Electrical Stimulation for the Treatment of Pain and Muscle Rehabilitation (for Kentucky Only)

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Instructions for Use

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Related Policies

- Durable Medical Equipment, Orthotics, Medical Supplies, and Repairs/Replacements (for Kentucky Only)
- Implanted Electrical Stimulator for the Spinal Cord (for Kentucky Only)
- Occipital Nerve Injections and Ablation (Including Occipital Neuralgia and Headache) (for Kentucky Only)

Application

This Medical Policy only applies to the state of Kentucky.

Coverage Rationale

Transcutaneous electrical nerve stimulator (TENS) is proven and medically necessary in certain circumstances. For medical necessity clinical coverage criteria, refer to the InterQual® CP: Durable Medical Equipment, Transcutaneous Electrical Nerve Stimulation (TENS).

Click here to view the InterQual® criteria.

Functional electrical stimulation (FES) is proven and medically necessary as a component of a comprehensive ambulation rehabilitation program in individuals with lower limb paralysis due to spinal cord injury (SCI) when all the following criteria are met:

- Demonstration of intact lower motor units (L1 and below) (both muscle and peripheral nerves)
- Muscle and joint stability for weight bearing at upper and lower extremities that can demonstrate balance and control to maintain an upright support posture independently
- Demonstration of brisk muscle contraction
- Demonstration of sensory perception sufficient for muscle contraction
- Demonstration of a high level of motivation, commitment, and cognitive ability for device use
- Ability to transfer independently
- Demonstration of independent standing tolerance for at least 3 minutes
- Demonstration of hand and finger function to manipulate controls
- Post-recovery from SCI and restorative surgery of at least 6 months
- Absence of hip and knee degenerative disease
- Absence of history of long bone fracture secondary to osteoporosis

FES is unproven and not medically necessary due to insufficient evidence of efficacy for treating any other indication not listed above.

Neuromuscular electrical stimulation (NMES) is proven and medically necessary for treating any of the following indications:

- Disuse muscle atrophy if:
  - The nerve supply to the muscle is intact; and
  - The disuse muscle atrophy is not of neurological origin but results from other conditions, such as casting, splinting, or contractures

  or
- When used as part of a comprehensive lower limb rehabilitation program following total knee arthroplasty; or
- To improve upper extremity function in persons with partial paralysis following stroke when used as part of a comprehensive rehabilitation program

NMES is unproven and not medically necessary due to insufficient evidence of efficacy for treating any condition not meeting the criteria above.

The following are unproven and not medically necessary due to insufficient evidence of efficacy:

- Interferential therapy (IFT) for treating musculoskeletal disorders/injuries, or to facilitate healing of nonsurgical soft tissue injuries or bone fractures
- Microcurrent electrical nerve stimulation (MENS)
- Percutaneous electrical nerve stimulation (PENS) or percutaneous neuromodulation therapy (PNT)
- Percutaneous electrical nerve field stimulation (PENFS)
- Percutaneous peripheral nerve stimulation (PNS)*
- Peripheral subcutaneous field stimulation (PSFS) or peripheral nerve field stimulation (PNFS)
- Pulsed electromagnetic field stimulation (PEMF) [also known as pulsed electrical stimulation (PES)]
- Restorative neurostimulation
- Scrambler therapy
- Translingual stimulation for gait rehabilitation

*For information regarding percutaneous peripheral nerve stimulation for occipital neuralgia and headache, refer to the Medical Policy titled Occipital Nerve Injections and Ablation (Including Occipital Neuralgia and Headache) (for Kentucky Only).

Note: For information regarding dorsal root ganglion (DRG) stimulation, refer to the Medical Policy titled Implanted Electrical Stimulator for Spinal Cord (for Kentucky Only).

Medical Records Documentation Used for Reviews

Benefit coverage for health services is determined by the federal, state, or contractual requirements, and applicable laws that may require coverage for a specific service. Medical records documentation may be required to assess whether the member meets the clinical criteria for coverage but does not guarantee coverage of the services requested.

The patient's medical record must contain documentation that fully supports the medical necessity for the requested services. This documentation includes, but is not limited to, relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures. Documentation supporting the medical necessity should be legible, maintained in the patient's medical record, and must be made available upon request.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
0278T	Transcutaneous electrical modulation pain reprocessing (e.g., scrambler therapy), each treatment session (includes placement of electrodes)
0783T	Transcutaneous auricular neurostimulation, set-up, calibration, and patient education on use of equipment

CPT Code	Description
63650	Percutaneous implantation of neurostimulator electrode array, epidural
63655	Laminectomy for implantation of neurostimulator electrodes, plate/paddle, epidural
63663	Revision including replacement, when performed, of spinal neurostimulator electrode percutaneous array(s), including fluoroscopy, when performed
63664	Revision including replacement, when performed, of spinal neurostimulator electrode plate/paddle(s) placed via laminotomy or laminectomy, including fluoroscopy, when performed
63685	Insertion or replacement of spinal neurostimulator pulse generator or receiver, requiring pocket creation and connection between electrode array and pulse generator or receiver
64555	Percutaneous implantation of neurostimulator electrode array; peripheral nerve (excludes sacral nerve)
64567	Percutaneous electrical nerve field stimulation, cranial nerves, without implantation
64596	Insertion or replacement of percutaneous electrode array, peripheral nerve, with integrated neurostimulator, including imaging guidance, when performed; initial electrode array
64597	Insertion or replacement of percutaneous electrode array, peripheral nerve, with integrated neurostimulator, including imaging guidance, when performed; each additional electrode array (List separately in addition to code for primary procedure)
64598	Revision or removal of neurostimulator electrode array, peripheral nerve, with integrated neurostimulator
64999	Unlisted procedure, nervous system

*__Note__: The following are the only FES devices verified by the Centers for Medicare & Medicaid Services (CMS) Pricing, Data Analysis, and Coding (PDAC) to be reported with HCPCS code E0770:

