Medical Coverage Policy

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Electrical Stimulation Therapy and Devices in a Home Setting

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note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This Coverage Policy addresses outpatient, non-implantable electrical simulation therapy and devices used in the home setting 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 injury
  - 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 not covered or reimbursable.

Electrical stimulation therapy for any other chronic wound indication including but not limited to prevention of a pressure injury is not covered or reimbursable.

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 not covered or reimbursable.

Transcutaneous Electrical Nerve Stimulation (TENS)
A transcutaneous electrical nerve stimulator (TENS) (HCPCS Codes 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.

The use of TENS (HCPCS Codes E0720, E0730, E0733) and related supplies (HCPCS Codes A4541, A4595) for ANY other indication, including devices for the treatment of migraine headaches (e.g., Cefaly), are not covered or reimbursable.

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 not covered or reimbursable.

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® Plus) (HCPCS Code E1399)
- electrical sympathetic stimulation therapy (HCPCS Code E1399)
- electrotherapeutic point stimulation (ETPS℠) (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 Code S8130)
- microcurrent electrical nerve stimulation (MENS), including frequency-specific microcurrent (FSM) stimulation (HCPCS Code E1399)
- percutaneous electrical nerve stimulation (PENS)/percutaneous neuromodulation therapy (PNT) (HCPCS Code E1399)
- percutaneous electrical nerve field stimulation (PENFS) (e.g., IB-Stim) (CPT Code 64567)
- threshold/therapeutic electrical stimulation (TES) (HCPCS Code E1399)
- transcutaneous afferent patterned stimulation (TAPS) neuromodulation therapy (e.g., Cala kIQ™; Felix™ NeuroAI™) (HCPCS Code E0734)
- transcutaneous auricular neurostimulation (tAN) (e.g., Sparrow Ascent®) (HCPCS Code E0721)
- transcutaneous electrical acupoint stimulation (TEAS) (CPT Code 0783T)

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

Coding Information

Notes:

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

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
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 bypasss graft(s) of the right leg with ulceration
I70.641-I70.649	Atherosclerosis of nonbiological bypasss graft(s) of the left leg with ulceration

ICD-10-CM Diagnosis Codes	Description
I70.65	Atherosclerosis of nonbiological bypasss 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-I83.009	Varicose veins of unspecified lower extremity with ulcer
I83.011-I83.019	Varicose veins of right lower extremity with ulcer
I83.021-I83.029	Varicose veins of left lower extremity with ulcer
I83.201-I83.209	Varicose veins of unspecified lower extremity with both ulcer and inflammation
I83.211-I83.219	Varicose veins of right lower extremity with both ulcer and inflammation
I83.221-I83.229	Varicose veins of left lower extremity with both ulcer and inflammation
I87.011	Postthrombotic syndrome with ulcer of right lower extremity
I87.012	Postthrombotic syndrome with ulcer of left lower extremity
I87.013	Postthrombotic syndrome with ulcer of bilateral lower extremity
I87.031	Postthrombotic syndrome with ulcer and inflammation of right lower extremity
I87.032	Postthrombotic syndrome with ulcer and inflammation of left lower extremity
I87.033	Postthrombotic syndrome with ulcer and inflammation of bilateral lower extremity
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
L89.113	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
L89.213	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
L89.313	Pressure ulcer of right buttock, stage 3
L89.314	Pressure ulcer of right buttock, stage 4

ICD-10-CM Diagnosis Codes	Description
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
L89.513	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
L89.613	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
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
L97.111-L97.119	Non-pressure chronic ulcer of right thigh
L97.121-L97.129	Non-pressure chronic ulcer of left thigh
L97.211-I97.219	Non-pressure chronic ulcer of right calf
L97.221-L97.229	Non-pressure chronic ulcer of left calf
L97.311-L97.319	Non-pressure chronic ulcer of right ankle
L97.321-L97.329	Non-pressure chronic ulcer of left ankle
L97.411-L97.419	Non-pressure chronic ulcer of right heel and midfoot
L97.421-L97.429	Non-pressure chronic ulcer of left heel and midfoot
L97.501-L97.509	Non-pressure chronic ulcer of other part of unspecified foot
L97.511-L97.519	Non-pressure chronic ulcer of other part of right foot
L97.521-L97.529	Non-pressure chronic ulcer of other part of left foot
L97.801-L97.809	Non-pressure chronic ulcer of other part of unspecified lower leg
L97.811-L97.819	Non-pressure chronic ulcer of other part of right lower leg
L97.821-L97.829	Non-pressure chronic ulcer of other part of left lower leg
L97.911-L97.919	Non-pressure chronic ulcer of unspecified part of right lower leg

ICD-10-CM Diagnosis Codes	Description
L97.921-L97.929	Non-pressure chronic ulcer of unspecified part of left lower leg
L98.411-L98.419	Non-pressure chronic ulcer of buttock
L98.421-L98.429	Non-pressure chronic ulcer of back
L98.431-L98.439	Non-pressure chronic ulcer of abdomen
L98.441-L98.449	Non-pressure chronic ulcer of chest
L98.451-L98.459	Non-pressure chronic ulcer of neck
L98.461-L98.469	Non-pressure chronic ulcer of face
L98.471-L98.479	Non-pressure chronic ulcer of groin
L98.491-L98.499	Non-pressure chronic ulcer of skin of other sites
L98.A	Non-pressure chronic ulcer of upper limb, not elsewhere classified
L98.A111-L98.A119	Non-pressure chronic ulcer of right upper arm
L98.A121-L98.A129	Non-pressure chronic ulcer of left upper arm
L98.A19-L98.A199	Non-pressure chronic ulcer of unspecified upper arm
L98.A211-L98.A219	Non-pressure chronic ulcer of right forearm
L98.A221-L98.A229	Non-pressure chronic ulcer of left forearm
L98.A29-L98.A299	Non-pressure chronic ulcer of unspecified forearm
L98.A311-L98.A319	Non-pressure chronic ulcer of right hand
L98.A321-L98.A329	Non-pressure chronic ulcer of left hand
L98.A391-L98.A399	Non-pressure chronic ulcer of unspecified hand

Not Covered or Reimbursable:

ICD-10-CM Diagnosis Codes	Description
	All other codes

Not Covered or Reimbursable when used to report electrical stimulation therapy for any other chronic wound indication including but not limited to prevention of a pressure injury:

HCPCS Codes	Description
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

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-M62.5A9	Muscle wasting and atrophy, not elsewhere classified

Not Covered or Reimbursable when used to report NMES and related supplies for any other indication, including idiopathic scoliosis and heart failure:

HCPCS Codes	Description
A4595	Electrical stimulator supplies, 2 lead, per month, (e.g., TENS, NMES)
E0744	Neuromuscular stimulator for scoliosis
E0745	Neuromuscular stimulator, electronic shock unit

ICD-10-CM Diagnosis Codes	Description
	All other codes

Transcutaneous Electrical Nerve Stimulator (TENS)

