronic Low Back Pain (CAG-00429N)	6/8/2012
LCD	CGS Administrators, LLC; Noridian Healthcare Solutions, LLC	Transcutaneous Electrical Joint Stimulation Devices (TEJSD) (L34821)	01/01/2020
LCD	CGS Administrators, LLC;	Transcutaneous Electrical Nerve Stimulators (TENS) (L33802)	01/01/2020

	Contractor	Determination Name/Number	Revision Effective Date
	Noridian Healthcare Solutions, LLC		
LCD	First Coast Service Options, Inc.	Wound care (L37166)	7/23/2020
LCD	Novitas Solutions, Inc.	Wound care (L35125)	7/23/2020
LCD	Wisconsin Physicians Service Insurance Corporation	Wound care (L37228)	1/28/2021
LCD	CGS Administrators, LLC	Physical Therapy – Home Health (L33942)	09/26/2019
LCD	Palmetto GBA	Home Health Occupational Therapy (L34560)	10/10/2019
LCD	Novitas Solutions, Inc.	Therapy and Rehabilitation Services (PT, OT) (L35036)	11/14/2019
LCD	First Coast Service Options, Inc.	Therapy and Rehabilitation Services (L33413)	10/1/2019
LCA	Novitas Solutions, Inc.	Auricular Stimulation (Electro-Acupuncture Device) (A55240)	1/21/2020
LCA	Palmetto GBA	Outpatient Occupational Therapy (A53064)	2/25/2021
LCA	Wisconsin Physicians Service Insurance Corporation	Percutaneous Electrical Nerve STIMULATION (PENS) and Percutaneous Neuromodulation Therapy (PNT) (A56062)	7/30/2020

Note: Please review the current Medicare Policy for the most up-to-date information.

Coding/Billing Information

- Note:** 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Electrical Stimulation Therapy

Chronic Wound Healing

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

HCPCS Codes	Description
G0281	Electrical stimulation, (unattended), to one or more areas, for chronic Stage III and Stage IV pressure ulcers, arterial ulcers, diabetic ulcers, and venous stasis ulcers not demonstrating measurable signs of healing after 30 days of conventional care, as part of a therapy plan of care

ICD-10-CM Diagnosis Codes	Description
E08.40- E08.49	Diabetes mellitus due to underlying condition with neurological complications
E08.51- E08.59	Diabetes mellitus due to underlying condition with circulatory complications
E08.65	Diabetes mellitus due to underlying condition with hyperglycemia

ICD-10-CM Diagnosis Codes	Description
E09.40- E09.49	Drug or chemical induced diabetes mellitus with neurological complications
E09.51- E09.59	Drug or chemical induced diabetes mellitus with circulatory complications
E10.40- E10.49	Type 1 diabetes mellitus with neurological complications
E10.51- E10.59	Type 1 diabetes mellitus with circulatory complications
E11.40- E11.49	Type 2 diabetes mellitus with neurological complications
E11.51- E11.59	Type 2 diabetes mellitus with circulatory complications
E13.40- E13.49	Other specified diabetes mellitus with neurological complications
E13.51- E13.59	Other specified diabetes mellitus with circulatory complications
I70.231- I70.239	Atherosclerosis of native arteries of right leg with ulceration
I70.241- I70.249	Atherosclerosis of native arteries of left leg with ulceration
I70.25	Atherosclerosis of native arteries of other extremities with ulceration
I70.331- I70.339	Atherosclerosis of unspecified type of bypass graft(s) of the right leg with ulceration
I70.341- I70.349	Atherosclerosis of unspecified type of bypass graft(s) of the left leg with ulceration
I70.35	Atherosclerosis of unspecified type of bypass graft(s) of other extremity with ulceration
I70.431- I70.439	Atherosclerosis of autologous vein bypass graft(s) of the right leg with ulceration
I70.441- I70.449	Atherosclerosis of autologous vein bypass graft(s) of the left leg with ulceration
I70.45	Atherosclerosis of autologous vein bypass graft(s) of other extremity with ulceration
I70.531- I70.539	Atherosclerosis of nonautologous biological bypass graft(s) of the right leg with ulceration
I70.541- I70.549	Atherosclerosis of nonautologous biological bypass graft(s) of the left leg with ulceration
I70.55	Atherosclerosis of nonautologous biological bypass graft(s) of other extremity with ulceration
I70.631- I70.639	Atherosclerosis of nonbiological bypass graft(s) of the right leg with ulceration
I70.641- I70.649	Atherosclerosis of nonbiological bypass graft(s) of the left leg with ulceration
I70.65	Atherosclerosis of nonbiological bypass graft(s) of other extremity with ulceration
I70.731- I70.739	Atherosclerosis of other type of bypass graft(s) of the right leg with ulceration
I70.741- I70.749	Atherosclerosis of other type of bypass graft(s) of the left leg with ulceration
I70.75	Atherosclerosis of other type of bypass graft(s) of other extremity with ulceration
I77.3	Arterial fibromuscular dysplasia
I77.89	Other specified disorders of arteries and arterioles
I83.001- I83.029	Varicose veins of lower extremities with ulcer

ICD-10-CM Diagnosis Codes	Description
I83.201- I83.229	Varicose veins of lower extremities with both ulcer and inflammation
I87.011- I87.019	Postthrombotic syndrome with ulcer
I87.031- I87.039	Postthrombotic syndrome with ulcer and inflammation
L89.003	Pressure ulcer of unspecified elbow, stage 3
L89.004	Pressure ulcer of unspecified elbow, stage 4
L89.013	Pressure ulcer of right elbow, stage 3
L89.014	Pressure ulcer of right elbow, stage 4
L89.023	Pressure ulcer of left elbow, stage 3
L89.024	Pressure ulcer of right elbow, stage 4
L89.103	Pressure ulcer of unspecified part of back, stage 3
L89.104	Pressure ulcer of unspecified part of back, stage 4
L89.113	Pressure ulcer of right upper back, stage 3
L89.114	Pressure ulcer of right upper back, stage 4
L89.123	Pressure ulcer of left upper back, stage 3
L89.124	Pressure ulcer of left upper back, stage 4
L89.133	Pressure ulcer of right lower back, stage 3
L89.134	Pressure ulcer of right lower back, stage 4
L89.143	Pressure ulcer of left lower back, stage 3
L89.144	Pressure ulcer of left lower back, stage 4
L89.153	Pressure ulcer of sacral region, stage 3
L89.154	Pressure ulcer of sacral region, stage 4
L89.203	Pressure ulcer of unspecified hip, stage 3
L89.204	Pressure ulcer of unspecified hip, stage 4
L89.213	Pressure ulcer of right hip, stage 3
L89.214	Pressure ulcer of right hip, stage 4
L89.223	Pressure ulcer of left hip, stage 3
L89.224	Pressure ulcer of left hip, stage 4
L89.303	Pressure ulcer of unspecified buttock, stage 3
L89.304	Pressure ulcer of unspecified buttock, stage 4
L89.313	Pressure ulcer of right buttock, stage 3
L89.314	Pressure ulcer of right buttock, stage 4
L89.323	Pressure ulcer of left buttock, stage 3
L89.324	Pressure ulcer of left buttock, stage 4
L89.43	Pressure ulcer of contiguous site of back, buttock and hip, stage 3
L89.44	Pressure ulcer of contiguous site of back, buttock and hip, stage 4
L89.503	Pressure ulcer of unspecified ankle, stage 3
L89.504	Pressure ulcer of unspecified ankle, stage 4
L89.513	Pressure ulcer of right ankle, stage 3
L89.514	Pressure ulcer of right ankle, stage 4
L89.523	Pressure ulcer of left ankle, stage 3
L89.524	Pressure ulcer of left ankle, stage 4
L89.603	Pressure ulcer of unspecified heel, stage 3
L89.604	Pressure ulcer of unspecified heel, stage 4
L89.613	Pressure ulcer of right heel, stage 3
L89.614	Pressure ulcer of right heel, stage 4
L89.623	Pressure ulcer of left heel, stage 3
L89.624	Pressure ulcer of left heel, stage 4
L89.813	Pressure ulcer of head, stage 3

ICD-10-CM Diagnosis Codes	Description
L89.814	Pressure ulcer of head, stage 4
L89.893	Pressure ulcer of other site, stage 3
L89.894	Pressure ulcer of other site, stage 4
L89.93	Pressure ulcer of unspecified site, stage 3
L89.94	Pressure ulcer of unspecified site, stage 4
L97.101- L97.929	Non-pressure chronic ulcer of lower limb, not elsewhere classified
L98.411- L98.499	Non-pressure chronic ulcer of skin, not elsewhere classified

Considered Experimental/Investigational/Unproven:

ICD-10-CM Diagnosis Codes	Description
	All other codes

Considered Experimental/Investigational/Unproven:

HCPCS Codes	Description
E0769	Electrical stimulation or electromagnetic wound treatment device, not otherwise classified
G0282	Electrical stimulation, (unattended), to one or more areas, for wound care other than described in G0281

ICD-10-CM Diagnosis Codes	Description
	All codes

Auricular Electroacupuncture

Considered Experimental/Investigational/Unproven:

HCPCS Codes	Description
S8930	Electrical stimulation of auricular acupuncture points; each 15 minutes of personal one-on-one contact with patient

ICD-10-CM Diagnosis Codes	Description
	All codes

Transcutaneous Electrical Modulation Pain Reprocessing (TEMPR)

Considered Experimental/Investigational/Unproven:

CPT®* Codes	Description
0278T	Transcutaneous electrical modulation pain reprocessing (eg, scrambler therapy), each treatment session (includes placement of electrodes)

ICD-10-CM Diagnosis Codes	Description
	All codes

Home Electrical Stimulation Devices (Electrical Stimulators)

Neuromuscular Electrical Stimulation (NMES)

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

HCPCS Codes	Description
A4595	Electrical stimulator supplies, 2 lead, per month, (e.g., TENS, NMES)
E0745	Neuromuscular stimulator, electronic shock unit

ICD-10-CM Diagnosis Codes	Description
M62.50- M62.59	Muscular wasting and atrophy, not elsewhere classified

Considered Experimental/Investigational/Unproven:

ICD-10-CM Diagnosis Codes	Description
	All other codes

Neuromuscular Electrical Stimulation for Scoliosis

Considered Experimental/Investigational/Unproven:

HCPCS Codes	Description
E0744	Neuromuscular stimulator for scoliosis

Transcutaneous Electrical Nerve Stimulator (TENS)

Considered medically necessary when used to report in-home use as an adjunct to conventional post-operative pain management within 30 days of surgery:

HCPCS Codes	Description
A4595	Electrical stimulator supplies, 2 lead, per month, (e.g., TENS, NMES)
E0720	Transcutaneous electrical nerve stimulation (TENS) device, 2 lead, localized stimulation
E0730	Transcutaneous electrical nerve stimulation (TENS) device, 4 or more leads, for multiple nerve stimulation

ICD-10-CM Diagnosis Codes	Description
G89.12	Acute post-thoracotomy pain

ICD-10-CM Diagnosis Codes	Description
G89.18	Other acute postprocedural pain

Considered Experimental/Investigational/Unproven

ICD-10-CM Diagnosis Codes	Description
	All other codes

Considered Experimental/Investigational/Unproven:

HCPCS Codes	Description
K1016	Transcutaneous electrical nerve stimulator for electrical stimulation of the trigeminal nerve
K1017	Monthly supplies for use of device coded at K1016

Considered Experimental/Investigational/Unproven:

ICD-10-CM Diagnosis Codes	Description
	All other codes

Conductive Garment

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

HCPCS Codes	Description
E0731	Form fitting conductive garment for delivery of TENS or NMES (with conductive fibers separated from the patient's skin by layers of fabric)

ICD-10-CM Diagnosis Codes	Description
M62.50- M62.59	Muscular wasting and atrophy, not elsewhere classified
G89.12	Acute post-thoracotomy pain
G89.18	Other acute postprocedural pain

Considered Experimental/Investigational/Unproven:

ICD-10-CM Diagnosis Codes	Description
	All other codes

Other Electrical Stimulation Therapy

Considered Experimental/Investigational/Unproven when used to report or used in conjunction with any electrical stimulator device indicated in this coverage policy as experimental, investigational or unproven:

HCPCS Codes	Description
64999	Unlisted procedure, nervous system
E0740	Non-implanted pelvic floor electrical stimulator, complete system
E0762	Transcutaneous electrical joint stimulation device system, includes all accessories
E0764	Functional neuromuscular stimulation, transcutaneous stimulation of sequential muscle groups of ambulation with computer control, used for walking by spinal cord injured, entire system, after completion of training program
E0765	FDA approved nerve stimulator, with replaceable batteries, for treatment of nausea and vomiting
E0770	Functional electrical stimulator, transcutaneous stimulation of nerve and/or muscle groups, any type, complete system, not otherwise specified.
E1399	Durable medical equipment, miscellaneous
K1002	Cranial electrotherapy stimulation (CES) system, includes all supplies and accessories, any type
K1018	External upper limb tremor stimulator of the peripheral nerves of the wrist
K1019	Monthly supplies for use of device coded at K1018
S8130	Interferential current stimulator, 2 channel
S8131	Interferential current stimulator, 4 channel

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References

1. Adunsky A, Ohry A; DDCT Group. Decubitus direct current treatment (DDCT) of pressure ulcers: results of a randomized double-blinded placebo controlled study. Arch Gerontol Geriatr. 2005. Nov-Dec;41(3):261-9.
2. Agency for Healthcare Research and Quality (AHRQ). Effective Health Care Program. Comparative effectiveness review: number 169. Noninvasive treatments for low back pain. Full report. Feb 2016. Accessed Jun 10, 2021. Available at URL address: https://effectivehealthcare.ahrq.gov/sites/default/files/back-pain-treatment_research_executive.pdf
3. Akai M, Hayashi K. Effect of electrical stimulation on musculoskeletal systems: a meta-analysis of controlled clinical trials. Bioelectromagnetics. 2002;23(2):132-43.
4. Almeida CC, Silva VZMD, Júnior GC, Liebano RE, Durigan JLQ. Transcutaneous electrical nerve stimulation and interferential current demonstrate similar effects in relieving acute and chronic pain: a systematic review with meta-analysis. Braz J Phys Ther. 2018 Sep - Oct;22(5):347-354.
5. Ambrosini E, Ferrante S, Pedrocchi A, Ferrigno G, Molteni F. Cycling induced by electrical stimulation improves motor recovery in postacute hemiparetic patients: a randomized controlled trial. Stroke. 2011 Apr;42(4):1068-73.
6. Amer-Cuenca JJ, Goicoechea C, Girona-López A, Andreu-Plaza JL, Palao-Román R, Martínez-Santa G, Lisón JF. Pain relief by applying transcutaneous electrical nerve stimulation (TENS) during unsedated colonoscopy: a randomized double-blind placebo-controlled trial. Eur J Pain. 2011 Jan;15(1):29-35.
7. American Academy of Neurology. Assessment: efficacy of transcutaneous electric nerve stimulation in the treatment of pain in neurologic disorders (an evidence-based review). 2010 (reaffirmed 2015; 2018). Accessed Jun 10, 2021. Available at URL address: <https://www.aan.com/Guidelines/home/GuidelineDetail/382>

8. American Academy of Orthopedic Surgeons (AAOS). Clinical practice guideline: Treatment of osteoarthritis of the knee. 2nd edition. 2013. Accessed Jun 10, 2021. Available at URL address: <https://www.aaos.org/globalassets/quality-and-practice-resources/osteoarthritis-of-the-knee/auc-non-arthroplasty-treatment-osteoarthritis-knee.pdf>
9. American College of Foot and Ankle Surgeons (ACFAS). Diabetic foot disorders: a clinical practice guideline. Pathway 3. 2006. Accessed Jun 10, 2021. Available at URL address: https://www.acfas.org/uploadedFiles/Healthcare_Community/Education_and_Publications/Clinical_Practice_Guidelines/DiabeticCPG-small.pdf
10. American College of Obstetricians and Gynecologists (ACOG). Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No. 189: Nausea and Vomiting of Pregnancy. *Obstet Gynecol*. 2018 Jan; 131(1):e15-e30. Accessed June 10, 2021. Available at URL address: <https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2018/01/nausea-and-vomiting-of-pregnancy>
11. American College of Physicians. Clinical guidelines and recommendations. Noninvasive treatments for acute, subacute, and chronic low back pain: a clinical practice guideline from the American College of Physicians. Apr 4, 2017. Accessed Jun 10, 2021. Available at URL address: https://www.acpjournals.org/doi/10.7326/M16-2367?_ga=2.235704321.1298480642.1623339163-942234550.1623339162&
12. American Heart Association's (AHA)/American Stroke Association (ASA). Comprehensive overview of nursing and interdisciplinary rehabilitation care of the stroke patient. 2010. Accessed June 10, 2021. Available at URL address: <http://stroke.ahajournals.org/content/41/10/2402>
13. American Migraine Foundation. Neuromodulation for migraine treatment: an overview. 2020. Accessed Jun 10, 2021. Available at URL address: <https://americanmigrainefoundation.org/resource-library/neuromodulation-for-migraine-treatment/>
14. American Society of Anesthesiologists Task Force on Chronic Pain Management; American Society of Regional Anesthesia and Pain Medicine. Practice guidelines for chronic pain management: an updated report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine. 2010. Accessed Jun 10, 2021. Available at URL address: <https://pubs.asahq.org/anesthesiology/article/112/4/810/10691/Practice-Guidelines-for-Chronic-Pain-ManagementAn>
15. Anderson CA, Omar MI, Campbell SE, Hunter KF, Cody JD, Glazener CMA. Conservative management for postprostatectomy urinary incontinence. *Cochrane Database of Systematic Reviews* 2015, Issue 1. Art. No.: CD001843.
16. Arena R, Pinkstaff S, Wheeler E, Peberdy MA, Guazzi M, Myers J. Neuromuscular electrical stimulation and inspiratory muscle training as potential adjunctive rehabilitation options for patients with heart failure. *J Cardiopulm Rehabil Prev*. 2010 Jul-Aug;30(4):209-23.
17. Atamaz FC, Durmaz B, Baydar M, Demircioglu OY, Iyiyapici A, Kuran B, Oncel S, Sendur OF. Comparison of the efficacy of transcutaneous electrical nerve stimulation, interferential currents, and shortwave diathermy in knee osteoarthritis: a double-blind, randomized, controlled multicenter study. *Arch Phys Med Rehabil*. 2012 May;93(5):748-56.
18. Azatcam G, Atalay NS, Akkaya N, Sahin F, Aksoy S, Zincir O, Topuz O. Comparison of effectiveness of Transcutaneous Electrical Nerve Stimulation and Kinesio Taping added to exercises in patients with myofascial pain syndrome. *J Back Musculoskelet Rehabil*. 2017;30(2):291-298. doi: 10.3233/BMR-150503.

19. Bai HY, Bai HY, Yang ZQ. Effect of transcutaneous electrical nerve stimulation therapy for the treatment of primary dysmenorrhea. *Medicine (Baltimore)*. 2017 Sep;96(36):e7959.
20. Barclay TH, Barclay RD. A clinical trial of cranial electrotherapy stimulation for anxiety and comorbid depression. *J Affect Disord*. 2014 Aug;164:171-7.
21. Barrett CL, Mann GE, Taylor PN, Strike P. A randomized trial to investigate the effects of functional electrical stimulation and therapeutic exercise on walking performance for people with multiple sclerosis. *Mult Scler*. 2009 Apr;15(4):493-504.
22. Bauer P, Krewer C2, Golaszewski S3, Koenig E2, Müller F2. Functional electrical stimulation-assisted active cycling--therapeutic effects in patients with hemiparesis from 7 days to 6 months after stroke: a randomized controlled pilot study. *Arch Phys Med Rehabil*. 2015 Feb;96(2):188-96.
23. Bax L, Staes F, Verhagen A. Does neuromuscular electrical stimulation strengthen the quadriceps femoris? A systematic review of randomised controlled trials. *Sports Med*. 2005;35(3):191-212.
24. Bedwell C, Dowswell T, Neilson JP, Lavender T. The use of transcutaneous electrical nerve stimulation (TENS) for pain relief in labour: a review of the evidence. *Midwifery*. 2011 Oct;27(5):e141-8.
25. Bello Y, Phillips T. Recent advances in wound healing. *JAMA*. 2000 Feb;283:716-8.
26. Berghmans B, Hendriks E, Bernards A, de Bie R, Omar MI. Electrical stimulation with non-implanted electrodes for urinary incontinence in men. *Cochrane Database of Systematic Reviews* 2013, Issue 6. Art. No.: CD001202. DOI:10.1002/14651858.CD001202.pub5.
27. Bethoux F, Rogers HL, Nolan KJ, Abrams GM, Annaswamy TM, Brandstater M, Browne B, Burnfield JM, Feng W, Freed MJ, Geis C, Greenberg J, Gudesblatt M, Ikramuddin F, Jayaraman A, Kautz SA, Lutsep HL, Madhavan S, Meilahn J, Pease WS, Rao N, Seetharama S, Sethi P, Turk MA, Wallis RA, Kuffa C. The effects of peroneal nerve functional electrical stimulation versus ankle-foot orthosis in patients with chronic stroke: a randomized controlled trial. *Neurorehabil Neural Repair*. 2014 Sep;28(7):688-97.
28. Bioness, Inc. NESS L300 Foot Drop System. 2018. Accessed Jun 10, 2021. Available at URL address: <http://www.bioness.com/Products.php>
29. Binny J, Joshua Wong NL, Garga S, et al. Transcutaneous electric nerve stimulation (TENS) for acute low back pain: systematic review. *Scand J Pain*. 2019;19(2):225-233.
30. Bjordal JM, Johnson MI, Ljunggreen AE. Transcutaneous electrical nerve stimulation (TENS) can reduce postoperative analgesic consumption. A meta-analysis with assessment of optimal treatment parameters for postoperative pain. *Eur J Pain*. 2003;7(2):181-8.
31. Blum K, Chen AL, Chen TJ, Prihoda TJ, Schoolfield J, DiNubile N, Waite RL, Arcuri V, Kerner M, Braverman ER, Rhoades P, Tung H. The H-Wave device is an effective and safe non-pharmacological analgesic for chronic pain: a meta-analysis. *Adv Ther*. 2008 Jul;25(7):644-57.
32. Boomershine C. Fibromyalgia. *Medscape. Drugs & Diseases. Rheumatology*. Updated Apr 23, 2020. Accessed Aug 10, 2021. Available at URL address: <https://emedicine.medscape.com/article/329838-overview#a6>
33. Bonnevie T, Gravier FE, Debeaumont D, Viacroze C, Muir JF, Cuvelier A, Netchitaïlo M, Roy AL, Quieffin J, Marques MH, Médrinal C, Dupuis J, Tardif C. Home-based Neuromuscular Electrical Stimulation as an Add-on to Pulmonary Rehabilitation Does Not Provide Further Benefits in Patients

With Chronic Obstructive Pulmonary Disease: A Multicenter Randomized Trial. *Arch Phys Med Rehabil.* 2018 Aug;99(8):1462-1470.