- Deluxe Digital Electronic Muscle Stimulator (Drive Medical)
- NESS L300 and H200 devices (Bioness)
- Odstock ODFS Pace FES System (Odstock Medical/Boston Brace)
- WalkAide (Innovative Neurotronics)

HCPCS Code	Description
A4438	Adhesive clip applied to the skin to secure external electrical nerve stimulator controller, each
A4543	Supplies for transcutaneous electrical nerve stimulator, for nerves in the auricular region, per month
A4544	Electrode for external lower extremity nerve stimulator for restless legs syndrome
A4556	Electrodes (e.g., apnea monitor), per pair
A4557	Lead wires (e.g., apnea monitor), per pair
A4593	Neuromodulation stimulator system, adjunct to rehabilitation therapy regime, controller
A4594	Neuromodulation stimulator system, adjunct to rehabilitation therapy regime, mouthpiece, each
A4595	Electrical stimulator supplies, 2 lead, per month, (e.g., TENS, NMES)
E0720	Transcutaneous electrical nerve stimulation (TENS) device, two-lead, localized stimulation
E0721	Transcutaneous electrical nerve stimulator for nerves in the auricular region
E0730	Transcutaneous electrical nerve stimulation (TENS) device, four or more leads, for multiple nerve stimulation
E0731	Form-fitting conductive garment for delivery of TENS or NMES (with conductive fibers separated from the patient's skin by layers of fabric)
E0743	External lower extremity nerve stimulator for restless legs syndrome, each
E0744	Neuromuscular stimulator for scoliosis
E0745	Neuromuscular stimulator, electronic shock unit
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

HCPCS Code	Description
E0770*	Functional electrical stimulator, transcutaneous stimulation of nerve and/or muscle groups, any type, complete system, not otherwise specified
E1399	Durable medical equipment, miscellaneous
L8678	Electrical stimulator supplies (external) for use with implantable neurostimulator, per month
L8679	Implantable neurostimulator, pulse generator, any type
L8680	Implantable neurostimulator electrode, each
L8682	Implantable neurostimulator radiofrequency receiver
L8685	Implantable neurostimulator pulse generator, single array, rechargeable, includes extension
L8686	Implantable neurostimulator pulse generator, single array, nonrechargeable, includes extension
L8687	Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension
L8688	Implantable neurostimulator pulse generator, dual array, nonrechargeable, includes extension
S8130	Interferential current stimulator, 2 channel
S8131	Interferential current stimulator, 4 channel

Description of Services

Electrical stimulators provide direct, alternating, pulsating and/or pulsed waveform forms of energy. The devices are used to exercise muscles, demonstrate a muscular response to stimulation of a nerve, relieve pain, relieve incontinence, and provide test measurements. Electrical stimulators may have controls for setting the pulse length, pulse repetition frequency, pulse amplitude, and triggering modes. Electrodes for such devices may be indwelling, implanted transcutaneous, or surface.

Functional Electrical Stimulation

Functional electrical stimulation (FES) is the direct application of electric current to intact nerve fibers in a coordinated fashion to cause involuntary but purposeful contraction. FES bypasses the central nervous system and targets motor neurons innervating either skeletal muscle or other organ systems. Electrodes may be on the surface of the skin or may be surgically implanted along with a stimulator. FES is categorized as therapeutic and functional. Therapeutic FES typically enables resistive exercise, with the goal of preventing muscular atrophy and promoting cardiovascular conditioning. Functional FES enables or enhances standing, ambulation, grasping, pinching, reaching, respiration, bowel or bladder voiding, or ejaculation. The two goals of FES are mutually supportive (Hayes, 2017).

Interferential Therapy

Interferential therapy (IFT) 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 that are placed on the skin over the targeted area producing a low-frequency current. IFT delivers a crisscross current resulting in deeper muscle penetration. Electric cell-signaling treatment is a form of IFT that uses ultra-high digital frequency energy. NEO GeneSys 2k is an electric cell-signaling treatment device (Hayes, 2023;, updated 2025). 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 (Hayes, 2008).

Microcurrent Electrical Nerve Stimulation Therapy

Microcurrent electrical nerve stimulation (MENS) therapy is intended for pain relief and to facilitate wound healing, delivering current in the microampere range. One microampere (μA) equals 1/1,000th of a milliampere (mA). By comparison, transcutaneous electrical nerve stimulation (TENS) therapy delivers currents in the milliampere range causing muscle contraction, pulsing, and tingling sensations. The microcurrent stimulus is subsensorial, so users cannot detect it. Although microcurrent devices are approved in the category of TENS for regulatory convenience, in practical use they are in no way similar and cannot be compared with TENS in their effect (Curtis, et al. 2010; Zuim, et al. 2006). MENS is also referred to as frequency-specific microcurrent therapy, microelectrical therapy, microcurrent therapy, or microelectrical neurostimulation. Examples of MENS devices currently in use include, but are not limited to, Algonix®, Alpha-Stim®100, Electro-Myopulse 75L, electro-Lyoscope 85P, KFH Energy, MENS 2000-D, MICROCURRENT, Myopulse 75C, and Micro Plus™.

Neuromuscular Electrical Stimulation

Neuromuscular electrical stimulation involves the use of transcutaneous application of electrical currents to cause muscle contractions. The goals of neuromuscular electrical stimulation are to promote reinnervation, to prevent or retard disuse atrophy, relax muscle spasms, and promote voluntary control of muscles in individuals who have lost muscle function due to surgery, neurological injury, or a disabling condition (Hayes, 2008).

Percutaneous Electrical Nerve Stimulation

Percutaneous electrical nerve stimulation (PENS), also known as percutaneous neuromodulation therapy, is a conservative, minimally invasive treatment for pain in which acupuncture-like needles connected through a cable to an external power source are inserted into the skin. Electroacupuncture is one of the many forms of PENS therapy (Rodriguez Lagos et al., 2023). PENS needle placement differs from TENS in that it is percutaneous instead of cutaneous and differs from spinal cord stimulation in that electrodes are not permanently implanted. The mechanism of action of PENS is theorized to modulate the hypersensitivity of nerves from which the persistent pain arises, potentially involving endogenous opioid-like substances.