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)
E0720	Transcutaneous electrical nerve stimulation (TENS) device, 2 lead, localized stimulation

HCPCS Codes	Description
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
G89.18	Other acute postprocedural pain

Not Covered or Reimbursable when used to report TENS and related supplies for any other indication, including devices for the treatment of migraine headaches (e.g., Cefaly):

HCPCS Codes	Description
A4541	Monthly supplies for use of device coded at E0733
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
E0733	Transcutaneous electrical nerve stimulator for electrical stimulation of the trigeminal nerve

ICD-10-CM Diagnosis Codes	Description
	All other codes

<u>Conductive Garment</u>

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-M62.5A9	Muscle wasting and atrophy, not elsewhere classified
G89.12	Acute post-thoracotomy pain
G89.18	Other acute postprocedural pain

Not Covered or Reimbursable:

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:

CPT®* Codes	Description
64567	Percutaneous electrical nerve field stimulation, cranial nerves, without implantation (Code effective 1/1/2026)
0720T	Percutaneous electrical nerve field stimulation, cranial nerves, without implantation (Code deleted 12/31/2025)
0783T	Transcutaneous auricular neurostimulation, set-up, calibration, and patient education on use of equipment

HCPCS Codes	Description
E0721	Transcutaneous electrical nerve stimulator for nerves in the auricular region
E0734	External upper limb tremor stimulator of the peripheral nerves of the wrist
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
E0770	Functional electrical stimulator, transcutaneous stimulation of nerve and/or muscle groups, any type, complete system, not otherwise specified
E1399	Durable medical equipment, miscellaneous
S8130	Interferential current stimulator, 2 channel

General Background

Electrical Stimulation Therapy

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.

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 injuries (previously known as pressure ulcers or bed sores), 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 injuries, 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], 2003).

A pressure injury 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 (Wester, 2023, CMS, 2003).

When evaluating pressure injuries, a staging system is typically used that measures tissue destruction by classifying wounds according to the tissue layers involved. In 2016, the National Pressure Injury Advisory Panel (NPIAP) updated the stages of pressure injuries. 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 (James, 2026; CMS, 2003).

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 (James, 2026).

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, and surgical debridement (James, 2026). Other therapeutic options may include bioengineered skin substitutes and a variety of synthetic dressings.

U.S. Food and Drug Administration (FDA): According to the Centers for Medicare & Medicaid Services (CMS) decision memorandum (2003), 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 injuries, venous stasis ulcers, arterial ulcers, and neuropathic diabetic foot ulcers. Meta-analyses, systematic reviews, randomized controlled trials, and other prospective comparative studies investigating ES for the treatment of chronic wounds have reported significant improvement in healing and decrease in wound size or complete healing compared to placebo or no stimulation. There is high variability as to which type of electrical current and application protocol is the most effective for the ulcer type (Arora, et al., 2020; Smith, et al., 2013; Houghton, et al., 2010; Regan, et al., 2009; Jünger, et al., 2008; Janković and Binić, 2008; Adunsky, et al., 2005; Houghton, et al., 2003; Akai and Hayashi, 2002; Peters, et al.; 2001).

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. 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) (K080661). 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) (K110350) 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 have reported that NMES was as effective as, or more effective than, exercise (Bax, et al., 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 various other 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 are primarily 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., decreased 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 comparing NMES to no exercise or placebo NMES for the treatment of advanced COPD (eight studies; n=126), chronic heart failure (two studies; n=76) or thoracic cancer (one 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. The inclusion criteria were: age ≥ 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 > 35kg/m^2; pregnancy or potential pregnancy; peripheral neuropathy; contraindication to cardiopulmonary exercise testing (CPET); progressive cancer; cardiac pacemaker; and implanted cardiodefibrillator. 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 (Bonnevie, 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., stoke, 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 were or planned to become pregnant. The intervention group (n=14) received NMES assigned by un-blinded 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 [Fmax], maximal isometric tension [Tmax], maximum shortening velocity [Vmax], and maximum power production [Pmax] 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 was 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 were no statistically significant differences 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 2022 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.

In a 2021 clinical practice guideline on the management of pelvis and musculoskeletal extremity injury and surgery, the American Academy of Orthopaedic Surgeons (AAOS) stated that neuromuscular electrical stimulation should be used in conjunction with standard treatment to improve function but AAOS noted that no significant difference is seen in pain. The recommendation was given a "strong" rating based upon evidence from two high quality and one moderate quality study. Due to inconsistent results, the AAOS reported there is a need for larger studies with an emphasis on heterogenous treatment effects and that further research on the effect on opioid use and pain are needed.

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 cleared 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, Tiawan), the StimPad™ TENS System (AEMED, Inc. West Palm Beach, FLA), JKH Stimulator Plus (JKH USA, LLC, Diamond Bar, CA), the ReBuilder® (Micromed, Inc., Essex Junction, VT), TENS Stimulator InTENSity 10 (Shenzhen Dongdixin Technology Co., Ltd., Shenzhen, CN), 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 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 cleared via the FDA 510(k) premarket notification process as 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 and Silberstein, 2018).

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; essential tremor; 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 ≥ 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 did not support TENS for the treatment of acute pain.

Attention-Deficit/Hyperactivity Disorder (ADHD): The use of TENS targeting the trigeminal nerve has been proposed as a treatment option for attention-deficit/hyperactivity disorder (ADHD). The literature is limited primarily to small pilot and feasibility studies. Further research in the form of high quality studies evaluating long-term effects is needed to determine the safety and effectiveness of TENS for this indication (McGough, et al., 2019; McGough, et al., 2015).

Back Pain: 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 condition (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.

Jauregui 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: Püsküllüoğlu et al. (2022) conducted a systematic review of seven randomized controlled trials evaluating the efficacy of TENS in treating pain or chemotherapy-induced peripheral neuropathy, versus sham TENS, no treatment, or standard care in adult patients with cancer. Sample sizes ranged 24-50; follow ups ranged from one hour to 12 months; and treatment protocols ranged from a one-time application to multiple treatments up to 12 weeks. Heterogeneity in study design, patient population, comparator groups, outcomes, treatment duration and administration, and length of follow-up limited the ability to draw any firm conclusions. Limitations in the data precluded quantitative meta-analysis. The authors concluded that while TENS appears generally safe, the data did not support the recommendation of TENS as a standard treatment for cancer pain or chemotherapy-induced peripheral neuropathy.

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. Hurlow et al. (2012) conducted an updated review, wherein 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.

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) which assessed 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 considered 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.

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, 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.