34. Borriero L, Moffa AH, Martin D, Loo CK, Brunoni AR. Transcranial Direct Current Stimulation in the Acute Depressive Episode: A Systematic Review of Current Knowledge. *J ECT.* 2018 Sep;34(3):153-163.
35. Brissot R, Gallien P, Le Bot MP, Beaubras A, Laisné D, Beillot J, Dassonville J. Clinical experience with functional electrical stimulation-assisted gait with Parastep in spinal cord-injured patients. *Spine (Phila Pa 1976).* 2000 Feb 15;25(4):501-8.
36. Brosseau L, Yonge K, Welch V, Marchand S, Judd M, Wells GA, Tugwell P. Transcutaneous electrical nerve stimulation (TENS) for the treatment of rheumatoid arthritis in the hand. *Cochrane Database of Systematic Reviews* 2003, Issue 3. Art. No.: CD004377. DOI: 10.1002/14651858.CD004377
37. Bruce-Brand RA, Walls RJ, Ong JC, Emerson BS, O'Byrne JM, Moyna NM. Effects of home-based resistance training and neuromuscular electrical stimulation in knee osteoarthritis: a randomized controlled trial. *BMC Musculoskelet Disord.* 2012 Jul 3;13(1):118.
38. Buchmuller A, Navez M, Milletre-Bernardin M, Pouplin S, Presles E, Lantéri-Minet M, Tardy B, Laurent B, Camdessanché JP; Lombotens Trial Group. Value of TENS for relief of chronic low back pain with or without radicular pain. *Eur J Pain.* 2012 May;16(5):656-65.
39. Burns JL, Blackwell SJ. Plastic surgery lower extremity. In: Townsend: Sabiston Textbook of Surgery. 18th ed. Philadelphia, PA: Saunders Elsevier, 2007. Ch. 73.
40. Cameron M, Lonergan E, Lee H. Transcutaneous Electrical Nerve Stimulation (TENS) for dementia. *Cochrane Database of Systematic Reviews* 2003. Updated 2005. Issue 3.
41. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determinations (LCDs) alphabetical index. Accessed Jun 10, 2021. Available at URL address: <https://www.cms.gov/medicare-coverage-database/indexes/lcd-alphabetical-index.aspx>
42. Centers for Medicare and Medicaid Services (CMS). National Coverage Determination (NCDs) alphabetical index. Accessed Jun 10, 2021. Available at URL address: <https://www.cms.gov/medicare-coverage-database/indexes/ncd-alphabetical-index.aspx>
43. Chao LF, Zhang AL, Liu HE, Cheng MH, Lam HB, Lo SK. The efficacy of acupoint stimulation for the management of therapy-related adverse events in patients with breast cancer: a systematic review. *Breast Cancer Res Treat.* 2009 Nov;118(2):255-67.
44. Chen J, Tu Q, Miao S, Zhou Z, Hu S. Transcutaneous electrical acupoint stimulation for preventing postoperative nausea and vomiting after general anesthesia: A meta-analysis of randomized controlled trials. *Int J Surg.* 2020;73:57-64.
45. Chen LX, Zhou ZR, Li YL, Ning GZ, Li Y, Wang XB, Feng SQ. Transcutaneous electrical nerve stimulation in patients with knee osteoarthritis: evidence from randomized-controlled trials. *Clin J Pain.* 2016 Feb;32(2):146-54.
46. Cherian JJ, Harrison PE, Benjamin SA, Bhave A, Harwin SF, Mont MA. Do the effects of transcutaneous electrical nerve stimulation on knee osteoarthritis pain and function last? *J Knee Surg.* 2016 Aug;29(6):497-501.
47. Cherian JJ, Jauregui JJ, Leichliter AK, Elmallah RK, Bhave A, Mont MA. The effects of various physical non-operative modalities on the pain in osteoarthritis of the knee. *Bone Joint J.* 2016 Jan;98-B(1 Suppl A):89-94.

48. Chiu HC, Ada L. Effect of functional electrical stimulation on activity in children with cerebral palsy: a systematic review. *Pediatr Phys Ther.* 2014 Fall;26(3):283-8.
49. Chou DE, Gross GJ, Casadei CH, Yugrakh MS. External Trigeminal Nerve Stimulation for the Acute Treatment of Migraine: Open-Label Trial on Safety and Efficacy. *Neuromodulation.* 2017 Oct;20(7):678-683.
50. Chou R, Qaseem A, Snow V, Casey D, Cross JT, Shekelle P, Owens D. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American college of physicians and the American pain society. *Annals of Internal Medicine.* Oct 2, 2007. 147(7):492-504.
51. Competitive Technologies. Calmare. 2021. Accessed Jun 10, 2021. Available at URL address: <http://www.calmarett.com/>
52. Cooper BC; International College of Cranio-Mandibular Orthopedics (ICCMO). Temporomandibular disorders: A position paper of the International College of Cranio-Mandibular Orthopedics (ICCMO). *Cranio.* 2011 Jul;29(3):237-44.
53. Coyne PJ, Wan W, Dodson P, Swainey C, Smith TJ. A trial of Scrambler therapy in the treatment of cancer pain syndromes and chronic chemotherapy-induced peripheral neuropathy. *J Pain Palliat Care Pharmacother.* 2013 Dec;27(4):359-64.
54. Crowe L, Caulfield B. Aerobic neuromuscular electrical stimulation--an emerging technology to improve haemoglobin A1c in type 2 diabetes mellitus: results of a pilot study. *BMJ Open.* 2012 Jun 14;2(3). pii: e000219.
55. Dailey DL, Vance CGT, Rakel BA, Zimmerman MB, Embree J, Merriwether EN, Geasland KM, Chimenti R, Williams JM, Golchha M, Crofford LJ, Sluka KA. Transcutaneous Electrical Nerve Stimulation Reduces Movement-Evoked Pain and Fatigue: A Randomized, Controlled Trial. *Arthritis Rheumatol.* 2020 May;72(5):824-836.
56. Dali C, Hansen F, Pedersen S, Skov L, Hilden J, Bjornskov I, et al. Threshold electrical stimulation (TES) in ambulant children with CP: a randomized double-blind placebo-controlled clinical trial. *Dev Med Child Neurol.* 2002 Jun;44(6):364-9.
57. De Gennaro M, Capitanucci ML, Mosiello G, Zaccara A. Current state of nerve stimulation technique for lower urinary tract dysfunction in children. *J Urol.* 2011 May;185(5):1571-7.
58. de Lima Pimentel R, Duque AP, Moreira BR, Rodrigues LF Junior. Acupuncture for the Treatment of Cardiovascular Diseases: A Systematic Review. *J Acupunct Meridian Stud.* 2019 Apr;12(2):43-51.
59. de Oliveira Melo M, Aragão FA, Vaz MA. Neuromuscular electrical stimulation for muscle strengthening in elderly with knee osteoarthritis - a systematic review. *Complement Ther Clin Pract.* 2013 Feb;19(1):27-31.
60. Demirtürk F, Akbayrak T, Karakaya IC, Yüksel I, Kirdi N, Demirtürk F, Kaya S, Ergen A, Beksac S. Interferential current versus biofeedback results in urinary stress incontinence. *Swiss Med Wkly.* 2008 May 31;138(21-22):317-21.
61. Department of Veterans Affairs Health Services Research and Development Services. A systematic evidence review of non-pharmacological interventions for behavioral symptoms of dementia. March 2011. Accessed Jun 10, 2021. Available at URL address: www.hsrd.research.va.gov/publications/esp/Dementia-Nonpharm.pdf

62. Department of Veterans Affairs Health Services Research and Development Services. Management of stroke rehabilitation. 2019. Accessed Jun, 10, 2021. Available at URL address: <https://www.healthquality.va.gov/guidelines/Rehab/stroke/VADoDStrokeRehabCPGFinal8292019.pdf>
63. Desmeules F, Boudreault J, Roy JS, Dionne CE, Frémont P, MacDermid J6. Efficacy of transcutaneous electrical nerve stimulation for rotator cuff tendinopathy: a systematic review. *Physiotherapy*. 2016 Mar;102(1):41-9.
64. Di Fiore P, Bussone G, Galli A, Didier H, Peccarisi C, D'Amico D, Frediani F. Transcutaneous supraorbital neurostimulation for the prevention of chronic migraine: a prospective, open-label preliminary trial. *Neurol Sci*. 2017 May;38(Suppl 1):201-206.
65. Edenfield AL, Amundsen CL, Wu JM, et al. Posterior tibial nerve stimulation for the treatment of fecal incontinence: A systematic evidence review. *Obstet Gynecol Surv*. 2015;70(5):329-341.
66. Elboim-Gabyzon M, Andrawus Najjar S, Shtarker H. Effects of transcutaneous electrical nerve stimulation (TENS) on acute postoperative pain intensity and mobility after hip fracture: A double-blinded, randomized trial. *Clin Interv Aging*. 2019;14:1841-1850. Published 2019 Oct 29.
67. Elsner B, Kugler J, Pohl M, Mehrholz J. Transcranial direct current stimulation (tDCS) for improving aphasia in adults with aphasia after stroke. *Cochrane Database of Systematic Reviews* 2019, Issue 5. Art. No.: CD009760. DOI: 10.1002/14651858.CD009760.pub4.
68. Elsner B, Kugler J, Pohl M, Mehrholz J. Transcranial direct current stimulation (tDCS) for idiopathic Parkinson's disease. *Cochrane Database of Systematic Reviews* 2016, Issue 7. Art. No.: CD010916. DOI: 10.1002/14651858.CD010916.pub2.
69. Elsner B, Kugler J, Pohl M, Mehrholz J. Transcranial direct current stimulation (tDCS) for improving aphasia in patients after stroke. *Cochrane Database of Systematic Reviews* 2013a, Issue 6. Art.No.: CD009760. DOI: 10.1002/14651858.CD009760.pub2.
70. Eraifej J, Clark W, France B, Desando S, Moore D. Effectiveness of upper limb functional electrical stimulation after stroke for the improvement of activities of daily living and motor function: a systematic review and meta-analysis. *Syst Rev*. 2017 Feb 28;6(1):40.
71. Ertas G, Bengi Sener E, Kaya C, Ozkan F, Ustun YB, Koksall E. Effects of P6 acustimulation with the ReliefBand on postoperative nausea and vomiting in patients undergoing gynecological laparoscopy. *Holist Nurs Pract*. 2015 Jan-Feb;29(1):6-12.
72. Escortell-Mayor E, Riesgo-Fuertes R, Garrido-Elustondo S, Asúnsolo-Del Barco A, Díaz-Pulido B, Blanco-Díaz M, Bejerano-Álvarez E; TEMA-TENS Group. Primary care randomized clinical trial: manual therapy effectiveness in comparison with TENS in patients with neck pain. *Man Ther*. 2011 Feb;16(1):66-73.
73. Facci LM, Nowotny JP, Tormem F, Trevisani VF. Effects of transcutaneous electrical nerve stimulation (TENS) and interferential currents (IFC) in patients with nonspecific chronic low back pain: randomized clinical trial. *Sao Paulo Med J*. 2011;129(4):206-16.
74. Farr J, Mont MA, Garland D, Caldwell JR, Zizic TM. Pulsed electrical stimulation in patients with osteoarthritis of the knee: follow up in 288 patients who had failed non-operative therapy. *Surg Technol Int*. 2006;15:227-33.
75. Fary RE, Carroll GJ, Briffa TG, Briffa NK. The effectiveness of pulsed electrical stimulation in the management of osteoarthritis of the knee: results of a double-blind, randomized, placebo-controlled, repeated-measures trial. *Arthritis Rheum*. 2011 May;63(5):1333-42. doi: 10.1002/art.30258.

76. Feng X, Ye T, Wang Z, Chen X, Cong W, Chen Y, Chen P, Chen C, Shi B, Xie W. Transcutaneous acupoint electrical stimulation pain management after surgical abortion: A cohort study. *Int J Surg*. 2016 Jun;30:104-8.
77. Fernández-Tenorio E, Serrano-Muñoz D, Avendaño-Coy J, Gómez-Soriano J. Transcutaneous electrical nerve stimulation for spasticity: A systematic review. *Neurologia*. 2019;34(7):451-460.
78. Ferrante S, Pedrocchi A, Ferrigno G, Molteni F. Cycling induced by functional electrical stimulation improves the muscular strength and the motor control of individuals with post-acute stroke. *Europa Medicophysica-SIMFER 2007 Award Winner*. *Eur J Phys Rehabil Med*. 2008 Jun;44(2):159-67.
79. Ferreira AP, Costa DR, Oliveira AI, Carvalho EA, Conti PC, Costa YM, Bonjardim. Short-term transcutaneous electrical nerve stimulation reduces pain and improves the masticatory muscle activity in temporomandibular disorder patients: a randomized controlled trial. *J Appl Oral Sci*. 2017 Mar-Apr;25(2):112-120.
80. Field-Fote EC, Roach KE. Influence of a locomotor training approach on walking speed and distance in people with chronic spinal cord injury: a randomized clinical trial. *Phys Ther*. 2011 Jan;91(1):48-60.
81. Frequency specific microcurrent. 2020. Accessed Jun 10, 2021. Available at URL address: <http://www.frequency-specific.com/>
82. Freynet A, Falcoz PE. Is transcutaneous electrical nerve stimulation effective in relieving postoperative pain after thoracotomy? *Interact Cardiovasc Thorac Surg*. 2010 Feb;10(2):283-8.
83. Fuentes JP, Armijo Olivo S, Magee DJ, Gross DP. Effectiveness of interferential current therapy in the management of musculoskeletal pain: a systematic review and meta-analysis. *Phys Ther*. 2010 Sep;90(9):1219-38.
84. Garland D, Holt P, Harrington JT, Caldwell J, Zizic T, Cholewczynski J. A 3-month, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of a highly optimized, capacitively coupled, pulsed electrical stimulator in patients with osteoarthritis of the knee. *Osteoarthritis Cartilage*. 2007 Jun;15(6):630-7.
85. George AT, Kalmar K, Sala S, Kopanakis K, Panarese A, Dudding TC, Hollingshead JR, Nicholls RJ, Vaizey CJ. Randomized controlled trial of percutaneous versus transcutaneous posterior tibial nerve stimulation in faecal incontinence. *Br J Surg*. 2013 Feb;100(3):330-8.
86. Giangregorio L, Craven C, Richards K, Kapadia N, Hitzig SL, Masani K, Popovic MR. A randomized trial of functional electrical stimulation for walking in incomplete spinal cord injury: effects on body composition. *J Spinal Cord Med*. 2012 Sep;35(5):351-60.
87. Gibson W, Wand BM, Meads C, Catley MJ, O'Connell NE. Transcutaneous electrical nerve stimulation (TENS) for chronic pain - an overview of Cochrane Reviews. *Cochrane Database of Systematic Reviews* 2019, Issue 4. Art. No.: CD011890. DOI: 10.1002/14651858.CD011890.pub3.
88. Gibson W, Wand BM, O'Connell NE. Transcutaneous electrical nerve stimulation (TENS) for neuropathic pain in adults. *Cochrane Database Syst Rev*. 2017 Sep 14;9:CD011976. doi: 10.1002/14651858.CD011976.pub2.
89. Giggins OM, Fullen BM, Coughlan GF. Neuromuscular electrical stimulation in the treatment of knee osteoarthritis: a systematic review and meta-analysis. *Clin Rehabil*. 2012 Feb 9.
90. Goode PS, Burgio KL, Johnson TM 2nd, Clay OJ, Roth DL, Markland AD, Burkhardt JH, Issa MM, Lloyd LK. Behavioral therapy with or without biofeedback and pelvic floor electrical stimulation for

persistent postprostatectomy incontinence: a randomized controlled trial. *JAMA*. 2011 Jan 12;305(2):151-9.