Percutaneous Electrical Nerve Field Stimulation

Percutaneous electrical nerve field stimulation targets central pain pathways via the auricular branch of the vagus nerve using alternating frequencies of low-voltage stimulation. While the exact mechanism responsible for the analgesic effects remains unknown, percutaneous electrical nerve field stimulation has been proposed as a method of pain relief in disorders such as irritable bowel syndrome (ECRI 2024; revised 2025).

Percutaneous Peripheral Nerve Stimulation

Peripheral nerve stimulation (PNS) is a type of neuromodulation therapy in which an electrode(s) is implanted or placed near a peripheral nerve (i.e., nerve located outside the brain and spinal cord) that subserves the painful dermatome. The electrode(s) delivers electrical impulses to the affected nerve to disrupt the transmission of pain signals thereby reducing the level of pain (International Neuromodulation Society, 2019). Implanted PNS devices include systems such as the StimRouter Neuromodulation System, SPRINT PNS System, and Freedom Peripheral Nerve Stimulator (previously known as StimQ).

Peripheral Nerve Field Stimulation

Peripheral nerve field stimulation, also referred to as peripheral subcutaneous field stimulation, is a technique used when the field to be stimulated is not well defined or does not fit exactly within the area served by any one or two peripheral nerves. Different from spinal cord stimulation or PNS, the peripheral nerve field stimulation electrode arrays are implanted within the subcutaneous tissue of the painful area, (Abejon and Krames, 2009).

Pulsed Electromagnetic Field Stimulation

Pulsed electromagnetic field stimulation, also referred to as pulsed electrical stimulation, is hypothesized to facilitate bone formation and cartilage repair and to alter inflammatory cell function. Some chondrocyte and osteoblast functions are mediated by electrical fields induced in the extracellular matrix by mechanical stresses. Electrostatic and electrodynamic fields may also alter cyclic adenosine monophosphate or DNA synthesis in cartilage and bone cells (Farr et al., 2006).

Restorative Neurostimulation

Restorative neurostimulation is a minimally invasive method of innervating the multifidus muscle of the lower back to override the underlying cycle of lumbar multifidus muscle degeneration. It is intended to be used as a rehabilitative therapy for individuals with impaired neuromuscular control associated with mechanical chronic low back pain. After the neurostimulation device is implanted, isolated electrical impulses are stimulated by way of self-anchoring leads placed next to the medial branch of the dorsal ramus (Hayes, 2022). The ReActiv8 Implantable Neurostimulation System is an example of a restorative neurostimulation system.

Scrambler Therapy

Scrambler therapy [also referred to as Calmare® Pain Therapy (Calmare Therapeutics Inc.) or transcutaneous electronic modulation pain reprocessing therapy] is a noninvasive, transdermal treatment that is designed for the symptomatic relief of chronic pain. Treatment is performed by applying electrodes corresponding to the dermatome on the skin, just above and below the area of pain. The device provides electrical signals via the electrodes presenting nonpain information to the painful area using continuously changing, variable, nonlinear waveforms (Hayes, 2021).

Transcutaneous Electrical Nerve Stimulation

TENS is a therapeutic modality device that uses electric current delivered through electrodes placed on the surface of the skin to decrease the perception of pain by activating peripheral nerves inhibiting the transmission of afferent pain nerve impulses and/or stimulating the release of endorphins. A TENS unit must be distinguished from other electrical stimulators (e.g., neuromuscular stimulators), which are used to directly stimulate muscles and/or motor nerves (Teoli and Dua, 2025).

Translingual Stimulation

Translingual stimulation is a noninvasive method used to elicit neural changes by stimulating the trigeminal and facial cranial nerves. Input from neurostimulation and physical therapy are thought to enhance neuroplasticity and enable the brain to restructure and relearn motor skills (ECRI, 2021).

Clinical Evidence

Functional Electrical Stimulation

Functional electrical stimulation (FES) has demonstrated promising benefits across various neurological and musculoskeletal (MSK) conditions, particularly in individuals with spinal cord injury (SCI), cerebral palsy (CP), stroke, multiple sclerosis (MS), and chronic heart failure (CHF). Evidence suggests that FES can improve muscle strength, aerobic capacity, respiratory function, gait parameters, and quality of life (QOL), especially when used in combination with exercise programs. However, its effectiveness varies depending on the condition, injury severity, and timing of the intervention. Limitations include small sample sizes, inconsistent protocols, short follow-up periods, and mixed results in long-term functional outcomes. Some studies found negligible effects on very weak muscles or no significant improvements compared with conventional therapies. Additionally, the quality of evidence is often rated low due to methodological concerns, such as lack of blinding, heterogeneity in study designs, and limited generalizability. Further high-quality, large-scale randomized controlled trials (RCTs) are needed to establish optimal treatment parameters and confirm the long-term efficacy of FES across diverse patient populations of individuals.

Spinal Cord Injury

Xiangli et al. (2025) conducted a systematic review and meta-analysis to evaluate the efficacy of FES used alone or as an adjunct to exercise (rowing/cycling) as a way to improve respiratory function and aerobic capacity in individuals with SCI. Using 23 RCTs and self-controlled studies (n = 314), the authors assessed outcomes of forced vital capacity (FVC), peak expiratory flow, maximal expiratory/inspiratory pressure, and peak oxygen uptake (VO_2peak). The authors concluded that when used as a stand-alone intervention, FES significantly improved expiratory function, with increases in peak expiratory flow [standardized mean difference (SMD), 0.42; p = 0.007], maximal expiratory pressure (SMD, 0.93; p = 0.008), and FVC (SMD, 0.37; p = 0.03). However, no significant improvement was found for maximal inspiratory pressure (p = 0.38). When FES was combined with exercise, it significantly enhanced aerobic capacity. This was illustrated by improvements in VO_2peak for both FES-assisted rowing (SMD, 0.35; p = 0.03) and FES-assisted cycling (SMD, 0.24; p = 0.0003) compared with exercise alone. No significant effects on peak ventilation were observed. A limitation of the study is the number of studies addressing a few outcomes, particularly FES combined with cycling and the maximal inspiratory pressure analysis, thus limiting the statistical value of these specific findings. Additional research, with larger sample sizes, is needed since the study did not address the effectiveness and clinical utility of the technology compared with those of standards of care.