Diabetes: Lu et al. (2023) conducted a randomized, placebo-controlled trial (n=160) to evaluate the clinical efficacy of TENS on blood glucose control in patients with type 2 diabetes. All patients received a TENS device wherein impulses were transmitted via patches placed on the bilateral abdominal wall. Patients randomized to the TENS (treatment) group received full-frequency wave resonant impulses with mixed frequencies ranging from 1–20,000 Hz, whereas patients in the placebo group were treated with "ineffective" pulse waves with frequencies from 1–30 Hz. All subjects were directed to use the device 60 minutes per day, at least five days per week for 20 consecutive weeks. The study inclusion criteria were: age 30–80; type 2 diabetes on stable oral antidiabetic medications; HbA1c between 7.5–10%; and able to self-administer treatment. The exclusion criteria included: new diagnosis of myocardial infarction, coronary artery bypass surgery, coronary artery stenting, transient ischemic attack, cerebrovascular accident, angina, congestive heart failure (NYHA III-IV), ventricular rhythm disturbances, or thromboembolic disease; history of pancreatitis; on insulin therapy (except for short term uses under seven days) or injectables within three months; women with a positive pregnancy test, planning to become pregnant during the trial, breastfeeding, or judged to be using inadequate contraceptive methods; prior intra-abdominal or gastrointestinal tract surgery; major abdominal trauma within six months; implanted electrical stimulation devices; elevated liver enzymes or bilirubin; active liver disease; moderate to severe renal impairment; blood dyscrasias; acute metabolic complications; malignancy within five years; and history of drug or alcohol abuse within one year. The primary outcome measure was change in HbA1c. Other outcome measures included percentage of subjects who achieved HbA1c target of < 7%; change in fasting plasma glucose; change in mean 7-point self-monitored blood glucose; weight; changes in certain biomarkers; and adverse events. Follow ups occurred at two, four, eight, 12, 16, and 20 weeks. Ultimately 155 subjects were included in the intention to treat analysis. After 20 weeks, HbA1c decreased from 8.1% to 7.9% in the TENS group (−0.2% [95% confidence interval (CI) −0.4% to −0.1%]) and from 8.1% to 7.8% in the placebo group (−0.3% [95% CI −0.5% to −0.2%]); the between-group difference was not statistically significant (p=0.821). There were also no statistically significant differences between the groups in the remaining glycemic parameters. There were nine serious adverse events reported, four in the TENS group and five in the placebo group; none were reportedly related to the TENS device. Limitations of the study included strict study eligibility and exclusion criteria which may limit applicability of findings to other patient populations, and the relatively short duration of follow up. The authors concluded that TENS did not demonstrate a statistically significant difference in HbA1c reduction as compared to placebo.

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 reportedly 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 transcutaneous tibial nerve stimulation 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: 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 trail 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 ≥ 30% or ≥ 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 ≥ 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: 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 with short-term follow-ups (e.g., two hours to four months) (Chou, et al., 2017; Di Fiore, et al., 2017; Przeklasa-Muszyńska, et al., 2017; Vikelis, et al., 2017; Miller, et al., 2016).

Kuruvilla et al. (2022) conducted a randomized sham-controlled trial (n=607) to evaluate the efficacy and safety of external trigeminal nerve stimulation (e-TNS; specifically, the Cefaly device) in treating migraine attacks. All subjects received a migraine diary and e-TNS device to record and treat a qualifying migraine (i.e., moderate to severe headache intensity with at least one migraine-associated symptom) within four hours of onset, for a two-hour treatment session. Subjects were instructed to not take any acute migraine medications prior to or during e-TNS therapy, but were able to take medications as needed after the two-hour session was completed. For the treatment group and the sham group, devices used identical biphasic symmetrical pulses. The sham device delivered low frequency pulses of 3 Hz, while the treatment device produced high frequency pulses of 100 Hz. Electrical pulses were transmitted transcutaneously via a supraorbital electrode placed on the forehead. The trial inclusion criteria were: age 18 to 65; at least a one-year history of migraine with or without aura; migraine onset before age 50; and experiencing between two and eight moderate or severe migraine attacks per month. The exclusion criteria included: difficulty distinguishing migraine attacks from tension-type headaches; > 15 headache days per month; supraorbital nerve blocks or Botox treatment in the prior four months; migraine aura without headache; change in migraine prophylaxis treatment in the previous three months; other primary headache disorders, except rare tension-type headaches per month; secondary headache disorders; and presence of a pacemaker or implanted or wearable defibrillator. The primary outcome measures included freedom from pain and resolution of the most bothersome migraine-associated symptom (MBS) at two hours from the beginning of e-TNS therapy. The secondary outcome measures included pain relief at two hours (i.e., reduction of a moderate/severe headache to a mild/no headache); resolution of any migraine-associated symptom at two hours; sustained pain freedom (i.e., pain freedom at two hours and 24 hours without the use of anti-migraine medication); sustained pain relief at 24 hours (i.e., mild or no headache at two and 24 hours without the use of anti-migraine medication); and use of a rescue medication between 2–24 hours after the beginning of an e-TNS session. The patient diary and e-TNS device were collected after two months. Five hundred thirty eight patients (89%) were

included in the intention-to-treat analysis (treatment group, n=259, sham group, n=279). The percentage of subjects experiencing freedom from pain at two hours after beginning e-TNS was higher in the treatment group (25.5%) compared to the sham group (18.3%; p=0.043). Similarly, the percentage of patients with resolution of MBS at two hours was higher in the treatment group (56.4%) versus the sham group (42.3%; p<0.01). Reported pain relief at two hours was higher in the treatment group (69.5%) than sham (55.2%; p=0.001); absence of all migraine-associated symptoms at two hours was higher in the treatment group (42.5%) than sham (34.1%; p=0.044); and sustained pain freedom and pain relief at 24 hours was higher in the treatment group (22.8% and 45.9%) than in the sham group (15.8% and 34.4%; p=0.039 and p=0.006, respectively). There was no statistically significant difference between the groups in the use of acute migraine medications between two and 24 hours post-treatment (31.7% of the treatment group and 37.6% of the sham group required rescue migraine medications after e-TNS treatment). More patients in the treatment group reported an adverse event (8.5%) compared to sham (2.9%; p<0.01), most commonly forehead paresthesias, discomfort, or burning. Limitations of the study included the unknown potential therapeutic effect of the sham e-TNS; the reliance on self-reported outcomes; and limited/one-time follow up. Further, the baseline number of headache years, average headache severity, and usual anti-migraine treatments were not recorded, thus any potential effects on outcomes could not be assessed.

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.

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. (2013) 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: Reichenbach et al. (2022) conducted a randomized, placebo-controlled trial to investigate the efficacy of transcutaneous electrical nerve stimulation (TENS) in adults with symptomatic knee osteoarthritis (OA). A total of 220 participants were randomized to receive either active TENS (n=108) or placebo TENS (n=112) over a three week treatment period. The study was conducted in the facility setting. Inclusion criteria required subjects to be ≥ 18 years; have radiographically confirmed knee OA; persistent knee pain for ≥ six months, and radiographic evidence of at least one osteophyte at the tibiofemoral joint. The primary outcome was knee pain intensity measured by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale at three weeks. Secondary outcomes included WOMAC function and stiffness subscales and global score, overall knee pain per visual analogue scale (VAS), emotional status (hospital anxiety and depression scale), participation, analgesic use, and adverse events. Follow-up assessments were conducted at baseline, one week, three weeks

(end of treatment), and three months. No statistically significant differences were observed between groups for the primary outcome (mean difference 0.06; 95% CI −0.41 to 0.29; p=0.74) or any secondary outcomes (all p>0.05). Adverse event rates were similar between groups, with no serious adverse events reported. Limitations of the study include the inability to blind treating therapists and limited generalizability to individuals with severe pain due to underrepresentation. The authors concluded that TENS does not provide clinically meaningful benefits over placebo in the management of knee OA, and further trials in this population are not warranted.