91. Greif R, Laciny S, Mokhtarani M, Doufas AG, Bakhshandeh M, Dorfer L, Sessler DI. Transcutaneous electrical stimulation of an auricular acupuncture point decreases anesthetic requirement. *Anesthesiology*. 2002 Feb;96(2):306-12.
92. Guido EH. Effects of sympathetic therapy on chronic pain in peripheral neuropathy subjects. *Am J Pain Mgmt*. 2002;12:31-34.
93. Gundog M, Atamaz F, Kanyilmaz S, Kirazli Y, Celepoglu G. Interferential current therapy in patients with knee osteoarthritis: comparison of the effectiveness of different amplitude-modulated frequencies. *Am J Phys Med Rehabil*. 2012 Feb;91(2):107-13.
94. Hamilton A, Wakely L, Marquez J. Transcranial Direct-Current Stimulation on Motor Function in Pediatric Cerebral Palsy: A Systematic Review. *Pediatr Phys Ther*. 2018 Oct;30(4):291-301.
95. Hayes Inc. Hayes Brief. P-Stim (Biegler GmbH) Auricular Electroacupuncture for Pain Management. Lansdale, PA: Hayes, Inc. Dec 31, 2012; annual review Dec 10, 2014. Archived.
96. Hayes Inc. Hayes Directory Report. Functional electrical stimulation for rehabilitation following spinal cord injury. Lansdale, PA: Hayes, Inc. Nov 16, 2017; reviewed Nov 14, 2019.
97. Hayes Inc. Hayes Directory Report. Pelvic floor electrical stimulation for the treatment of urinary incontinence. Lansdale, PA: Hayes, Inc. Published Feb 25, 2016. Reviewed Feb 6, 2017; Feb 8, 2018; Jan 8, 2019; Feb 11, 2020.
98. Hayes Inc. Health Technology Assessment. Percutaneous electrical nerve stimulation for treatment of low back pain. Lansdale, PA: Hayes, Inc. Published Feb 9, 2017; reviewed Feb 9, 2018; Jan 10, 2019.
99. Hayes Inc. Hayes Directory Report. Transcranial direct current stimulation for depression. Lansdale, PA: Hayes, Inc. Published Dec 7, 2017; reviewed Feb 24, 2020.
100. Hayes, Inc. Emerging technology report. NSS-2 Bridge system for opioid withdrawal. Lansdale, PA: Hayes, Inc. Published Dec 2017.
101. Hayes Inc. Evidence analysis research brief (search and summary). Bioness L300 Foot Drop System (Bioness) for patients with traumatic brain injury. Lansdale, PA: Hayes, Inc. Published Apr 6, 2018; archived May 6, 2019.
102. Hayes Inc. Evidence analysis research brief (search and summary). H-Wave (electronic Waveform Lab Inc.) for the treatment of low back pain. Lansdale, PA: Hayes, Inc. Published Jun 27, 2018a; archived Jul 21, 2019.
103. Hayes Inc. Evidence analysis research brief (search and summary). H-Wave (electronic Waveform Lab Inc.) for the treatment of lower extremity pain. Lansdale, PA: Hayes, Inc. Published Jun 21, 2018b; archived Jul 27, 2019.
104. Hayes Inc. Health technology assessment. Functional electrical stimulation (FES) for treatment of foot drop in multiple sclerosis patients. Lansdale, PA: Hayes, Inc. Jul 16, 2015. Reviewed Jun 16, 2016; Jun 27, 2017; archived Aug 16, 2018.
105. Hayes Inc. Health technology assessment. Scrambler/Calmare pain therapy (Calmare Therapeutics Inc.) for the management of pain not related to cancer. Lansdale, PA: Hayes, Inc. Apr 6, 2020.

106. Hayes Inc. Health technology assessment. Scrambler/Calmare pain therapy (Calmare Therapeutics Inc.) for the management of chronic pain related to cancer or cancer treatment. Lansdale, PA: Hayes, Inc. Mar 30, 2020.
107. Hayes Inc. Health technology assessment. Transcutaneous electrical nerve stimulation for chronic low back pain. Lansdale, PA: Hayes, Inc. Sept 21, 2018. Annual review Dec 2, 2019.
108. Hayes Inc. Health technology assessment. Transcutaneous electrical nerve stimulation for knee osteoarthritis. Lansdale, PA: Hayes, Inc. Jan 30, 2019. Annual review Mar 25, 2020.
109. Hayes Inc. Hayes technology brief. Microcurrent electrical therapy for the treatment of musculoskeletal pain. Lansdale, PA: Hayes, Inc. Oct 26, 2018. Annual Review Dec 10, 2019
110. Hein E, Nowak M, Kiess O, Biermann T, Bayerlein K, Kornhuber J, Kraus T. Auricular transcutaneous electrical nerve stimulation in depressed patients: a randomized controlled pilot study. *J Neural Transm.* 2013 May;120(5):821-7.
111. Helmreich, RJ, Shiao, SY, and Dune, LS. Meta-analysis of acustimulation effects on nausea and vomiting in pregnant women. *Explore (NY).* 2006;2(5):412-421.
112. Hill K, Cavalheri V, Mathur S, Roig M, Janaudis-Ferreira T, Robles P, Dolmage TE, Goldstein R. Neuromuscular electrostimulation for adults with chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews* 2018, Issue 5. Art. No.: CD010821. DOI: 10.1002/14651858.CD010821.pub2.
113. Hocking B. ETPS neuropathic acupuncture. Ch 54. In: Weiner RS (editor). *Pain management: a practical guide for clinicians*, sixth edition. CRC Press: Washington D.C. 2002: Pgs 667-690.
114. Holzer A, Leitgeb U, Spacek A, Wenzl R, Herkner H, Kettner S. Auricular acupuncture for postoperative pain after gynecological surgery: a randomized controlled trail. *Minerva Anesthesiol.* 2011 Mar;77(3):298-304.
115. Horrocks EJ, Thin N, Thaha MA, Taylor SJ, Norton C, Knowles CH. Systematic review of tibial nerve stimulation to treat faecal incontinence. *Br J Surg.* 2014 Apr;101(5):457-68.
116. Hou S, Huh B, Kim HK, Kim KH, Abdi S. Treatment of Chemotherapy-Induced Peripheral Neuropathy: Systematic Review and Recommendations. *Pain Physician.* 2018 Nov;21(6):571-592.
117. Houghton P, Kincaid C, Lovell M, Campbell K, Keast D, Woodbury M, et al. Effect of electrical stimulation on chronic leg ulcer size and appearance. *Phys Ther.* 2003;83(1):17-28.
118. Houghton PE, Campbell KE, Fraser CH, Harris C, Keast DH, Potter PJ, Hayes KC, Woodbury MG. Electrical stimulation therapy increases rate of healing of pressure ulcers in community-dwelling people with spinal cord injury. *Arch Phys Med Rehabil.* 2010 May;91(5):669-78.
119. Howlett OA, Lannin NA, Ada L, McKinstry C. Functional electrical stimulation improves activity after stroke: a systematic review with meta-analysis. *Arch Phys Med Rehabil.* 2015 May;96(5):934-43.
120. Hsu SS, Hu MH, Wang YH, Yip PK, Chiu JW, Hsieh CL. Dose-response relation between neuromuscular electrical stimulation and upper-extremity function in patients with stroke. *Stroke.* 2010 Apr;41(4):821-4.
121. Hui-Chan CW, Ng SS, Mak MK. Effectiveness of a home-based rehabilitation programme on lower limb functions after stroke. *Hong Kong Med J.* 2009 Jun;15(3 Suppl 4):42-6.

122. Hungerford DS, Maclaughlin EJ, Mines CM, Deveshwar S, Elliott C, Tuber JS, Principe JR, Ford TL, Schechtman J, Zizic TM. Synergistic effect of using a transcutaneous electrical joint stimulator and an unloading brace in treating osteoarthritis of the knee. *Am J Orthop (Belle Mead NJ)*. 2013 Oct;42(10):456-63.
123. Hurlow A, Bennett MI, Robb KA, Johnson MI, Simpson KH, Oxberry SG. Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults. *Cochrane Database of Systematic Reviews* 2012, Issue 3. Art. No.: CD006276. DOI: 10.1002/14651858.CD006276.pub3..
124. Innovative Health Solutions Inc. NSS-2 Bridge product research. 2018. Accessed Jun 10, 2021. Available at URL address: <https://i-h-s.com/healthcare-professionals/nss-2-research/>
125. Janković A, Binić I. Frequency rhythmic electrical modulation system in the treatment of chronic painful leg ulcers. *Arch Dermatol Res*. 2008 Aug;300(7):377-83.
126. Jauregui JJ, Cherian JJ, Gwam CU, Chughtai M, Mistry JB, Elmallah RK, Harwin SF, Bhave A, Mont MA. A Meta-Analysis of Transcutaneous Electrical Nerve Stimulation for Chronic Low Back Pain. *Surg Technol Int*. 2016 Apr;28:296-30.
127. Jerez-Roig J, Souza DL, Espelt A, Costa-Marín M, Belda-Molina AM. Pelvic floor electrostimulation in women with urinary incontinence and/or overactive bladder syndrome: a systematic review. *Actas Urol Esp*. 2013 Jul-Aug;37(7):429-44.
128. Jin DM, Xu Y, Geng DF, Yan TB. Effect of transcutaneous electrical nerve stimulation on symptomatic diabetic peripheral neuropathy: a meta-analysis of randomized controlled trials. *Diabetes Res Clin Pract*. 2010 Jul;89(1):10-5.
129. Johnson MI, Bjordal JM. Transcutaneous electrical nerve stimulation for the management of painful conditions: focus on neuropathic pain. *Expert Rev Neurother*. 2011 May;11(5):735-53.
130. Johnson MI, Claydon LS, Herbison GP, Jones G, Paley CA. Transcutaneous electrical nerve stimulation (TENS) for fibromyalgia in adults. *Cochrane Database of Systematic Reviews* 2017, Issue 10. Art. No.: CD012172. DOI: 10.1002/14651858.CD012172.pub
131. Johnson MI, Paley CA, Howe TE, Sluka KA. Transcutaneous electrical nerve stimulation for acute pain. *Cochrane Database of Systematic Reviews* 2015a, Issue 6. Art. No.: CD006142. DOI: 10.1002/14651858.CD006142.pub3.
132. Johnson MI, Mulvey MR, Bagnall AM. Transcutaneous electrical nerve stimulation (TENS) for phantom pain and stump pain following amputation in adults. *Cochrane Database of Systematic Reviews* 2015b, Issue 8. Art. No.: CD007264. DOI: 10.1002/14651858.CD007264.pub3.
133. Jones S, Man WDC, Gao W, Higginson IJ, Wilcock A, Maddocks M. Neuromuscular electrical stimulation for muscle weakness in adults with advanced disease. *Cochrane Database of Systematic Reviews* 2016, Issue 10. Art. No.: CD009419. DOI: 10.1002/14651858.CD009419.pub3.
134. Jünger M, Arnold A, Zuder D, Stahl HW, Heising S. Local therapy and treatment costs of chronic, venous leg ulcers with electrical stimulation (Dermapulse): a prospective, placebo controlled, double blind trial. *Wound Repair Regen*. 2008 Jul-Aug;16(4):480-7.
135. Kafri M, Laufer Y. Therapeutic effects of functional electrical stimulation on gait in individuals post-stroke. *Ann Biomed Eng*. 2015 Feb;43(2):451-66.
136. Kajbafzadeh AM, Sharifi-Rad L, Mozafarpour S, Ladi-Seyedian SS. Efficacy of transcutaneous interferential electrical stimulation in treatment of children with primary nocturnal enuresis: a randomized clinical trial. *Pediatr Nephrol*. 2015 Jul;30(7):1139-45.