Chen et al. (2025a) conducted an 8-week, assessor-blinded RCT with concealed allocation, an intention-to-treat analysis, and blinded outcome assessors. Overall, 60 participants (30 randomized to each group) with recent SCI were recruited from three SCI units in Australia and Bangladesh. Participant inclusion criteria included a recent complete or incomplete SCI (less than 6 months); age 18 years or older; absence of other neurological injury or condition; weakness, with grade 1 or 2 strength on the 6-point manual muscle test in a major muscle group, affecting one side of the body (i.e., knee, wrist, elbow flexors or extensors, ankle plantar flexors or dorsiflexors); and the ability to continue physiotherapy on an outpatient basis if discharged from inpatient. Participant exclusion criteria included the inability to evoke a strong, electrically stimulated contraction in the target group muscle; inability to cooperate with treatment (cognitive impairment or medical condition); inability to speak the local language well enough to complete an informed consent; or any condition preventing training or testing of the targeted muscle group. A major muscle group of the upper or lower limb with grade 1 or grade 2 strength on a standard 6-point manual muscle test was selected. Participants were randomized to either a control group or an experimental (treatment) group. Participants in the experimental group received strength training combined with electrical stimulation and usual care for a targeted muscle group for 8 weeks, once a day, three times per week (24 total training sessions). Participants in the control group received usual care for the targeted muscle group, with no more than two strength training sessions/week (two sets of 10 contractions). Participant assessments were taken by a blinded

assessor at baseline and again at 8 weeks. Voluntary muscle strength on a modified 12-point manual muscle test was the primary outcome measurement. Participants' perception of strength, ability, and function to perform self-selected goals were the three secondary outcome measurements. Results of the voluntary strength mean at 8 weeks between the groups was 0.7 out of 13 points, for which clinical worthwhile treatment was deemed as 1 point. The secondary outcomes did not determine a clinically important effect. The study concluded that 8 weeks of strength training combined with electrical stimulation has a negligible effect on the strength of very weak muscles. Limitations of the study include strength training doses that may have failed to demonstrate a clear treatment effect, frequency of weekly treatment sessions, and sensitivity of the 13-point manual muscle test.

Manaf et al. (2024) completed a nonrandomized, pre-post, government-funded university hospital study to determine the feasibility and preliminary effects of high-intensity interval training (HIIT) using FES cycling exercise (FES-LCE) on changes in thigh muscle volume and muscle strength in individuals with incomplete SCI. There were eight individuals with incomplete SCI; six were women and two were men, with an average age of 50 years, stable SCI paraplegia, and an average of 6.75 years since injury. Individuals with uncontrolled spasticity or pain and/or medical contraindications (e.g., heart problems, severe autonomic dysreflexia, very low or high blood pressure, weight-bearing severely infected skin pressure sores) were excluded. The intervention was to participate in the HIIT FES-LCE (85%-90% peak watts; 4 × 4-minute intervals) three times a week (over 6 weeks). The primary outcomes of adherence, individuals' acceptability, and adverse events were measured. The secondary outcomes were muscle strength (peak torque) and leg volume changes. Findings revealed high levels of adherence; satisfaction; positive feedback; no serious adverse events; and notable improvements in the hamstring muscle (18.2%-23.3%), leg volume (1.7%-18.2%), and isometric peak torque of the quadriceps (range, 13.9%-25.6%). Limitations of the study include the presence of individuals with lumbar and T12 injuries, which may have resulted in denervation in their lower limb muscles. Denervated muscles do not respond to electrical stimulation, per the inclusion criteria. Observed responses to electrical stimulation of the lower limb muscles could originate from nerves or unaffected muscles, which can be the case in incomplete injuries. The study assessed HIIT's effect in conjunction with electrical stimulation on muscles that have volitional control instead of those that are solely denervated. In addition, the HIIT FES-LCE did not compare this intervention with other exercise interventions, deeming comparison between two exercise interventions unclear for adherence and effectiveness. Previous physical activity lifestyles of the individuals were not captured, making it difficult to determine the extent of interventional improvement in physical fitness. Finally, a control group was not included, leading to difficulties establishing cause-and-effect relationships between HIIT FES-LCE and observed improvements. The authors concluded that future research is needed to explore the long-term effects and determine optimal protocols for this intervention.

Hayes published an Evidence Analysis Research Brief addressing home-based FES for rehabilitation following SCI based on a review of six abstracts, including one RCT that was reported in three of the abstracts and one single-arm study that was reported in the other three abstracts. The brief stated that there is not enough published, peer-reviewed literature to evaluate the evidence related to home-based FES for rehabilitation following SCI and that they did not find any clinical position statements or guidelines that addressed home-based FES for this indication; it was concluded that there is no/unclear support for its use in individuals undergoing rehabilitation following SCI (2024).