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 group. 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 draws; 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 conclusions regarding the impact of TENS on pain relief for knee osteoarthritis could not be made.

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 rheumatoid arthritis of the hand.

Rotator Cuff Tendinopathy: Desmueles 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: 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 criterial 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 included: 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-stoke 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.

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.

Urinary 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: In 2023, the National Institute for Health and Care Excellence (NICE) published guidance on the use of transcutaneous electrical trigeminal nerve stimulation for the treatment of attention deficit hyperactivity disorder (ADHD). NICE determined the evidence for the safety and efficacy of this treatment was inadequate in both quality and quantity, and thus should only be used in a research context.

The Department of Veterans Affairs and Department of Defense (VA/DoD) stated in a 2022 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 a 2022 interventional procedure guidance, NICE stated that transcutaneous electrical stimulation of the supraorbital nerve for treating an acute migraine attack is adequate but, for treating subsequent attacks, is limited in quality and quantity. For treating acute migraine, the procedure should only be used with special arrangements for clinical governance, consent and audit or research. The document further noted the evidence for preventing migraine is inadequate in quality, and thus, when used for migraine prevention, the procedure should only be used in the context of research.

In a guideline on the assessment and management of chronic pain, NICE (2021) did 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 their 2021 clinical practice guideline for the management of non-arthroplasty osteoarthritis of the knee, the American Academy of Orthopaedic Surgeons (AAOS) provided a "limited" recommendation for the use of TENS to improve pain and/or function in patients with knee osteoarthritis (OA). The recommendation was based upon two high quality studies and one moderate quality study that found that TENS was effective in reducing pain associated with OA but

not in improving function. TENS was given a "limited" recommendation because of inconsistent evidence. Future research was recommended with larger randomized controlled trial examining the long-term effectiveness of the intervention.

The American College of Physicians (ACP) and American Academy of Family Physicians (AAFP) 2020 guideline on the management of acute pain from non-low back musculoskeletal injuries in adults suggested clinicians treat such individuals with transcutaneous electrical nerve stimulation (TENS) to reduce pain (Grade: Conditional recommendation [benefits probably outweigh risks and burden, or vice versa, but there is appreciable uncertainty]; Low-certainty evidence [confidence in the effect estimate is limited: the true effect may be substantially different from the estimated effect]) (Qaseem, et al., 2020).

The VA/DoD stated in a 2023 clinical practice guideline on the management of headache that a recommendation either for or against the use of supraorbital electrical stimulation or external trigeminal nerve 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 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 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).

In a 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 (AAN, 2024).

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) cleared 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

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.) which was cleared by the FDA via the 510(k) premarket notification process.

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 to determine the clinical utility of electroceutical therapy in the treatment of individuals with acute or chronic pain are lacking.

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 chronic intractable pain, diabetic peripheral neuropathy, post-surgical pain, muscle re-education, and thrombosis prevention.

U.S. Food and Drug Administration (FDA): The Neufit Neubie device originally received FDA clearance through the 510(k) premarket notification 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® Plus device (EMSI) received FDA clearance in 2014 through the 510(k) process as a Class II medical device. It is capable of providing TENS and electrical muscle stimulation therapy.

Per the FDA indications for use, 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 peer-reviewed published literature to support the use of combination devices for the treatment of any condition. As such, conclusions about the safety and efficacy of the use of combination units cannot be made.

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 systemically 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 cleared via the FDA 510(k) premarket notification process. Two such devices are the Dynatron STS and the Dynatron STS RX, a home device (Dynatronics Corp.). The devices are proposed for symptomatic relief of chronic intractable pain and/or management of post-traumatic or post-surgical pain.

Literature Review: The evidence in the published peer-reviewed scientific literature is insufficient to support the safety and effectiveness of electrical sympathetic stimulation therapy. Studies are primarily in the form of case series and retrospective reviews with small patient populations and short-term follow-ups (Guido, 2002).

Electrotherapeutic Point Stimulation (ETPS^{SM})
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). 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.

U.S. Food and Drug Administration (FDA): The TENS US Unit is cleared by the FDA as the TENS Pro 900 (Acumed Medical Supplies, LTD, Stanford, CT) for the treatment of chronic intractable pain. The device was cleared 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)
Functional electrical stimulation (FES), also known as functional neuromuscular stimulation (FNS), aims to replace stimuli from damaged (nonintact) nerve pathways to assist with functional movement and reduce spasticity in individuals with neurological impairments, such as spinal cord injury or stroke. This differs from neuromuscular electrical stimulation (NMES), which is used to treat disuse atrophy when the nerve supply to a muscle is intact (i.e., in individuals without neurologic impairment). FES is typically delivered at high intensity for short durations—20 minutes to an hour—several times a week over months.

FES has been proposed for multiple indications, including:

- assisting with ambulation in individuals with paraplegia
- improving gait disorders such as foot drop, hemiplegia after stroke, cerebral injury, or incomplete spinal cord injury
- as a means of stationary exercise to prevent or reduce muscle atrophy (e.g., cycle ergometers [FES bicycles])
- providing range of motion and function in individuals with upper limb paralysis or hemiplegia
- as a modality for acute and chronic conditions with impaired respiratory function

There are numerous types of FES devices, which vary widely in design and proposed indication for use. Examples of FES devices include:

- Cionic Neural Sleeve NS-200 (Cionic Inc.)
- Ergys2 Rehabilitation System (Therapeutic Alliance, Inc.)
- H200 (Bioness Medical, Inc.)
- L300 Go (Bioness Medical, Inc.)
- MyoCycle (MYOLYN, Inc.)
- MyndMove 2.0 (MyndTec, Inc.)
- ODFS® Pace (Odstock Medical Ltd.)
- Parastep® I System (Sigmedics, Inc.)
- ReGrasp (Rehabtronics Inc.)
- RT300 (Restorative Therapies, Inc.)
- WalkAide® (Innovative Neurotronics)

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 cleared by the FDA 510(k) process as Class II devices. Examples include the RT300 FES cycle ergometer (Restorative Therapies, Inc.), cleared 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". The WalkAide System is cleared 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.

Literature Review
There is insufficient evidence in the published peer-reviewed scientific literature to establish the safety and effectiveness of functional electrical stimulation used in a home setting, for any indication. Studies have been performed primarily in the inpatient or clinic setting and are limited by small and heterogenous subject populations; heterogeneity in active and control group treatments, outcome measures, and instruments used; lack of blinding; high risk of bias; variation in FES delivery, stimulated muscles, stimulation intensity and type; and conflicting outcomes.