137. Kang RW, Lewis PB, Kramer A, Hayden JK, Cole BJ. Prospective randomized single-blinded controlled clinical trial of percutaneous neuromodulation pain therapy device versus sham for the osteoarthritic knee: a pilot study. *Orthopedics*. 2007 Jun;30(6):439-45.
138. Kavirajan HC, Lueck K, Chuang K. Alternating current cranial electrotherapy stimulation (CES) for depression. *Cochrane Database of Systematic Reviews* 2014, Issue 7. Art. No.: CD010521. DOI: 10.1002/14651858.CD010521.pub2.
139. Kerr C, McDowell B, Cosgrove A, Walsh D, Bradbury I, McDonough. Electrical stimulation in cerebral palsy: a randomized controlled trial. *Dev Med Child Neurol*. 2006 Nov;48(11):870-6.
140. Kim KH, Lee MS, Kim TH, Kang JW, Choi TY, Lee JD. Acupuncture and related interventions for symptoms of chronic kidney disease. *Cochrane Database of Systematic Reviews* 2016, Issue 6. Art. No.: CD009440. DOI: 10.1002/14651858.CD009440.pub2
141. Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J, Callahan L, Copenhaver C, Dodge C, et. al. 2019 American College of Rheumatology/ Arthritis Foundation Guideline for the management of osteoarthritis of the hand, hip, and knee. *Arthritis Care & Research*. Vol. 72, No. 2, Feb 2020, pp 149-162.
142. Kovacic K, Hainsworth K, Sood M, et al. Neurostimulation for abdominal pain-related functional gastrointestinal disorders in adolescents: a randomised, double-blind, sham-controlled trial. *Lancet Gastroenterol Hepatol*. 2017;2(10):727-737.
143. Kovacs FM, Urrútia G, Alarcón JD. Surgery versus conservative treatment for symptomatic lumbar spinal stenosis: a systematic review of randomized controlled trials. *Spine (Phila Pa 1976)*. 2011 Sep 15;36(20):E1335-51.
144. Krasaelap A, Sood MR, Li BUK, et al. Efficacy of Auricular Neurostimulation in Adolescents With Irritable Bowel Syndrome in a Randomized, Double-Blind Trial. *Clin Gastroenterol Hepatol*. 2020;18(9):1987-1994.e2.
145. Kroeling P, Gross A, Goldsmith CH, Burnie SJ, Haines T, Graham N, Brant A. Electrotherapy for neck pain. *Cochrane Database of Systematic Reviews* 2009, Issue 4. Art. No.: CD004251. DOI: 10.1002/14651858.CD004251.pub4.
146. La Marca R, Nedeljkovic M, Yuan L, Maercker A, Ehlert U. Effects of auricular electrical stimulation on vagal activity in healthy men: Evidence from a three-armed randomized trial. *Clin Sci (Lond)*. 2009 Nov 9.
147. Lan F, Ma YH, Xue JX, Wang TL, Ma DQ. Transcutaneous electrical nerve stimulation on acupoints reduces fentanyl requirement for postoperative pain relief after total hip arthroplasty in elderly patients. *Minerva Anesthesiol*. 2012 Apr 24.
148. Labrunée M, Boned A, Granger R, Bousquet M, Jordan C, Richard L, Garrigues D, Gremeaux V, Sénard JM, Pathak A, Guiraud T. Improved Walking Claudication Distance with Transcutaneous Electrical Nerve Stimulation: An Old Treatment with a New Indication in Patients with Peripheral Artery Disease. *Am J Phys Med Rehabil*. 2015 Nov;94(11):941-9.
149. Lauritsen CG, Silberstein SD. Rationale for electrical parameter determination in external trigeminal nerve stimulation (eTNS) for migraine: A narrative review. *Cephalalgia*. 2018 Aug 23:333102418796781.
150. Lee A, Chan SKC, Fan LTY. Stimulation of the wrist acupuncture point PC6 for preventing postoperative nausea and vomiting. *Cochrane Database of Systematic Reviews* 2015, Issue 11. Art.

No.: CD003281. DOI: 10.1002/14651858.CD003281.pub4.

151. Lee SC, Park KS, Moon JY, Kim EJ, Kim YC, Seo H, Sung JK, Lee da J. An exploratory study on the effectiveness of "Calmare therapy" in patients with cancer-related neuropathic pain: A pilot study. *Eur J Oncol Nurs*. 2016 Apr;21:1-7.
152. Li J, Song Y. Transcutaneous electrical nerve stimulation for postoperative pain control after total knee arthroplasty: A meta-analysis of randomized controlled trials. *Medicine (Baltimore)*. 2017 Sep;96(37):e8036.
153. Lieber RL, Silva PD, Daniel DM. Equal effectiveness of electrical and volitional strength training for quadriceps femoris muscles after anterior cruciate ligament surgery. *J Orthop Res*. 1996 Jan;14(1):131-8.
154. Lin S, Sun Q, Wang H, Xie G. Influence of transcutaneous electrical nerve stimulation on spasticity, balance, and walking speed in stroke patients: A systematic review and meta-analysis. *J Rehabil Med*. 2018 Jan 10;50(1):3-7.
155. Liu M, Fan S, Xu Y, Cui L. Non-invasive brain stimulation for fatigue in multiple sclerosis patients: A systematic review and meta-analysis. *Mult Scler Relat Disord*. 2019;36:101375.
156. Liu Y, Xu G, Luo M, Teng HF. Effects of Transcutaneous Electrical Nerve Stimulation at Two Frequencies on Urinary Incontinence in Poststroke Patients: A Randomized Controlled Trial. *Am J Phys Med Rehabil*. 2016 Mar;95(3):183-93.
157. Lu ML, He J, Lu S. Electrical stimulation therapy for slow transit constipation in children: a systematic review. *Int J Colorectal Dis*. 2015 May;30(5):697-702.
158. Maddocks M, Gao W, Higginson IJ, Wilcock A. Neuromuscular electrical stimulation for muscle weakness in adults with advanced disease. *Cochrane Database of Systematic Reviews* 2013, Issue 1. Art. No.: CD009419. DOI: 10.1002/14651858.CD009419.pub2.
159. Maddocks M, Nolan CM, Man WD, Polkey MI, Hart N, Gao W, Rafferty GF, Moxham J, Higginson IJ. Neuromuscular electrical stimulation to improve exercise capacity in patients with severe COPD: a randomised double-blind, placebo-controlled trial. *Lancet Respir Med*. 2016 Jan;4(1):27-36.
160. Magis D, Sava S, d'Elia TS, Baschi R, Schoenen J. Safety and patients' satisfaction of transcutaneous supraorbital neurostimulation (tSNS) with the Cefaly® device in headache treatment: a survey of 2,313 headache sufferers in the general population. *J Headache Pain*. 2013 Dec 1;14:95.
161. Mangold S, Schuster C, Keller T, Zimmermann-Schlatter A, Ettlin T. Motor training of upper extremity with functional electrical stimulation in early stroke rehabilitation. *Neurorehabil Neural Repair*. 2009 Feb;23(2):184-90.
162. Mao JJ, Bowman MA, Xie SX, Bruner D, DeMichele A, Farrar JT. Electroacupuncture Versus Gabapentin for Hot Flashes Among Breast Cancer Survivors: A Randomized Placebo-Controlled Trial. *J Clin Oncol*. 2015 Nov 1;33(31):3615-20.
163. Marineo G. Untreatable pain resulting from abdominal cancer: new hope from biophysics? *JOP*. 2003 Jan;4(1):1-10.
164. Marineo G, Iorno V, Gandini C, Moschini V, Smith TJ. Scrambler therapy may relieve chronic neuropathic pain more effectively than guideline-based drug management: results of a pilot, randomized, controlled trial. *J Pain Symptom Manage*. 2012 Jan;43(1):87-95. doi: 10.1016/j.jpainsymman.2011.03.015.

165. Martimbianco ALC, Porfírio GJM, Pacheco RL, Torloni MR, Riera R. Transcutaneous electrical nerve stimulation (TENS) for chronic neck pain. *Cochrane Database of Systematic Reviews* 2019, Issue 12. Art. No.: CD011927
166. Martimbianco ALC, Torloni MR, Andriolo BNG, Porfírio GJM, Riera R. Neuromuscular electrical stimulation (NMES) for patellofemoral pain syndrome. *Cochrane Database of Systematic Reviews* 2017, Issue 12. Art. No.: CD011289. DOI: 10.1002/14651858.CD011289.pub2.
167. Matthews A, Haas DM, O'Mathúna DP, Dowswell T. Interventions for nausea and vomiting in early pregnancy. *Cochrane Database of Systematic Reviews* 2015, Issue 9. Art. No.: CD007575. DOI: 10.1002/14651858.CD007575.pub4.
168. McCaughey EJ, Borotkanics RJ, Gollee H, Folz RJ, McLachlan AJ. Abdominal functional electrical stimulation to improve respiratory function after spinal cord injury: a systematic review and meta-analysis. *Spinal Cord*. 2016 Sep;54(9):628-39.
169. McClure D, Greenman SC, Koppolu SS, Varvara M, Yaseen ZS, Galynker II. A Pilot Study of Safety and Efficacy of Cranial Electrotherapy Stimulation in Treatment of Bipolar II Depression. *J Nerv Ment Dis*. 2015 Nov;203(11):827-35.
170. Medi-Stem, Inc. Frequently used modalities. 2014. Accessed Jun 10, 2021. Available at URL address: <https://www.medi-stim.com/overview.html>
171. Miller L, McFadyen A, Lord AC, Hunter R, Paul L, Rafferty D, Bowers R, Mattison P3 Functional Electrical Stimulation for Foot Drop in Multiple Sclerosis: A Systematic Review and Meta-Analysis of the Effect on Gait Speed. *Arch Phys Med Rehabil*. 2017 Jul;98(7):1435-1452.
172. Miller S, Sinclair AJ, Davies B, Matharu M. Neurostimulation in the treatment of primary headaches. *Pract Neurol*. 2016 Oct;16(5):362-75.
173. Mills PB, Dossa F. Transcutaneous Electrical Nerve Stimulation for Management of Limb Spasticity: A Systematic Review. *Am J Phys Med Rehabil*. 2016 Apr;95(4):309-18.
174. Mello LF, Nóbrega LF, Lemos A. Transcutaneous electrical stimulation for pain relief during labor: a systematic review and meta-analysis. *Rev Bras Fisioter*. 2011 May-Jun;15(3):175-84.
175. Miranda A, Taca A. Neuromodulation with percutaneous electrical nerve field stimulation is associated with reduction in signs and symptoms of opioid withdrawal: a multisite, retrospective assessment. *Am J Drug Alcohol Abuse*. 2018;44(1):56-63.
176. Moll I, Vles JSH, Soudant DLHM, Witlox AMA, Staal HM, Speth LAWM, Janssen-Potten YJM, Coenen M, Koudijs SM, Vermeulen RJ. Functional electrical stimulation of the ankle dorsiflexors during walking in spastic cerebral palsy: a systematic review. *Dev Med Child Neurol*. 2017 Dec;59(12):1230-1236.
177. Monga AK, Tracey MR, Subbaroyan J. A systematic review of clinical studies of electrical stimulation for treatment of lower urinary tract dysfunction. *Int Urogynecol J*. 2012 Aug;23(8):993-1005.
178. Mont MA, Hungerford DS, Caldwell JR, Hoffman KC, He YD, Jones LC, Zizic TM. Pulsed electrical stimulation to defer TKA in patients with Knee Osteoarthritis. *Orthopedics*. 2006;29:887.
179. Moon JY, Kurihara C, Beckles JP, Williams KE, Jamison DE, Cohen SP. Predictive factors associated with success and failure for Calmare (Scrambler) therapy: a multicenter analysis. *Clin J Pain*. 2015 Aug;31(8):750-6.