Máté et al. (2023) conducted a systematic review and meta-analysis to examine the evidence for the potential of hybrid FES cycling to improve cardiorespiratory fitness in people with mobility disability related to an SCI. The systematic review included 13 published studies (10 uncontrolled acute exercise session studies and three uncontrolled training studies), with six of the studies included in the meta-analyses. In 12 studies, the individuals had SCI, with the time since injury ranging from 2 to 13.6 years. Some studies only included individuals with a complete SCI, while other studies had a mixture of individuals with complete and incomplete injuries. Most studies were considered to have fair methodological quality. There was a total of 119 individuals included in the 13 studies (102 men and 17 women). The authors reported that (1) hybrid FES cycling was moderately more effective than arm crank ergometry in increasing peak volume of oxygen consumption (VO_2peak) from rest in the 10 studies (125 individuals) that reported VO_2peak and that (2) there was a large effect on the increase of VO_2peak from rest for hybrid FES cycling compared with FES cycling in the five studies (36 individuals) that reported on hybrid FES cycling compared with FES cycling. The authors also reported that longitudinal training with hybrid FES cycling showed a significant improvement in VO_2peak from prior to the intervention to post intervention in the three studies (22 individuals) that reported on aerobic fitness after hybrid FES cycling. Limitations of the study include the small sample sizes of the included studies; individuals included in the subanalyses; heterogeneity of the study designs and inclusion criteria among the studies; and publication bias and a lack of individual participant data, as three of the studies appeared to have the same participant data for acute bouts of hybrid FES cycling and arm crank ergometry (but were only included once in the meta-analysis). The authors concluded that hybrid FES cycling can improve cardiorespiratory fitness in people with SCI and that there is emerging evidence that hybrid FES cycling might increase aerobic fitness in people with mobility disability related to central nervous system (CNS) disorders.

In a systematic review by Bekhet et al. (2022), the effect of using neuromuscular electrical stimulation (NMES) or FES or both on training on body composition parameters in individuals with SCI was evaluated. The review included 46 studies, with a total sample size of 414 individuals, that evaluated NMES loading exercise and FES cycling exercise used in training. The authors reported that there was an average increase in the muscle cross-sectional area of 26% (n = 33) and that 15 studies reported changes (both increase and decrease) in lean mass or fat-free mass, with a range from -4% to 35%. Limitations noted include the broad inclusion criteria for other interventions that made it difficult to determine the benefits that were due specifically to the electrical stimulation; broad variability of NMES/FES parameters used across the studies; small sample sizes; variability of the levels of SCI included; wide range of study designs (case reports, crossover, prospective, and retrospective), with a limited number of RCTs; and variability in durations and interventions. The authors concluded that the systematic review showed that the use of NMES/FES resulted in robust muscle hypertrophy and an increase in lean mass and fat-free mass, with inconclusive evidence about reduction in intramuscular mass. They recommended multicenter RCTs to consolidate previous research findings on body composition and to reach consensus about the most effective stimulation parameters needed to improve body composition in persons with SCI. The studies reviewed included the Griffin (2009) study, previously summarized in this policy.

Hayes published a Health Technology Assessment on FES for rehabilitation following complete and incomplete SCI in adults, adolescents, and children. The literature search was designed to identify studies that assessed the effectiveness and safety of FES in individuals with SCI. Fifteen studies, reported in 21 articles, were included, of which nine were RCTs and six were pretest/posttest studies in nine to 70 individuals with an SCI. FES was used for therapeutic or functional applications and compared with standard care [e.g., physical therapy (PT), occupational therapy, exercise without FES, electrical stimulation without exercise]. Outcome measurements were walking ability, hand function, muscle strength, muscle atrophy, bone loss, QOL, health complications, and cardiovascular and respiratory outcomes through a follow-up time frame of 0 to 40 months.

In adults with complete motor SCI, six of seven studies found improved muscle strength, enabled independent ambulation, improved grasp strength, and increased cough capacity; the seventh study found that FES did not weaken bone loss in individuals with acute SCI. Two studies were rated as fair quality, and five were rated as very poor quality, yielding a Hayes rating of C. However, a body of evidence that is large in size and low in quality suggests that FES appears to improve health outcomes in adults with complete motor SCI.

Adults with incomplete motor SCI from three fair-quality RCTs, limited by a small sample size and lack of long-term follow-up, showed that FES improved muscle strength in both studies. However, in two studies, there was no significant improvement in muscle endurance, walking ability, bone mineral density, and functional/QOL outcomes, leading to a Hayes rating of C.

Children and adolescents with complete motor SCI had mixed FES effectiveness. One study found that children with implanted electrodes to enable standing and walking could perform some activities of daily living (ADL) faster and with greater independence than without FES; while the second study found greater muscle strength, other outcome measures [including muscle volume, bone mineral density, and cardiovascular and respiratory health (except for oxygen uptake)] were not improved. Fair and very low-quality evidence in the two studies, due to inconsistent results, yielded a Hayes rating of D2.

FES use in children and adolescents with incomplete motor SCI concluded insufficient evidence for this population, as no studies met the inclusion criteria, yielding a Hayes rating of D2 (Hayes 2017; updated 2022).

Sadowsky et al. (2013) conducted a single-center cohort study to examine the effect of long-term lower extremity FES cycling on the physical integrity and functional recovery in people with chronic SCI. Overall, 25 participants with chronic SCI (at least 16 months following injury) who received FES during cycling were matched by age, gender, injury level, severity, and duration of injury to 20 people with SCI who received range of motion (ROM) and stretching. The main outcome measure was change in neurological function, which comprised motor, sensory, and combined motor-sensory scores, assessed by the American Spinal Injury Association Impairment scale. Response was defined as a ≥ 1-point improvement. FES was associated with an 80% combined motor-sensory score responder rate compared with 40% in controls. An average 9.6 combined motor-sensory score point loss among controls was offset by an average 20-point gain among FES participants. Quadriceps muscle mass was, on average, 36% higher and intra-/intermuscular fat 44% lower in the FES group. Hamstring and quadriceps muscle strength was 30% and 35% greater, respectively, in the FES group. QOL and daily function measures were significantly higher in the FES group. The authors concluded that receiving FES during cycling in chronic SCI may provide substantial physical integrity benefits, including enhanced neurological and functional performance, increased muscle size and force-generation potential, reduced spasticity, and improved QOL.