Cerebral Palsy: Moll et al. (2017) conducted a systematic review to assess the effect of FES on 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.

Chiu and Ada (2014) conducted a systematic review to determine the effectiveness of FES versus 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 versus 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 foot drop, hemiplegia due to stroke, cerebral injury, or incomplete spinal cord injury. Randomized controlled trials and case series have primarily included small patient populations with short-term follow-ups, and heterogeneous treatment regimens and outcome measures (Esnouf, et al., 2010; Stein, et al., 2010; Nooijen, et al., 2009; 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 (AFOs) 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. AFOs. 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). The meta-analysis indicated 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) (n=22), overground training with electrical stimulation (OG) (n=18) (WalkAide), and treadmill-based training with locomotor robot (LR) (Lokomat Robotic Gait Orthosis) (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 ($p \leq 0.01$). 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 unknown optimal training dosage for improving walking speed and distance; focus on walking rather than other aspects of walking (e.g., producing optimal kinematics); most subjects used a wheelchair as their primary means of mobility thus the amount of change qualified as meaningful 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 included the small patient population, short-term 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, WalkAide, 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.

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: Studies investigating FES using Parastep were published in 2000 or earlier, 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 a stable neurologic and orthopedic status and were 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 0.15 6 ± 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.

Stroke Rehabilitation: Randomized controlled trials using various FES devices have evaluated FES cycling (MOTOmed®, RECK GmbH) 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 with standard rehabilitation vs. rehabilitation alone (n=20) (Ferrante, et al., 2008); and with arm and hand rehabilitation comparing FES (Compex Motion, Compex SA) to conventional therapy (n=23) (Mangold, et al., 2009). Some studies reported no significant differences with FES. Meta-analyses of controlled trials have reported no significant improvement in functional motor ability, and mixed results for gait speed and improvement with ADLs when FES was used for stroke rehabilitation; trials were conducted primarily or exclusively in the inpatient or clinic settings (Matsumoto, et al., 2023; da Cunha, et al., 2021; Kristensen, et al., 2021; Busk, et al., 2020; Pollock, et al., 2014; Pomeroy, et al., 2006). Due to the small patient populations, short-term follow-ups, and conflicting results, the effectiveness of home FES for stroke rehabilitation has not been established.

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 and 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 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 ≥ 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 U.S. Department of Veteran's Affairs (VA/DoD) 2024 practice guideline on the management of stroke rehabilitation suggested the use of neuromuscular electrical stimulation to improve motor outcomes in this population, with the strength of the recommendation given as "weak for". The recommendation noted that short-term improvements in upper and lower extremity motor function and activities of daily living (ADLs) may occur, but evidence was insufficient to confirm long-term sustainability. The group's confidence in the evidence was very low due to methodological limitations in the studies

evaluated. The guideline found insufficient evidence to recommend for or against contralaterally controlled FES to improve upper extremity motor outcomes and ADLs, or for neuromuscular electrical stimulation and pharyngeal electrical stimulation for dysphagia.

The 2016 American Heart Association/American Stroke Association guidelines for stroke rehabilitation stated that neuromuscular electrical stimulation (NMES)/FES for the management of post-stroke dysphagia was of uncertain benefit and was not recommended (Class of Recommendation: III; Level of Evidence: A). For the treatment of spasticity, the guideline noted that the adjunctive use of NMES may be reasonable to improve spasticity temporarily (Class of Recommendation: IIb; Level of Evidence: A), but there was insufficient evidence that the addition of NMES improved functional gait or hand use. For mobility issues, the guideline stated NMES was reasonable to consider as an alternative to an ankle-foot orthosis for foot drop, or for individuals with minimal volitional movement within the first few months after stroke or for individuals with shoulder subluxation (Class of Recommendation: IIa; Level of Evidence: A) (Winstein, et al., 2016).

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 cleared via the FDA 510(k) premarket notification process as 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. Evidence is primarily in the form of noncomparative retrospective studies, small case series, and literature reviews (Norwood, et al., 2024; Allen, et al., 2023; Bajaj, et al., 2023; Trinh, et al., 2023).

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=two studies) and increase functionality (n=two 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-Stim, 2014).

U.S. Food and Drug Administration (FDA): HVG stimulators are FDA-cleared via the 510(k) premarket notification process as a Class II device. An example of such a device is the CS3102 High Voltage Galvanic Stimulator (Control Solutions, Inc.).

Literature Review: 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 cleared via the FDA 510(k) premarket notification process as Class II devices. Examples of FDA-approved devices include the RS-4i Plus Sequential Stimulator (RS Medical, Vancouver, WA), IF 8000 (Biomotion, Madison, AL), and Flex-IT (EMSI, Inc., 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. Studies report mixed outcomes, includes some which found 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; Demirtürk, 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, Demirtürk 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 ($p<0.05$ 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.

Microcurrent Electrical Nerve Stimulation (MENS)
MENS involves the use of a device that delivers small amounts of electrical current (millionths of an amp) to purportedly help to 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 (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 other conditions (Frequency Specific Microcurrent [FSM], 2025).

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-cleared 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. Evidence primarily consists of studies with small patient populations and short-term follow-ups with conflicting outcomes, and in some cases reported outcomes were no better than placebo (Iijima and Takahashi, 2021; Rajpurohit, et al., 2010; Zuim, et al., 2006).

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 clearance by the FDA via the 510(k) process. PNT is

purportedly 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. The Vertis PNT Control Unit with a cervical electrode and cable also received 510(k) clearance.

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 pain or other disorders. Overall, studies have included small patient populations and short term follow-ups.

Back Pain: Weiner et al. (2008) conducted a randomized controlled trial (n=200) to evaluate the efficacy of PENS in adults with chronic low back pain. Patients were randomized to either 1) PENS, 2) brief electrical stimulation to control for treatment expectance (control-PENS), 3) PENS plus general conditioning and aerobic exercise (GCAE) or to 4) control-PENS plus GCAE. Treatment was delivered twice a week for six weeks to the 50 participants in each group. All groups reported significantly reduced pain (McGill Pain Questionnaire short form) and disability and improved gait velocity, which was sustained at six months. Significantly fewer fear avoidance beliefs were reported in the CGAE group compared to the non-CGAE group. Comparable reduced pain and function were reported by the PENS and control-PENS group, whether delivered for five minutes or 30 minutes. Thus, the exact dose of electrical stimulation needed for analgesia could not be determined. PENS and GCAE were more effective than PENS alone in reducing fear avoidance beliefs, but not in reducing pain or in improving physical function. There was a statistically significant improvement in chair rise time in the control-PENS plus CGAE compared to control-PENS alone. The overall drop-out rate was 8%.

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.