180. Moreno-Duarte I, Morse LR, Alam M, Bikson M, Zafonte R, Fregni F. Targeted therapies using electrical and magnetic neural stimulation for the treatment of chronic pain in spinal cord injury. *Neuroimage*. 2014 Jan 15;85 Pt 3:1003-13. doi: 10.1016/j.neuroimage.2013.05.097.
181. Moura CC, Chaves ECL, Cardoso ACLR, Nogueira DA, Azevedo C, Chianca TCM. Auricular acupuncture for chronic back pain in adults: a systematic review and meta-analysis. *Rev Esc Enferm USP*. 2019;53:e03461.
182. Mulvey MR, Bagnall AM, Johnson MI, Marchant PR. Transcutaneous electrical nerve stimulation (TENS) for phantom pain and stump pain following amputation in adults. *Cochrane Database of Systematic Reviews* 2010, Issue 5. Art. No.: CD007264. DOI: 10.1002/14651858.CD007264.pub2.
183. Murina F, Bianco V, Radici G, Felice R, Di Martino M, Nicolini U. Transcutaneous electrical nerve stimulation to treat vestibulodynia: a randomised controlled trial. *BJOG*. 2008 Aug;115(9):1165-70.
184. Nakagawa H, Kaiho Y, Namiki S, Ishidoya S, Saito S, Arai Y. Impact of sacral surface therapeutic electrical stimulation on early recovery of urinary continence after radical retropubic prostatectomy: a pilot study. *Adv Urol*. 2010:102751.
185. National Institute for Health and Care Excellence (NICE). NICE guideline. Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain. NG193. Apr 7, 2021. Accessed Jun 17, 2021. Available at URL address: Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain (nice.org.uk)
186. National Institute for Health and Clinical Excellence (NICE). Functional electrical stimulation for drop foot of central neurological origin. Jan 2009. Accessed Jun 10, 2021. Available at URL address: <http://guidance.nice.org.uk/IPG278>
187. National Institute for Health and Clinical Excellence (NICE). Interventional procedures guidance. Transcutaneous neuromuscular electrical stimulation for oropharyngeal dysphagia in adults. IPG634. Dec 19, 2018. Accessed Jun 17, 2021. Available at URL address: <https://www.nice.org.uk/guidance/ipg634/resources/transcutaneous-neuromuscular-electrical-stimulation-for-oropharyngeal-dysphagia-in-adults-pdf-1899874043109061>
188. National Institute for Health and Clinical Excellence (NICE). Low back pain and sciatica in over 16s: assessment and management. Nov 30, 2016. Last updated: Dec 11, 2020. Accessed Jun 10, 2021. Available at URL address: <https://www.nice.org.uk/guidance/NG59/chapter/Recommendations#non-invasive-treatments-for-low-back-pain-and-sciatica>
189. National Institute for Health and Clinical Excellence (NICE). Medtech innovation briefing (MIB56). ODFS Pace and Pace XL functional electrical stimulation devices for treating drop foot. Mar 2016. Accessed Jun 10, 2021. Available at URL address: <https://www.nice.org.uk/advice/mib56>
190. National Institute for Health and Clinical Excellence (NICE). NICE guideline. Urinary incontinence and pelvic organ prolapse in women: management. NG123. Apr 2, 2019. Accessed Jun 17, 2021. Available at URL address: <https://www.nice.org.uk/guidance/ng123/resources/urinary-incontinence-and-pelvic-organ-prolapse-in-women-management-pdf-66141657205189>
191. National Institute for Health and Clinical Excellence (NICE). Stroke rehabilitation CG 162. Jun 2013. Accessed Jun 10, 2021. Available at URL address: <http://guidance.nice.org.uk/CG162/NICEGuidance/pdf/English>
192. National Institute for Health and Clinical Excellence (NICE). IPG 559. Transcutaneous electrical stimulation of the supraorbital nerve for treating and preventing migraine. May 2016. Accessed Jun 10, 2021. Available at URL address: <https://www.nice.org.uk/guidance/ipg559>

193. National Institute of Health Pain Consortium. Disparities in pain care. 2021. Accessed Aug 4, 2021. Available at URL address: <https://www.ninds.nih.gov/sites/default/files/DisparitiesPainCare.pdf>
194. National Pressure Ulcer Advisory Panel. New 2014 prevention and treatment of pressure ulcers: clinical practice guideline. Accessed Jun 10, 2021. Available at URL address: <http://www.internationalguideline.com/>
195. National Pressure Ulcer Advisory Panel (NPUAP). Pressure Injury Stages. 2016. Accessed Jun 10, 2021. Available at URL address: <https://npiap.com/general/custom.asp?page=PressureInjuryStages>
196. National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel and Pan Pacific Pressure Injury Alliance. Prevention and Treatment of Pressure Ulcers: Quick Reference Guide. Emily Haesler (Ed.). Cambridge Media: Osborne Park, Western Australia; 2014. Accessed Jun 10, 2021. Available at URL address: <https://www.epuap.org/wp-content/uploads/2016/10/quick-reference-guide-digital-npuap-epuap-pppia-jan2016.pdf>
197. Nazligul T, Akpınar P, Aktas I, Unlu Ozkan F, Cagliyan Hartevioglu H. The effect of interferential current therapy on patients with subacromial impingement syndrome: a randomized, double-blind, sham-controlled study. *Eur J Phys Rehabil Med*. 2018 Jun;54(3):351-357.
198. Negm A, Lorbergs A, Macintyre NJ. Efficacy of low frequency pulsed subsensory threshold electrical stimulation vs placebo on pain and physical function in people with knee osteoarthritis: systematic review with meta-analysis. *Osteoarthritis Cartilage*. 2013 Sep;21(9):1281-9.
199. Ng SS, Hui-Chan CW. Does the use of TENS increase the effectiveness of exercise for improving walking after stroke? A randomized controlled clinical trial. *Clin Rehabil*. 2009 Dec;23(12):1093-103.
200. Ng RT, Lee WS, Ang HL, Teo KM, Yik YI, Lai NM. Transcutaneous electrical stimulation (TES) for treatment of constipation in children. *Cochrane Database of Systematic Reviews* 2016, Issue 11. Art. No.: CD010873. DOI: 10.1002/14651858.CD010873.pub4.
201. Nooijen CF, Ter Hoeve N, Field-Fote EC. Gait quality is improved by locomotor training in individuals with SCI regardless of training approach. *J Neuroeng Rehabil*. 2009 Oct 2;6:36.
202. Notaro P, Dell'Agnola CA, Dell'Agnola AJ, Amatu A, Bencardino KB, Siena S. Pilot evaluation of scrambler therapy for pain induced by bone and visceral metastases and refractory to standard therapies. *Support Care Cancer*. 2016 Apr;24(4):1649-54.
203. O'Connell NE, Marston L, Spencer S, DeSouza LH, Wand BM. Non-invasive brain stimulation techniques for chronic pain. *Cochrane Database Syst Rev*. 2018 Apr 13;4:CD008208. doi: 10.1002/14651858.CD008208.pub5.
204. Pachman DR, Weisbrod BL, Seisler DK, Barton DL, Fee-Schroeder KC, Smith TJ, Lachance DH, Liu H, Shelerud RA, Chevillat AL, Loprinzi CL. Pilot evaluation of Scrambler therapy for the treatment of chemotherapy-induced peripheral neuropathy. *Support Care Cancer*. 2015 Apr;23(4):943-51.
205. Page MJ, Green S, Mroczki MA, Surace SJ, Deitch J, McBain B, Lyttle N, Buchbinder R. Electrotherapy modalities for rotator cuff disease. *Cochrane Database of Systematic Reviews* 2016, Issue 6. Art. No.: CD012225. DOI: 10.1002/14651858.CD012225.
206. Pal S, Dixit R, Moe S, Godinho MA, Abas_ABL, Ballas_SK, Ram_S, Yousuf_UAM. Transcutaneous electrical nerve stimulation (TENS) for pain management in sickle cell disease. *Cochrane Database of Systematic Reviews* 2020, Issue 3. Art. No.: CD012762. DOI: 10.1002/14651858.CD012762.pub2.

207. Palmer S, Domaille M, Cramp F, Walsh N, Pollock J, Kirwan J, Johnson MI. Transcutaneous electrical nerve stimulation as an adjunct to education and exercise for knee osteoarthritis: a randomized controlled trial. *Arthritis Care Res (Hoboken)*. 2014 Mar;66(3):387-94.
208. Pereira S, Mehta S, McIntyre A, Lobo L, Teasell RW. Functional electrical stimulation for improving gait in persons with chronic stroke. *Top Stroke Rehabil*. 2012 Nov-Dec;19(6):491-8.
209. Peters E, Lavery L, Armstrong D, Fleischli J. Electric stimulation as an adjunct to heal diabetic foot ulcers: a randomized clinical trial. *Arch Phys Med Rehabil*. 2001;82:721-5.
210. Pieber K, Herceg M, Paternostro-Sluga T. Electrotherapy for the treatment of painful diabetic peripheral neuropathy: a review. *J Rehabil Med*. 2010 Apr;42(4):289-95.
211. Piquet M, Balestra C, Sava SL, Schoenen JE. Supraorbital transcutaneous neurostimulation has sedative effects in healthy subjects. *BMC Neurol*. 2011 Oct 28;11:135.
212. Postans N, Hasler J, Granat M, Maxwell D. Functional electric stimulation to augment partial weight-bearing supported treadmill training for patients with acute incomplete spinal cord injury: a pilot study. *Arch Phys Med Rehabil*. 2004;85:604-10.
213. Prenton S, Hollands KL, Kenney LP. Functional electrical stimulation versus ankle foot orthoses for foot-drop: A meta-analysis of orthotic effects. *J Rehabil Med*. 2016 Oct 5;48(8):646-656.
214. Prenton S, Hollands KL, Kenney LPJ, Onmanee P. Functional electrical stimulation and ankle foot orthoses provide equivalent therapeutic effects on foot drop: A meta-analysis providing direction for future research. *J Rehabil Med*. 2018 Feb 13;50(2):129-139.
215. Proctor M, Farquhar C, Stones W, He L, Zhu X, Brown J. Transcutaneous electrical nerve stimulation for primary dysmenorrhoea. *Cochrane Database of Systematic Reviews* 2002, Issue 1. Art. No.: CD002123. DOI: 10.1002/14651858.CD002123. Updated May 3, 2009.
216. Puhar I, Kapudija A, Kasaj A, Willershausen B, Zafiroopoulos GG, Bosnjak A, Plancak D. Efficacy of electrical neuromuscular stimulation in the treatment of chronic periodontitis. *J Periodontal Implant Sci*. 2011 Jun;41(3):117-22.
217. Przeklasa-Muszyńska A, Skrzypiec K, Kocot-Kępska M, Dobrogowski J, Wiatr M, Mika J. Non-invasive transcutaneous Supraorbital Neurostimulation (tSNS) using Cefaly® device in prevention of primary headaches. *Neurol Neurochir Pol*. 2017 Mar - Apr;51(2):127-134.
218. Rajpurohit B, Khatri SM, Metgud D, Bagewadi A. Effectiveness of transcutaneous electrical nerve stimulation and microcurrent electrical nerve stimulation in bruxism associated with masticatory muscle pain - A comparative study. *Indian J Dent Res* 2010;21:104-6.
219. Rapoport AM, Bonner JH, Lin T, Harris D, Gruper Y, Ironi, A, Cowan RP. Remote electrical neuromodulation (REN) in the acute treatment of migraine: a comparison with usual care and acute migraine medications. *J Headache Pain*. 2019;20(1):83. Published 2019 Jul 22.
220. Regan MA, Teasell RW, Wolfe DL, Keast D, Mortenson WB, Aubut JA; Spinal Cord Injury Rehabilitation Evidence Research Team. A systematic review of therapeutic interventions for pressure ulcers after spinal cord injury. *Arch Phys Med Rehabil*. 2009 Feb;90(2):213-31.
221. Resende L, Merriwether E, Rampazo ÉP, Dailey D, Embree J, Deberg J, Liebano RE, Sluka KA. Meta-analysis of transcutaneous electrical nerve stimulation for relief of spinal pain. *Eur J Pain*. 2018 Apr;22(4):663-678.