Additional evidence indicates that people with paraplegia can benefit from FES that exercises muscles without providing locomotion. In one study, electrically stimulated use of an exercise cycle by people with paraplegia restored muscle mass (Baldi et al., 1998). In another study, bone mineral density improved in some bones of individuals with SCI after use of the FES bicycle (Chen et al., 2005). While most studies involved individuals with many years of muscular atrophy, Baldi et al. included individuals with less than 4 months of atrophy. Moreover, electrically stimulated isometric exercise stimulated bone remineralization that was not observed with electrically stimulated walking (Needham-Shropshire, 1997). Even if the ambulation provided by devices such as the Parastep significantly improves, it will still only be usable by a subset of individuals with paraplegia such as those with T4 to T11 SCIs (Klose, 1997). Stationary electrically stimulated exercise can be performed by a much larger group of individuals, including people with tetraplegia. To summarize, electrically stimulated ambulation cannot be considered safer or more beneficial than electrically stimulated stationary exercise, unless the benefits of ambulation are shown to be superior in large-scale trials in which people with paraplegia are randomized to these two therapies. Further studies also need to be performed to confirm the benefits of electrically stimulated stationary exercise since the controlled trials conducted to date have used very small study populations and have assessed a limited set of outcome measures.

Cerebral Palsy

Elsharkawy et al. (2025) conducted an RCT in 30 participants with diplegic CP to evaluate the effect of the Universal Exercise Unit (UEU) vs FES on genu recurvatum in these children. Genu recurvatum causes the knee to hyperextend during the stance phase, often due to contracture or stiffness in the calf muscles. The children, between the ages of 4 and 8 years with diplegic CP and genu recurvatum, were randomly assigned to two groups. Both groups underwent UEU therapy to strengthen the hamstring and tibialis anterior muscles, while study group II received FES. The authors reported significant improvement in muscle strength and knee joint alignment following UEU and FES. However, UEU demonstrated superior outcomes compared with FES, potentially attributed to its stronger impact on the hamstring and tibialis anterior muscles. Additionally, FES indicated an enhanced active ankle dorsiflexion angle and strength as well as improvement in selective motor control and balance. Limitations of the study include that it only looked at one type of CP, and the participant age range was only between 4 and 8 years. Future research is necessary to further assess the clinical utility of FES technology in the CP population and evaluate the long-term clinical treatment protocols for this population.

A retrospective review conducted by Walters et al. (2025) evaluated the clinical data for patients who were diagnosed with CP and associated foot drop and treated with FES to help with their gait disorder. Objective and patient-reported outcome measures were used. The primary outcomes of walking speed and walking satisfaction were analyzed at 3 months after starting FES treatment. In a subset of 11 patients who had used FES for 4 years or longer, secondary analyses were completed to explore benefit over time. The authors indicated that a large number of missing data points could be related to the study being conducted during the COVID-19 pandemic and due to in-person visits transitioning to video appointments. The authors concluded that patient-reported walking satisfaction [numeric rating scale (NRS)] improved when comparing no-FES vs FES at 3 months and at 4 years. A limitation of this study was its timing, which took place during the COVID-19 pandemic and may have had a strong influence on the long-term follow-up rate, as many older adults with chronic health conditions limited activities and chose not to visit hospitals during this time. Further long-term clinical trials demonstrating the clinical efficacy of FES are necessary and needed to address the clinical impact of the technology on patient-centered outcomes.

Moll et al. (2023) conducted a randomized crossover trial that was conducted in 25 children with unilateral spastic CP to study if FES of the peroneal nerve can improve body functions, activities, and participation and if it could be an effective alternative treatment. Participants were aged 4 to 18 years (median age, 9 years 8 months; 60% male) who were classified by the Gross Motor Function Classification System as level I or II, with unilateral foot drop of central origin, and were currently undergoing treatment with an ankle-foot orthosis (AFO) or adapted shoes. The study treatment sequence was randomized, with each participant receiving 12 weeks of FES treatment (during which time each participant wore the WalkAide® device) and 12 weeks of conventional treatment (AFO or adapted shoes), separated by a 6-week washout period. Outcome measures included the Goal Attainment Scale, the Cerebral Palsy QOL questionnaire, and a three-dimensional gait analysis. The authors reported that 18 participants completed the trial and that the proportion of Goal Attainment Scale goals that were achieved was not significantly higher in the FES vs the conventional treatment phase. According to the authors, there were no changes found in the standard physical examination or regarding satisfaction with orthoses and participants' ability to dress themselves. The authors concluded that FES was not significantly worse than AFO; however, participant selection is critical, and a testing period and thorough follow-up are needed. Limitations of the study include the single-center design, high dropout rate, short follow-up period, and use of multiple physiotherapists performing the physical examinations.

In a prospective open-label study in children with hemiplegic CP–related foot drop who used dorsiflexion FES, Segal et al. (2023) assessed the effectiveness of the device over a 5-month period of use. The study included 15 participants who were at least 6 years of age who attended all appointments and who had good adherence. Each participant was assessed

by motor function tests and the measurement of ankle biomechanical parameters at baseline, after 1 month, and after 5 months. All testing was conducted by the same physiotherapist in the same order for all participants and at each visit. At baseline, tests were conducted while the child was wearing the dorsiflexion FES device (WalkAide) turned off, and at 1 and 5 months, each test was carried out first with the device switched off and then with it switched on. There were 11 participants who dropped out between enrollment and the 5-month mark: eight (72%) withdrew due to a lack of a positive effect of FES on gait (as perceived by the participant and family), and three (28%) withdrew for unrelated reasons. The authors reported that improvement was noted at the 1-month appointment, although the difference between month 1 and month 5 was not significant. Falling frequency questionnaires filled out by the parents revealed a trend toward improvement in stability, although the results were not statistically significant. Limitations of the study include the single-center design, small sample size, low retention rate, and lack of a control group.