Professional Societies/Organizations: In their 2021 clinical practice guideline for the management of non-arthroplasty osteoarthritis of the knee, the American Academy of Orthopaedic Surgeons (AAOS) provided a "limited" recommendation for the use of PENS to improve pain and/or function in patients with knee osteoarthritis (OA). The recommendation was based upon one high quality study that found that PENS combined with a Cox-2 inhibitor resulted in greater improvements in pain and function compared to sham PENS. PENS was given a "limited" recommendation because of feasibility issues which requires a practitioner trained in the technique which could limit access for some patients. Future research was recommended with larger randomized controlled trial examining the long-term effectiveness of the intervention.

Percutaneous Electrical Nerve Field Stimulation (PENFS)
Nonimplantable percutaneous electrical nerve field stimulation (or auricular neurostimulation) has been proposed for the treatment of various conditions, including substance use disorders and functional abdominal pain disorders (e.g., pain associated with irritable bowel syndrome [IBS]). PENFS devices are placed behind the ear, with electrodes placed in and around the ear to stimulate specific cranial nerves and periauricular occipital nerves, to purportedly reduce pain and opioid withdrawal symptoms.

U.S. Food and Drug Administration: In 2017, the FDA approved the NSS-2 Bridge™ (Masimo Corporation, Irvine, CA), a percutaneous nerve field stimulator for the treatment of substance use disorders. The NSS-2 Bridge is a battery-powered device proposed as an aid to reduce the symptoms of opioid withdrawal. The device emits electrical pulses to stimulate branches of cranial nerves V, VII, IX, X and the occipital nerves. Individuals can use the device for up to five days to treat acute symptoms that may be experienced during the physical withdrawal phase (e.g., sweating, gastrointestinal upset, agitation, insomnia and joint pain).

In 2019, the FDA approved the IB-Stim (Neuraxis, Inc., Carmel, IN) as a Class II device for functional abdominal pain relief. Specifically, IB-Stim (formerly Neuro-Stim) is a percutaneous electrical nerve field stimulator intended for use in individuals 11-18 years old, with functional abdominal pain associated with irritable bowel syndrome (IBS). Per the FDA indications for use, "the IB-Stim is intended to be used for 120 hours per week up to 3 consecutive weeks, through application to branches of Cranial Nerves V, VII, IX and X, and the occipital nerves identified by transillumination, as an aid in the reduction of pain when combined with other therapies for IBS." Subsequent updates to the indications for use have extended the intended treatment population from ages 8-21, the treatment duration from three to four weeks, and added functional dyspepsia as a treated indication.

Literature Review—PENFS for Functional Gastrointestinal Disorders: Evidence in the published peer-reviewed scientific literature is at present insufficient to support the safety and effectiveness of percutaneous electrical nerve field stimulation in the treatment of functional gastrointestinal disorders. Evidence consists primarily of noncomparative trials with small patient populations, short term follow-up, and mixed outcomes (Dorfman, et al., 2025; Kolacz, et al., 2025; Chogle, et al., 2024; Santucci, et al., 2024; Bora, et al., 2023; Castillo, et al., 2023; Chogle, et al., 2023; Santucci, et al., 2023; Santucci, et al., 2022). Additional comparative studies with large sample sizes and long-term follow-up are needed to confirm initial results, and to identify optimal target patient population and treatment parameters.

Kovacic et al. (2017) conducted a randomized controlled trial to evaluate the efficacy of 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 PENFS 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. In a subanalysis this study, Krasaelap et al. (2020) evaluated the effects of the Neuro-

Stim device on the subset of individuals with irritable bowel syndrome (IBS). Twenty seven subjects received PENFS, and 23 received the sham intervention. 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≤0.001) were all observed. These effects were not sustained at eight to twelve weeks after the completion of therapy. 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.

Literature Review—PENFS for Postoperative Pain Management: Investigators have explored the use of PENFS to manage acute and postoperative pain. Several trials have investigated the off-label use of NSS-2 Bridge (Masimo) to treat pain after abdominal, breast, and musculoskeletal surgeries, with mixed results. Ilfeld et al. conducted four randomized controlled trials comparing the effect of NSS-2 Bridge versus a sham device on postoperative pain and opioid use after cholecystectomy or hernia repair (2024); breast surgery (2025a); total hip arthroplasty (2025b); and total knee arthroplasty (2025c). Protocols and outcome measures were similar across the four trials. Each trial included 30 adult subjects (n=15 active group; n=15 sham group). All subjects had the study device placed in the recovery room; those in the active group received percutaneous auricular stimulation with the NSS-2 Bridge device, while those in the sham group had a nonfunctional sham device. Subjects were also discharged with a prescription for oxycodone to take as needed. All devices were worn for five days, then removed. Subjects were followed for the first eight days following their respective procedure, to assess opioid consumption and pain scores. In the post-knee arthroplasty and cholecystectomy/hernia repair studies, the active device subjects had significantly lower average pain scores, compared to those who had sham treatment. Oxycodone consumption was significantly lower in the active group in the post-op knee study, but not in the cholecystectomy/hernia repair study. For the post-breast surgery and post-total hip arthroplasty studies, there were no statistically significant differences between the active and sham groups in pain scores or oxycodone use. All studies were limited by the small sample sizes.

Literature Review—PENFS for Substance Use Disorders: Published studies investigating the safety and effectiveness of PENFS for substance use disorders are primarily in the form of small case series, prospective nonrandomized trials, and retrospective reviews with small patient populations (Miranda and Taca, 2018). There is currently insufficient evidence to support the use of this device for any indication including the treatment of pain or withdrawal symptoms related to substance use disorders.

Professional Societies/Organizations: On behalf of the European and North American Societies for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN/NASPGHAN), Groen at al. (2025) published guidelines for the treatment of irritable bowel syndrome (IBS) and functional abdominal pain (FAP) in children 4–18 years of age. The guidelines stated "Percutaneous Electrical Nerve Field Stimulation (PENFS) is suggested as a treatment option (Conditional recommendation, Moderate certainty evidence)". The recommendation was based upon the outcomes from one randomized trial (cited above—Kovacic et al. [2017]). The authors provided additional rationale for the conditional recommendation:

> "Despite moderate certainty of evidence, the pain intensity reduction was among the highest across all studied treatment options. This is a very new field in the treatment of [abdominal pain related disorders of gut–brain interaction] (AP-DGBIs) and has only been studied in a small population. The study included in these guidelines comes from a single

institution. This study shows that a favorable effect likely exists, but that its size has yet to be determined, which, in the context of limited availability and experience, does not create sufficient grounds for a strong recommendation for all children AP-DGBIs. The [Guideline Development Group] (GDG) notes that this treatment comes at a relatively high initial cost and requires weekly new device placement for the duration of the treatment course. Moreover, PENFS has only recently been implemented as a treatment option for AP-DGBIs and will likely undergo further development in the coming years. The GDG suggests that this treatment option may be utilized for patients who have shown considerable difficulty in achieving pain relief."