222. Ricci M, Fabbri L, Pirotti S, Ruffilli N, Foca F, Maltoni M. Scrambler therapy: what's new after 15 years? The results from 219 patients treated for chronic pain. *Medicine (Baltimore)*. 2019 Jan;98(2):e13895.
223. Ricci M, Pirotti S, Scarpi E, Burgio M, Maltoni M, Sansoni E, Amadori D. Managing chronic pain: results from an open-label study using MC5-A Calmare® device. *Support Care Cancer*. 2012 Feb;20(2):405-12. Epub 2011 Mar 11.
224. Rimmer CJ, Knowles CH, Lamparelli M, Durdey P, Lindsey I, Hunt L, Nugent K, Gill KA. Author information. Short-term Outcomes of a Randomized Pilot Trial of 2 Treatment Regimens of Transcutaneous Tibial Nerve Stimulation for Fecal Incontinence. *Dis Colon Rectum*. 2015 Oct;58(10):974-82.
225. Robb K, Oxberry SG, Bennett MI, Johnson MI, Simpson KH, Searle RD. A Cochrane systematic review of transcutaneous electrical nerve stimulation for cancer pain. *J Pain Symptom Manage*. 2009 Apr;37(4):746-53.
226. Roscoe JA, Morrow GR, Hickok JT, Bushunow P, Pierce HI, Flynn PJ, Kirshner JJ, Moore DF, Atkins JN. The efficacy of acupressure and acustimulation wrist bands for the relief of chemotherapy-induced nausea and vomiting. A University of Rochester Cancer Center Community Clinical Oncology Program multicenter study. *J Pain Symptom Manage*. 2003 Aug;26(2):731-42.
227. Rose KM, Taylor AG, Bourguignon C. Effects of cranial electrical stimulation on sleep disturbances, depressive symptoms, and caregiving appraisal in spousal caregivers of persons with Alzheimer's disease. *Appl Nurs Res*. 2009 May;22(2):119-25.
228. Rosen T, de Veciana M, Miller HS, Stewart L, Rebarber A, Slotnick RN. A randomized controlled trial of nerve stimulation for relief of nausea and vomiting in pregnancy. *Obstet Gynecol*. 2003 Jul;102(1):129-35.
229. Ruela LO, Lunes DH, Nogueira DA, Stefanello J, Gradim CVC. Effectiveness of auricular acupuncture in the treatment of cancer pain: randomized clinical trial. *Rev Esc Enferm USP*. 2018;52:e03402
230. Russo A, Tessitore A, Esposito F, Di Nardo F, Silvestro M, Trojsi F, De Micco R, Marcuccio L, Schoenen J, Tedeschi G. Functional Changes of the Perigenual Part of the Anterior Cingulate Cortex after External Trigeminal Neurostimulation in Migraine Patients. *Front Neurol*. 2017 Jun 15;8:282.
231. Sabato AF, Marineo G, Gatti A. Scrambler therapy. *Minerva Anestesiol*. 2005 Jul-Aug;71(7-8):479-82.
232. Sator-Katzenschlager SM, Scharbert G, Kozek-Langenecker SA, Szeles JC, Finster G, Schiesser AW, Heinze G, Kress HG. The short- and long-term benefit in chronic low back pain through adjuvant electrical versus manual auricular acupuncture. *Anesth Analg*. 2004 May;98(5):1359-64, table of contents.
233. Sator-Katzenschlager SM, Szeles JC, Scharbert G, Michalek-Sauberer A, Kober A, Heinze G, Kozek-Langenecker SA. Electrical stimulation of auricular acupuncture points is more effective than conventional manual auricular acupuncture in chronic cervical pain: a pilot study. *Anesth Analg*. 2003 Nov;97(5):1469-73.
234. Sbruzzi G, Ribeiro RA, Schaan BD, Signori LU, Silva AM, Irigoyen MC, Plentz RD. Functional electrical stimulation in the treatment of patients with chronic heart failure: a meta-analysis of randomized controlled trials. *Eur J Cardiovasc Prev Rehabil*. 2010 Jun;17(3):254-60.
235. Sbruzzi G, Silveira SA, Silva DV, Coronel CC, Plentz RD. Transcutaneous electrical nerve stimulation after thoracic surgery: systematic review and meta-analysis of 11 randomized trials. *Rev Bras Cir Cardiovasc*. 2012 Mar;27(1):75-87.

236. Schoenen J, Vandersmissen B, Jeanette S, Herroelen L, Vandenheede M, Gérard P, Magis D. Migraine prevention with a supraorbital transcutaneous stimulator: a randomized controlled trial. *Neurology*. 2013 Feb 19;80(8):697-704.
237. Schukro RP, Heiserer C, Michalek-Sauberer A, Gleiss A, Sator-Katzenschlager S. The effects of auricular electroacupuncture on obesity in female patients--a prospective randomized placebo-controlled pilot study. *Complement Ther Med*. 2014 Feb;22(1):21-5. doi: 10.1016/j.ctim.2013.10.002.
238. Scottish Intercollegiate Guidelines Network (SIGN). Management of chronic pain. Edinburgh: SIGN; 2013. (SIGN publication no. 136). [December 2013]. Revised Aug 2019. Available from URL: <https://www.sign.ac.uk/our-guidelines/management-of-chronic-pain/>
239. Seo HG, Bang MS, Chung SG, Jung SH, Lee SU. Effect of electrical stimulation on botulinum toxin a therapy in patients with chronic myofascial pain syndrome: a 16-week randomized double-blinded study. *Arch Phys Med Rehabil*. 2013 Mar;94(3):412-8.
240. Shekelle PG, Cook IA, Miake-Lye IM, Booth MS, Beroes JM, Mak S. Benefits and Harms of Cranial Electrical Stimulation for Chronic Painful Conditions, Depression, Anxiety, and Insomnia: A Systematic Review. *Ann Intern Med*. 2018 Mar 20;168(6):414-421.
241. Shimoura K, Iijima H, Suzuki Y, Aoyama T. Immediate effects of transcutaneous electrical nerve stimulation on pain and physical performance in individuals with preradiographic knee osteoarthritis: a randomized controlled trial. *Archives of Physical Medicine and Rehabilitation*, 2019-02-01, Volume 100, Issue 2, Pages 300-306.e1.
242. Sibbritt D, Peng W, Lauche R, Ferguson C, Frawley J, Adams J. Efficacy of acupuncture for lifestyle risk factors for stroke: a systematic review. *PLoS One*. 2018 Oct 26;13(10):e0206288.
243. Sillen MJ, Speksnijder CM, Eterman RM, Janssen PP, Wagers SS, Wouters EF, Uszko-Lencer NH, Spruit MA. Effects of neuromuscular electrical stimulation of muscles of ambulation in patients with chronic heart failure or COPD: a systematic review of the English-language literature. *Chest*. 2009 Jul;136(1):44-61.
244. Smart NA, Dieberg G, Giallauria F. Functional electrical stimulation for chronic heart failure: A meta-analysis. *Int J Cardiol*. Jan 10. 2013 Jul 15;167(1):80-6.
245. Smith ME, Totten A, Hickam DH, Fu R, Wasson N, Rahman B, Motu'apuaka M, Saha S. Pressure ulcer treatment strategies: a systematic comparative effectiveness review. *Ann Intern Med*. 2013 Jul 2;159(1):39-50.
246. Smith TJ, Razzak AR, Blackford AL, et al. A pilot randomized sham-controlled trial of mc5-a scrambler therapy in the treatment of chronic chemotherapy-induced peripheral neuropathy (CIPN). *J Palliat Care*. 2020;35(1):53-58.
247. Springer S, Khamis S. Effects of functional electrical stimulation on gait in people with multiple sclerosis - A systematic review. *Mult Scler Relat Disord*. 2017 Apr;13:4-12.
248. Starkweather AR1, Coyne P, Lyon DE, Elswick RK Jr, An K, Sturgill J. Decreased low back pain intensity and differential gene expression following Calmare®: results from a double-blinded randomized sham-controlled study. *Res Nurs Health*. 2015 Feb;38(1):29-38.
249. Stein RB, Everaert DG, Thompson AK, Chong SL, Whittaker M, Robertson J, Kuether G. Long-term therapeutic and orthotic effects of a foot drop stimulator on walking performance in progressive and nonprogressive neurological disorders. *Neurorehabil Neural Repair*. 2010 Feb;24(2):152-67.

250. Stein C, Fritsch CG, Robinson C, Sbruzzi G, Plentz RD. Effects of electrical stimulation in spastic muscles after stroke: systematic review and meta-analysis of randomized controlled trials. . *Stroke*. 2015 Aug;46(8):2197-205.
251. Stewart F, Berghmans B, Bø K, Glazener CMA. Electrical stimulation with non-implanted devices for stress urinary incontinence in women. *Cochrane Database of Systematic Reviews* 2017, Issue 12. Art. No.: CD012390. DOI: 10.1002/14651858.CD012390.pub2.
252. Suh HR, Han HC, Cho HY. Immediate therapeutic effect of interferential current therapy on spasticity, balance, and gait function in chronic stroke patients: a randomized control trial. *Clin Rehabil*. 2014 Sep;28(9):885-91.
253. Sun R, Dai W, Liu Y, Liu C, Liu Y, Gong Y, Sun X, Shi T, Song M. Non-needle acupoint stimulation for prevention of nausea and vomiting after breast surgery: A meta-analysis. *Medicine (Baltimore)*. 2019 Mar;98(10):e14713.
254. Sun K, Xing T, Zhang F, Liu Y, Li W, Zhou Z, Fang L, Yu L, Yan M. Perioperative Transcutaneous Electrical Acupoint Stimulation for Postoperative Pain Relief Following Laparoscopic Surgery: A Randomized Controlled Trial. *Clin J Pain*. 2017 Apr;33(4):340-347.
255. Suriya-amarit D, Gaogasigam C, Siriphorn A, Boonyong S. Effect of interferential current stimulation in management of hemiplegic shoulder pain. *Arch Phys Med Rehabil*. 2014 Aug;95(8):1441-6. doi: 10.1016/j.apmr.2014.04.002.
256. Tan C, Liu Y, Li W, Liu J, Chen L. Transcutaneous neuromuscular electrical stimulation can improve swallowing function in patients with dysphagia caused by non-stroke diseases: a meta-analysis. *J Oral Rehabil*. 2013 Jun;40(6):472-80.
257. Tan Z, Liu H, Yan T, Jin D, He X, Zheng X, Xu S, Tan C. The effectiveness of functional electrical stimulation based on a normal gait pattern on subjects with early stroke: a randomized controlled trial. *Biomed Res Int*. 2014;2014:545408.
258. Tan JY, Molassiotis A, Wang T, Suen LK. Adverse events of auricular therapy: a systematic review. *Evid Based Complement Alternat Med*. 2014;2014:506758.
259. Tan G, Rintala DH, Jensen MP, Richards JS, Holmes SA, Parachuri R, Lashgari-Saegh S, Price LR. Efficacy of cranial electrotherapy stimulation for neuropathic pain following spinal cord injury: a multi-site randomized controlled trial with a secondary 6-month open-label phase. *J Spinal Cord Med*. 2011;34(3):285-96.
260. Tao H, Wang T, Dong X, Guo Q, Xu H, Wan Q. Effectiveness of transcutaneous electrical nerve stimulation for the treatment of migraine: a meta-analysis of randomized controlled trials. *J Headache Pain*. 2018 May 29;19(1):42.
261. Taylor AG1, Anderson JG, Riedel SL, Lewis JE, Kinser PA, Bourguignon C. Cranial electrical stimulation improves symptoms and functional status in individuals with fibromyalgia. *Pain Manag Nurs*. 2013 Dec;14(4):327-35.
262. Theranica Bio-Electronics Ltd. Nerivio. 2019. Accessed Jun 10, 2021. Available at URL address: <https://theranica.com/technology/>
263. Thin NN, Horrocks EJ, Hotouras A, Palit S, Thaha MA, Chan CL, Matzel KE, Knowles CH. Systematic review of the clinical effectiveness of neuromodulation in the treatment of faecal incontinence. *Br J Surg*. 2013 Oct;100(11):