Zhu et al. (2022) conducted a meta-analysis to assess the effectiveness of FES devices in gait improvement in children with CP. Their analysis included nine studies, with a total of 282 children with CP; 140 children were in the FES treatment group, and 140 children were in the control group. The authors reported that the data showed that the walking speed and step length were increased after FES compared with those in the control group. The authors noted that the randomization scheme and result report used in most studies were low risk, although most studies had limitations in the blinding method of individuals, as most were single-blinded studies. The authors concluded that FES could increase walking speed and walking step length, which could improve the walking ability of children with CP. The authors recommended more research to support their findings.

In a parallel, three-group, randomized, unblinded, single-center, cross-sectional study by Sansare et al. (2021), the effect of two training approaches, cycling with and without FES assistance, to that of a no-intervention control group on the cardiorespiratory fitness of children with CP was examined. The study included 39 participants between the ages of 10 and 18 years. They were randomized to one of the three study groups: FES (received FES-assisted cycle training; n = 15), VOL (underwent volitional cycling only; n = 11), or CON (received no treatment intervention; n = 13), with participant characteristics among the groups showing no significant differences in age, height, weight, and body mass index (BMI) among the three groups. Both treatment groups underwent a setup/practice phase prior to baseline testing and then were asked to cycle continuously for 30 minutes, three times a week for 8 weeks, at the target cycling power corresponding to 50% to 80% of their Karvonen-predicted target heart rate during the baseline incremental test. All participants were assessed for cardiorespiratory fitness at three time points: prior to training (PRE), at the end of 8 weeks of training (POST), and during a washout period of 8 weeks (WO). An additional assessment was performed midway through training to account for increased cardiorespiratory capacity and motor learning effects, and new heart rate and power targets were set. The average adherence to the training protocol in both the cycling groups was 91.9%, with no significant difference between the FES and VOL groups. The authors concluded that the study showed that while FES-assisted cycling can enable children with CP to attain higher cycling cadences than cycling alone or without any intervention, it did not show any significant improvements in peak VO_2 (liters of oxygen per minute per kg body weight) and peak net heart rate (peak heart rate in beats per minute). They reported that the FES group made significant gains between PRE to POST and that all three study groups showed minimal changes between POST and WO, which the authors stated is indicative of the ability to maintain the gains made during training.

Moll et al. (2017) conducted a systematic review to assess the effect of FES of ankle dorsiflexors in children and adolescents with spastic CP during walking. A search, using predetermined terms, was conducted using PubMed/MEDLINE, Embase, the Physiotherapy Evidence Database (PEDro), Web of Science, CINAHL, and the Cochrane Library. Outcomes were reported according to the International Classification of Functioning, Disability, and Health (ICF). The ICF domains are classified by body and individual and societal perspectives by means of two lists: a list of structure and function and a list of domains of participation and activity. A total of 780 articles were identified, and after review, 14 articles were included, including two small RCTs. In total, 127 individuals received FES of the ankle dorsiflexors (14 bilaterally affected and 113 unilaterally affected). The individuals' ages ranged from 5 to 19 years, and the Gross Motor Function Classification System level ranged from I to III. The authors concluded that (1) at the ICF participation and activity level, there is limited evidence for a decrease in self-reported frequency of toe-drag and falls and (2) at the ICF body structure and function level, there is clear evidence (level I to III studies) that FES increased (active) ankle dorsiflexion angle and strength and improved selective motor control, balance, and gait kinematics but decreased walking speed. Adverse events included skin irritation and acceptance issues. The authors further stated that it cannot be concluded that FES (of the ankle dorsiflexors) improves functioning at the activity and participation level; however, current evidence supports the potential role of FES as an alternative to classic orthotic treatment. The authors recommended that future studies should focus on the domain of activity and participation.

Cerebrovascular Accident

Liu et al. (2025) conducted a retrospective study on clinical data from 150 patients, with an average age of 51 years, who had a stroke, had lower limb motor dysfunction, and were treated in a single hospital from January 2023 to January 2024,

to determine the efficacy of FES in improving motor control across three groups (50 patients each). Criteria inclusions included a stroke diagnosis based on Cerebrovascular Disease's fourth national conference; cranial computed tomography or magnetic resonance imaging (MRI) confirmation of the initial diagnosis, with between 1- and 12-month disease duration and a stable condition; foot inversion or foot drop on the affected side and willingness to participate in rehabilitation treatment (all patients); lower limb spasticity grade II or below on the Modified Ashworth Scale; stage II or above on the Brunnstrom scale for lower limb motor recovery; and the ability to walk with supervision or independently for at least 10 meters, without any type of assistive device. Exclusion criteria included severe cognitive or communication disorders; severe cardiopulmonary, renal, or hepatic impairment; cardiac pacemakers or psychiatric disorders; foot drop due to peripheral nerve injury; and noncontinuous treatment or missing follow-up data. Patients were divided into three groups: a conventional rehabilitation (control) group (35 male and 15 female patients), a conventional rehabilitation plus calf muscle functional stimulation (CPN-FES) group (34 male and 16 female patients), and a conventional rehabilitation plus tibialis anterior functional stimulation (TA-FES) group (37 male and 13 female patients). Patients in conventional rehabilitation underwent PT, acupuncture, occupational therapy, daily functional training, limb positioning, and position changes therapy. Training was conducted over a period of 8 weeks for 5 days a week and 40 minutes each session. Acupuncture was administered in 30-minute sessions, once daily for 8 weeks, 5 days a week. In the two remaining groups, FES sessions were 15 minutes daily, 5 days a week, over 8 weeks and performed by the same therapist. The collection of data included lower limb motor function, mental status, H-reflex changes, ADL, walking and balance abilities, and F-wave latency and amplitude. The study found that early rehabilitation integrated with FES markedly enhanced the recovery of patients with stroke. At the end of the 8 weeks of observation, there were improvements in lower limb motor function, cognitive status, ADL, walking, and balance. The greatest improvements were noted in the CPN-FES group, followed by the TA-FES group, and the control group demonstrated the least improvement. In addition, reduced muscle spasticity and improved nerve conduction were demonstrated through changes in H-reflex and F-wave measurements. The study concluded that FES in stroke rehabilitation patients appeared to improve functional outcomes and enhance motor control. Limitations of this study include its lack of a multicenter, double-blinded design, randomization, individualized FES parameters, patient adherence assessment, long-term follow-up, exploration of underlying mechanisms of treatment, and potential confounding factors control.