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 individual 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 cleared 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 Afferent Patterned Stimulation (TAPS)
Essential tremor (ET) and Parkinson's disease are neurological conditions with different causes, which both present with involuntary and rhythmic shaking or trembling. In ET, tremors occur most frequently in the hands and arms. Tremors in Parkinson's disease usually begin on one side of the body and progress to the other, are more forceful than in ET, and are accompanied by an array of other symptoms (e.g., stiffness, difficulty with balance and coordination) which worsen over time. Deep brain stimulation (DBS) is an established treatment for medically refractory essential tremor (ET) and Parkinson's disease, and involves the delivery of electrical impulses to an area of the brain responsible for movement via surgically implanted wires and electrodes. DBS is therefore an invasive neuromodulation therapy reserved for severe cases. Transcutaneous afferent patterned stimulation (TAPS) neuromodulation therapy has been proposed as a non-invasive treatment for essential tremor and tremor in Parkinson's disease. TAPS therapy is typically delivered via a wrist-worn device which purportedly provides deep brain stimulation (DBS) (i.e., to the thalamus) in a non-invasive manner via peripheral nerves in the wrist.

U.S. Food and Drug Administration (FDA): The Cala Trio device (Cala Health, Inc., Burlingame, CA) was granted FDA 510(k) clearance October 5, 2021 for the indication of "temporary relief of hand tremors in the treated hand following stimulation in adults with essential tremor". The wrist-worn device is purported to relieve essential tremor symptoms by applying TAPS to the median and radial nerves of a patient's wrist. The device consists of a rechargeable stimulator, a wrist-worn electrode band, and a base station to charge the device. The wrist-worn electrode band is integrated with electrodes placed at various intervals around the inner diameter of the band to target the median and radial nerves. This band is attached to the stimulator which contains a full color display and allows the user to calibrate, adjust stimulation parameters, set timers, and read instructions for stimulation delivery.

In November 2022, the FDA cleared the Cala kIQ™ device via the 510(k) premarket notification pathway as substantially equivalent to the Cala Trio. Per the FDA determination, the next generation Cala kIQ device, like the predicate Cala Trio device, is indicated for the "temporary

relief of hand tremors in the treated hand following stimulation in adults with essential tremor". In addition, the newer device "is indicated to aid in the temporary relief of postural and kinetic hand tremor symptoms that impact some activities of daily living in the treated hand following stimulation in adults with Parkinson's disease." The next generation kIQ device is reported to have increased maximum current density, increased maximum average power density, and an additional electrode, compared to the older Trio device.

The Felix™ NeuroAI™ Wristband was cleared by the FDA 510(k) process in July 2025, with the stated indication to "aid in tremor-related functional limitations in the upper limbs in adults with essential tremor." It is a wrist-worn device intended to deliver transcutaneous electrical stimulation to the peripheral nerves in the wrist, to purportedly lessen hand tremors and restore motor control. Per the manufacturer, the device incorporates an AI algorithm to continuously control the stimulation parameters of the device.

Literature Review: There is insufficient evidence in the published peer-reviewed scientific literature to support TAPS for the treatment of any condition, including but not limited to tremor in Parkinson's disease and essential tremor. The available literature is primarily limited to open label, single arm studies, and retrospective reviews that are further limited by short-term follow-ups, small patient populations, and heterogeneity of treatment parameters (Dewey, et al., 2025; Brillman, et al., 2023; Isaacson, et al., 2023; Lu, et al., 2023; Brillman, et al., 2022; Pascual-Valdunciel, et al., 2021; Isaacson, et al., 2020; Kim, et al., 2020; Yu, et al., 2020; Lin, et al., 2018).

Dai et al. (2023) conducted a randomized pragmatic trial (n=310) to evaluate the clinical benefit of adding transcutaneous afferent patterned stimulation (TAPS) to standard of care (SOC) in individuals with essential tremor (ET), versus SOC alone. All subjects were prescribed a TAPS device (Cala Trio™, Cala Health, San Mateo, CA), then randomized to treatment (TX) or standard of care (SOC) for one month of home use. Subjects in the TX group added TAPS to their physician-recommended care plan, while subjects in the SOC group continued with their physician-recommended regimen. The TX group was directed to use the device as needed for temporary relief of hand tremor, and to perform postural holds before and after stimulation sessions for measuring tremor power. Subjects in the SOC group were told to measure tremor power once a day with the device, without delivering stimulation. Study subjects were identified in the claims databases of a major payor. The study inclusion criteria were: a diagnosis of ET (as determined by claim data); age ≥ 22 years; with fully insured commercial health plan or/and Medicare Advantage with medical and pharmacy health insurance benefits for at least 12 months before the enrollment; and ability to sign informed consent. The exclusion criteria were: a diagnosis of Parkinson's disease, Alzheimer's disease/dementia, epilepsy, or thyroid disorders (as determined by claim data); presence of an implanted electronic medical device; history of an ET-related neurosurgery or magnetic resonance-guided focused ultrasound; persons who had used botulinum toxin as a therapeutic injection in the upper limb during the last six months; people who were pregnant or planned to become pregnant during the study; and individuals with hand skin lesions at the stimulation site. The study group was 66% male, 84% white, and 70% had received ET-related pharmacotherapy within the previous 12 months. The primary outcome measure was median tremor power as measured by the device. The secondary outcome measure was improvement in the Bain & Findley Activities of Daily Living (BF-ADL) upper limb score. The follow up period was one month. Two hundred seventy six subjects (133 TX, 143 SOC) were included in the modified intention-to-treat (mITT) analysis. At one month, tremor power in the TX group (0.017 ± 0.003 $(m/s^2)^2$) was significantly lower than tremor power in the SOC group (0.08 ± 0.014 $(m/s^2)^2$) in the mITT analysis ($p<0.0001$). One hundred thirty four subjects (43%) completed the BF-ADL ratings at baseline and one month. The changes in BF-ADL score from baseline to one month in the TX group (1.6 ± 0.43) were significantly greater than the changes observed in the SOC group (0.22 ± 0.37) ($p=0.0187$). No serious device-related adverse events

were reported. The study was limited by the open-label design; lack of medication usage data; between-group variability in collection of tremor data; use of the study device to collect outcome data; missing BF-ADL data; potential for selection bias; use of self-reported data; and lack of a placebo-controlled group. This study provided initial, one-month data as part of an ongoing open-label, crossover study.

Pahwa et al. (2019) conducted a randomized controlled study of 77 ET patients who received either treatment stimulation (n=40) or sham stimulation (n=37) delivered and worn on the wrist of the hand with more severe tremor. Tremor was evaluated before and immediately after the end of a single 40-minute stimulation session. The primary endpoint compared spiral drawing in the stimulated hand using the Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS) Archimedes spiral scores in both the treatment and sham groups. Additional endpoints included TETRAS upper limb tremor scores, subject-rated tasks from the Bain and Findley activities of daily living (ADL) scale before and after stimulation as well as clinical global impression-improvement (CGI-I) rating after stimulation. Subjects who received peripheral nerve stimulation did not show significantly greater improvement in the Archimedes spiral task compared to sham but did show significantly greater improvement in upper limb TETRAS tremor scores (p=0.017) compared to sham. Subject-rated improvements in ADLs were significantly greater with treatment (49% reduction) than with sham (27% reduction; p=0.001). A greater percentage of ET patients (88%) reported improvement in the stimulation group as compared to the sham group (62%) according to CGI-I ratings (p=0.019). No significant adverse events were reported. Author noted limitations of the study included the small patient population and short-term follow-up (i.e., immediately after a single treatment session).