264. Thin NN, Taylor SJ, Bremner SA, Emmanuel AV, Hounscome N, Williams NS, Knowles CH. Neuromodulation Trial Study Group. Randomized clinical trial of sacral versus percutaneous tibial nerve stimulation in patients with faecal incontinence. *Br J Surg*. 2015 Mar;102(4):349-58.
265. Thomas DR. Pressure ulcers. In: Rakel RE, Bope ET, editors. *Conn's Current Therapy*. 1st ed. Philadelphia, PA: W.B. Saunders; 2011. Section 13.
266. Tipton JM, McDaniel RW, Barbour L, Johnston MP, Kayne M, LeRoy P, Ripple ML. Putting evidence into practice: evidence-based interventions to prevent, manage, and treat chemotherapy-induced nausea and vomiting. *Clin J Oncol Nurs*. 2007 Feb;11(1):69-78.
267. Toth MJ, Tourville TW, Voigt TB, Choquette RH, Anair BM, Falcone MJ, Failla MJ, Stevens-Lapslae JE, Endres NK, Slauterbeck JR, Beynon BD. Utility of Neuromuscular Electrical Stimulation to Preserve Quadriceps Muscle Fiber Size and Contractility After Anterior Cruciate Ligament Injuries and Reconstruction: A Randomized, Sham-Controlled, Blinded Trial. *Am J Sports Med*. 2020 Aug;48(10):2429-2437.
268. Tsang HC, Lam CS, Chu PW, Yap J, Fung TY, Cheing GL. A randomized controlled trial of auricular transcutaneous electrical nerve stimulation for managing posthysterectomy pain. *Evid Based Complement Alternat Med*. 2011;2011:276769.
269. Tugtepe H, Thomas DT, Ergun R, Kalyoncu A, Kaynak A, Kastarli C, Dagli TE. The effectiveness of transcutaneous electrical neural stimulation therapy in patients with urinary incontinence resistant to initial medical treatment or biofeedback. *J Pediatr Urol*. 2015 Jun;11(3):137.e1-5.
270. U.S. Food and Drug Administration (FDA). 510(k) database. Product code BWK. Accessed Jun 10, 2021. Available at URL address: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmnm.cfm>
271. U.S. Food and Drug Administration (FDA). 510(k) database. Product code GXY. Accessed Jun 29, 2021. Available at URL address: <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmnm.cfm?ID=K023212>
272. US Food and Drug Administration. FDA grants marketing authorization of the first device for use in helping to reduce the symptoms of opioid withdrawal. Nov 15, 2017. Accessed Jun 10, 2021. Available at URL address: <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm585271.htm>
273. US Food and Drug Administration. IB-Stim. DEN180057. Jun 7, 2019. Accessed Jun 10, 2021. Available at URL address: https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN180057.pdf
274. US Food and Drug Administration. Nerivio Migra. DEN180059. May 20, 2019. Accessed Jun 10, 2021. Available at URL address: https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN180059.pdf
275. US Food and Drug Administration. NSS-2 Bridge. DEN170018. Nov 15, 2017. Accessed Jun 10, 2021. Available at URL address: https://www.accessdata.fda.gov/cdrh_docs/pdf17/DEN170018.pdf
276. U.S. Food and Drug Administration (FDA). Premarket approval (PMA) database. Accessed Jun 10, 2021. Available at URL address: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm>
277. VA/DoD Clinical practice guideline for diagnosis and treatment of low back pain. Washington, D.C.: Dept. of Veterans Affairs, Dept. of Defense, 2017. Available at URL address: <https://www.healthquality.va.gov/guidelines/Pain/lbp/VADoDLBPCPG092917.pdf>
278. VA/DoD Clinical practice guideline for the management of chronic insomnia disorder and obstructive sleep apnea. Washington, D.C.: Dept. of Veterans Affairs, Dept. of Defense, 2019. Available at URL address: <https://www.healthquality.va.gov/guidelines/CD/insomnia/VADoDSleepCPGFinal508.pdf>

279. VA/DoD Clinical practice guideline for the non-surgical management of hip & knee osteoarthritis. Washington, D.C.: Dept. of Veterans Affairs, Dept. of Defense, 2020. Available at URL address: <https://www.healthquality.va.gov/guidelines/CD/OA/VADoDOACPG.pdf>
280. VA/DoD Clinical practice guideline for the primary care management of ha. Washington, D.C.: Dept. of Veterans Affairs, Dept. of Defense, 2020. Available at URL address: <https://www.healthquality.va.gov/guidelines/pain/headache/VADoDHeadacheCPGFinal508.pdf>
281. Vafadar AK, Côté JN, Archambault PS. Effectiveness of functional electrical stimulation in improving clinical outcomes in the upper arm following stroke: a systematic review and meta-analysis. *Biomed Res Int.* 2015;2015:729768.
282. Valenza MC, Torres-Sánchez I, Cabrera-Martos I, Valenza-Demet G, Cano-Cappellacci M. Acute effects of contract-relax stretching vs. tens in young subjects with anterior knee pain: a randomized controlled trial. *J Strength Cond Res.* 2016 Aug;30(8):2271-8.
283. van Middelkoop M, Rubinstein SM, Kuijpers T, Verhagen AP, Ostelo R, Koes BW, van Tulder MW. A systematic review on the effectiveness of physical and rehabilitation interventions for chronic non-specific low back pain. *Eur Spine J.* 2011 Jan;20(1):19-39. Epub 2010 Jul 18.
284. Vikelis M, Dermitzakis EV, Spingos KC, Vasiliadis GG, Vlachos GS, Kararizou E. Clinical experience with transcutaneous supraorbital nerve stimulation in patients with refractory migraine or with migraine and intolerance to topiramate: a prospective exploratory clinical study. *BMC Neurol.* 2017 May 18;17(1):97.
285. Volpato HB, Szego P, Lenza M, Milan SL, Talerman C, Ferretti M. Femoral quadriceps neuromuscular electrical stimulation after total knee arthroplasty: a systematic review. *Einstein (Sao Paulo).* 2016 Jan-Mar;14(1):77-98.
286. Walsh DM, Howe TE, Johnson MI, Sluka KA. Transcutaneous electrical nerve stimulation for acute pain. *Cochrane Database of Systematic Reviews* 2009, Issue 2. Art. No.: CD006142. DOI: 10.1002/14651858.CD006142.pub2.
287. Weber DJ, Skidmore ER, Niyonkuru C, Chang CL, Huber LM, Munin MC. Cyclic functional electrical stimulation does not enhance gains in hand grasp function when used as an adjunct to onabotulinumtoxinA and task practice therapy: a single-blind, randomized controlled pilot study. *Arch Phys Med Rehabil.* 2010 May;91(5):679-86.
288. Weiner DK, Perera S, Rudy TE, Glick RM, Shenoy S, Delitto A. Efficacy of percutaneous electrical nerve stimulation and therapeutic exercise for older adults with chronic low back pain: a randomized controlled trial. *Pain.* 2008 Nov 30;140(2):344-57.
289. Woodson BT, Soose RJ, Gillespie MB, Strohl KP, Maurer JT, de Vries N, Steward DL, Baskin JZ, Badr MS, Lin HS, Padhya TA, Mickelson S, Anderson WM, Vanderveken OM, Strollo PJ Jr; STAR Trial Investigators. Three-Year Outcomes of Cranial Nerve Stimulation for Obstructive Sleep Apnea: The STAR Trial. *Otolaryngol Head Neck Surg.* 2016 Jan;154(1):181-8.
290. Wu LC, Weng PW, Chen CH, Huang YY, Tsuang YH, Chiang CJ. Literature Review and Meta-Analysis of Transcutaneous Electrical Nerve Stimulation in Treating Chronic Back Pain. *Reg Anesth Pain Med.* 2018 May;43(4):425-433.
291. Xu M, Zhou SJ, Jiang CC, Wu Y, Shi WL, Gu HH, Cai HD, Wang XQ. The Effects of P6 Electrical Acustimulation on Postoperative Nausea and Vomiting in Patients After Infratentorial Craniotomy. *J Neurosurg Anesthesiol.* 2012 Jun 22.

292. Yan T, Hui-Chan CW. Transcutaneous electrical stimulation on acupuncture points improves muscle function in subjects after acute stroke: a randomized controlled trial. *J Rehabil Med.* 2009 Apr;41(5): 312-6.
293. Yarnitsky D, Dodick DW, Grosberg BM, Burstein R, Ironi A, Harris D, Lin T, Silberstein SD. Remote electrical neuromodulation (REN) relieves acute migraine: a randomized, double-blind, placebo-controlled, multicenter trial. *Headache.* Sep 2019;59(8):1240-1252.
294. Yarnitsky D, Volokh L, Ironi A, Weller B, Shor M, Shifrin A, Granovsky Y. Nonpainful remote electrical stimulation alleviates episodic migraine pain. *Neurology.* 2017;88(13):1250-1255.
295. Yeh CH, Chiang YC, Hoffman SL, Liang Z, Klem ML, Tam WW, Chien LC, Suen LK. Efficacy of auricular therapy for pain management: a systematic review and meta-analysis. *Evid Based Complement Alternat Med.* 2014;2014:934670.
296. Yeh ML, Chang YC, Huang YY, Lee TY. A randomized controlled trial of auricular acupressure in heart rate variability and quality of life for hypertension. *Complement Ther Med.* 2015 Apr;23(2):200-9.
297. Yik YI, Hutson J, Southwell B. Home-Based Transabdominal Interferential Electrical Stimulation for Six Months Improves Paediatric Slow Transit Constipation (STC). *Neuromodulation.* 2018 Oct;21(7):676-681.
298. Yosephi MH, Ehsani F, Daghighi M, Zoghi M, Jaberzadeh S. The effects of trans-cranial direct current stimulation intervention on fear: A systematic review of literature. *J Clin Neurosci.* 2019 Apr;62:7-13.
299. Youssef T, Youssef M, Thabet W, Lotfy A, Shaat R, Abd-Elrazek E, Farid M. Randomized clinical trial of transcutaneous electrical posterior tibial nerve stimulation versus lateral internal sphincterotomy for treatment of chronic anal fissure. *Int J Surg.* 2015 Oct;22:143-8.
300. Yue C, Zhang X, Zhu Y, Jia Y, Wang H, Liu Y. Systematic Review of Three Electrical Stimulation Techniques for Rehabilitation After Total Knee Arthroplasty. *J Arthroplasty.* 2018 Jul;33(7):2330-2337.
301. Zeng C, Li H, Yang T, Deng ZH, Yang Y, Zhang Y, Lei GH. Electrical stimulation for pain relief in knee osteoarthritis: systematic review and network meta-analysis. *Osteoarthritis Cartilage.* 2015 Feb;23(2):189-202.
302. Zhang Q, Gao Z, Wang H, Ma L, Guo F, Zhong H, Xiong L, Wang Q. The effect of pre-treatment with transcutaneous electrical acupoint stimulation on the quality of recovery after ambulatory breast surgery: a prospective, randomised controlled trial. *Anaesthesia.* 2014 Aug;69(8):832-9.
303. Zhao HJ, Tan JY, Wang T, Jin L. Auricular therapy for chronic pain management in adults: A synthesis of evidence. *Complement Ther Clin Pract.* 2015 May;21(2):68-78.
304. Zhao W, Wang C, Li Z, Chen L, Li J, Cui W, Ding S, Xi Q, Wang F, Jia F, Xiao S, Guo Y, Zhao Y. Efficacy and safety of transcutaneous electrical acupoint stimulation to treat muscle spasticity following brain injury: a double-blinded, multicenter, randomized controlled trial. *PLoS One.* 2015 Feb 2;10(2):e0116976.
305. Zhiyuan W, Ming Y, Jie J, Yi W, Tiansheng H, Mingfen L, Zhijie H, Zhenzhen G, Pang LM. Effect of transcutaneous electrical nerve stimulation at acupoints on patients with type 2 diabetes mellitus: a randomized controlled trial. *J Tradit Chin Med.* 2015 Apr;35(2):134-40.
306. Zhu Y, Feng Y, Peng L. Effect of transcutaneous electrical nerve stimulation for pain control after total knee arthroplasty: A systematic review and meta-analysis. *J Rehabil Med.* 2017 Nov 21;49(9):700-704.

307. Zhu YP, Yao XD, Zhang SL, Dai B, Ye DW. Pelvic floor electrical stimulation for postprostatectomy urinary incontinence: a meta-analysis. *Urology*. 2012 Mar;79(3):552-5.
308. Zuim PR, Garcia AR, Turcio KH, Hamata MM. Evaluation of microcurrent electrical nerve stimulation (MENS) effectiveness on muscle pain in temporomandibular disorders patients. *J Appl Oral Sci*. 2006 Jan;14(1):61-6.

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