Professional Societies/Organizations: The International Essential Tremor Foundation (2021) stated in a guideline advisory that Cala Trio can be an adjunct to first or second line pharmacotherapy, although a specific recommendation for or against is not made and there is no indication that the treatment algorithm is based upon a review of the scientific literature.

Transcutaneous Auricular Neurostimulation (tAN)
Transcutaneous auricular neurostimulation (tAN), or transcutaneous nerve field stimulation, involves the delivery of electrical stimulation through the skin on and around the ear, to target branches of cranial nerves V (trigeminal nerve) and X (vagus nerve). This stimulation purportedly activates regions of the central brain to release endogenous opioids (endorphins), which then "fill" vacant opioid receptors in the brain to reduce or eliminate withdrawal symptoms. The technology has been proposed for the treatment of opioid withdrawal symptoms (when used in conjunction with standard treatments for opioid use disorder).

U.S. Food and Drug Administration (FDA): In 2021, the FDA cleared the Sparrow Therapy System (Spark Biomedical, Inc., San Diego, CA), a transcutaneous auricular nerve field stimulation device, via the 510(k) premarket approval process as a Class II device. The indications for use stated the Sparrow system "is intended to be used in patients experiencing opioid withdrawal in conjunction with standard symptomatic medications and other therapies for opioid withdrawal symptoms under the supervision of trained clinical personnel". The device is intended for use in clinical environments and/or in the home. The Sparrow Therapy System FDA submission cited the NSS-2 Bridge as the predicate device, the difference being that the NSS-2 Bridge device delivers stimulation percutaneously, versus transcutaneously with the Sparrow device. The newer Sparrow Ascent device was cleared by the FDA in 2023, with identical functioning and indications for use.

Literature Review: There is insufficient evidence in the published peer-reviewed scientific literature to support the effectiveness, safety, and long-term outcomes of home-use transcutaneous auricular neurostimulation or transcutaneous nerve field stimulation for any indication, and their use is considered investigational at this time.

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) has offered 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, Horsham, PA) is proposed for relief of nausea due to a number of causes. This device is available over the counter.

TEAS is also proposed for use in other conditions such as control of diabetes, glaucoma, 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; Zhao, et al., 2015; Zhiyuan, et al., 2015).

U.S. Food and Drug Administration (FDA): The original FDA clearance for these devices was for various models of the ReliefBand NST (Woodside Biomedical, Inc., San Diego, CA). Reported 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). Indications for ReliefBand have since expanded to include physician-diagnosed migraine, hangover, anxiety, and for use as an adjunct to antiemetics in reducing postoperative nausea.

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 Neiguan point 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 ($p\leq0.05$). 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 ($n<100$) 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. There was insufficient evidence to support electrical acustimulation for the treatment of nausea and vomiting in pregnancy.

Professional Societies/Organizations: In a 2018 practice bulletin (reaffirmed 2024), 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 studied 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.

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 or 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 was 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 limitation 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.

Health Equity Considerations

Health equity is the highest level of health for all people; health inequity is the avoidable difference in health status or distribution of health resources due to the social conditions in which people are born, grow, live, work, and age.

Social determinants of health are the conditions in the environment that affect a wide range of health, functioning, and quality of life outcomes and risks. Examples include safe housing, transportation, and neighborhoods; racism, discrimination and violence; education, job opportunities and income; access to nutritious foods and physical activity opportunities; access to clean air and water; and language and literacy skills.

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	Assessing Patient's Suitability for Electrical Nerve Stimulation Therapy (160.7.1)	6/19/2006
NCD	National	Durable Medical Equipment Reference List (280.1)	5/16/2023
NCD	National	Electrical Stimulation (ES) and Electromagnetic Therapy for the Treatment of Wounds (270.1)	7/1/2004
NCD	National	Electrotherapy for Treatment of Facial Nerve Paralysis (Bell's Palsy) (160.15)	Longstanding
NCD	National	Neuromuscular Electrical Stimulation (NMES) (160.12)	10/1/2006
NCD	National	Supplies Used in the Delivery of Transcutaneous Electrical Nerve Stimulation (TENS) and Neuromuscular Electrical Stimulation (NMES) (160.13)	7/14/1988
NCD	National	Transcutaneous Electrical Nerve Stimulation (TENS) for Acute Post-Operative Pain (10.2)	6/8/2012
NCD	National	Treatment of Motor Function Disorders with Electric Nerve Stimulation (160.2)	4/1/2003
LCD	CGS Administrators; Noridian Healthcare Solutions	External Upper Limb Tremor Stimulator Therapy (L39591)	4/7/2024
LCD	Palmetto GBA	Home Health Occupational Therapy (L34560)	6/9/2022
LCD	Palmetto GBA	Home Health Physical Therapy (L34564)	5/23/2024

	Contractor	Determination Name/Number	Revision Effective Date
LCD	CGS Administrators	Physical Therapy – Home Health (L33942)	6/27/2024
LCD	CGS Administrators; Noridian Healthcare Solutions	Transcutaneous Electrical Nerve Stimulators (TENS) (L33802)	1/1/2024
LCD	Multiple LCDs	Wound Care	Varies

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

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Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	• Added policy statement for functional electrical stimulation (FES).	1/15/2026
Annual Review	• Revised policy statements for transcutaneous electrical nerve stimulators.	10/15/2025
Annual Review/ Focused Review	• Added the following therapies/devices to the noncoverage policy statement: bioelectric nerve block; combination therapy; electrical sympathetic stimulation therapy; electrotherapeutic point stimulation; H-WAVE electrical stimulation; high-voltage galvanic stimulation; microcurrent electrical nerve stimulation; transcutaneous auricular neurostimulation; threshold/therapeutic electrical stimulation. • Removed the following therapies/devices from the policy statement: auricular electroacupuncture; cranial electrical	1/15/2025

Type of Revision	Summary of Changes	Date
	stimulation; pelvic floor electrical stimulation; transcutaneous electrical joint stimulation.	
Annual Review	• Revised noncoverage policy statements. • Removed the following therapies/devices from the policy statement: transcutaneous electrical modulation pain reprocessing; bioelectric nerve block; combination therapy; electrical sympathetic stimulation therapy; electrotherapeutic point stimulation; functional electrical stimulation; H-WAVE electrical stimulation; high-voltage galvanic stimulation; microcurrent electrical nerve stimulation; threshold/therapeutic electrical stimulation.	12/3/2023