An RCT conducted between September 2022 and February 2023 by Elhamrawy et al. (2024) aimed to determine the effects of FES for intrascapular muscles on trunk performance, balance, and scapular position in older participants who were post hemiparetic stroke. The secondary outcome was to evaluate functional performance of those participants. Inclusion criteria were participants 60 years of age or older (of both sexes); first-time right or left cerebrovascular accident (CVA) in the preceding 6 months, with damage to the cerebral cortex (confirmed by computed tomography, MRI, medical chart, or neurological examination); ability to stand and walk independently; and a Modified Ashworth Scale of less than or equal to 1 plus. Participants with shoulder dysfunction prior to or post stroke (dislocation or subluxation), upper limb splint usage, behavioral abnormalities, orthopedic or neurological problems, epilepsy, or paralysis neglect were excluded from participation. Overall, 51 participants were assessed for eligibility, and 17 were excluded for not meeting exclusion criteria (n = 12), for declining to participate (n = 3), or for other reasons (n = 2). There were 34 participants enrolled and randomized through a computer-based program into two groups (17 participants each): the control (CON) group and the FES group. The CON group underwent 45 minutes of core stabilization exercises (CSEs) only 4 days a week for 12 weeks. Each session consisted of balance and core stability exercises, in which each exercise was repeated 15 to 20 times. The FES group underwent FES to the paretic side of the intrascapular muscle 30 minutes a day, followed by 45 minutes of CSEs 4 days a week for the first 6 weeks, and then 45 minutes of CSEs only 4 days a week for the next 6 weeks. Results for spinal performance, scapular position, balance, and function at baseline were measured using the Trunk Impairment Scale (TIS) and Postural Assessment Scale for Stroke (PASS). A palpation meter was used in measuring the horizontal distance of the scapular position. Timed Up and Go (TUG) and the Berg Balance Scale (BBS) were used in evaluating fall prediction, functional mobility, and reaction rate. The Barthel Index assessed the participants' ability to perform ADL. Effect sizes were statistically measured with IBM SPSS Statistics, using Cohen d (d) for effect sizes by averaging the difference between baseline, 6-week, and 12-week results. There was not a significant difference between participants in their baseline assessments. There was a significant improvement in the CON group, with a large effect size (d between 1.1 and 3.7) at 6 and 12 weeks ($p \leq 0.001$) in the PASS, BBS, TUG, TIS, and Barthel Index. The scapular position was statistically insignificant but clinically significant in reduction at the 6- and 12-week comparison to baseline results ($p = 0.49496$, $d = 0.6$; $p = 0.4113$, $d = 0.8$). Significant improvements, with a large effect size (d between 1.9 and 8.9) at 6 and 12 weeks ($p \leq 0.0001$), were observed in the TUG, Barthel Index, TIS, PASS, and scapular position. Comparisons between the CON and FES groups showed significant differences ($p < 0.05$) at 6 and 12 weeks in the BBS, Barthel Index, and TIS and at 12 weeks only in the TUG and PASS. Scapular position was also in favor of the FES group ($p = 0.054$). A small sample size and lack of a true control group and long-term follow-up are the limitations of this study. The authors concluded that significant improvement was observed in shoulder muscle power, shoulder position, and scapular alignment in using FES for interscapular muscles. CSEs, in combination with FES, have a beneficial effect on improving balance, ADL, postural adjustment, scapular alignment, and trunk performance in older individuals who have had a stroke.

Galvão et al. (2024) conducted a systematic review and meta-analysis to analyze the efficacy and effectiveness of cycling using FES, either combined with exercise programs or alone, to improve strength, balance, trunk control, walking speed, walking distance, and ADL in individuals in early, subacute CVA recovery. The study included five RCTs, with 187 individuals (age range, 56-74 years) who were within 16 and 60 days of poststroke recovery. The authors reported that cycling using FES combined with exercise programs promoted relevant benefits in trunk control and walking distance and that cycling using FES alone compared with exercise programs promoted similar benefits in strength, balance, walking speed, walking distance, and ADL. Limitations of the study include the heterogeneity in the parameters used in the studies and in the FES; systems used; limited number of studies available for inclusion; and lack of standardization in the motor impairment definition of the individuals included in the studies. The authors concluded that their systematic review provided low- to moderate-quality evidence that cycling using FES may be an effective strategy to consider in improving motor function and activity outcomes in individuals in the early, subacute phase of CVA recovery.

Matsumoto et al. (2023) conducted a multicenter, randomized controlled, open-label trial in 203 adult Japanese participants, aged 25 to 85 years, who had experienced an initial stroke within 6 months of the study and had poststroke sequelae, including hemiplegic gait disorder (foot drop). The participants were divided into a treatment arm that received FES (n = 102) and a control group (n = 101); 84 participants in the FES group and 85 participants in the control group completed the study. The data of the primary outcome for 184 participants (92 in each group) were analyzed after excluding 19 participants who did not receive any intervention or whose data were not available. The participants in the FES group underwent a 40-minute training program, 5 days a week for 8 weeks, receiving FES via the WalkAide device, while participants in the control group received a 40-minute training program without FES, 5 days a week for 8 weeks. The authors reported that FES did not significantly improve the distance covered by poststroke participants with foot drop in the barefoot 6-Minute Walk Test (6MWT) and that there were no group differences in walking speed, cadence, or functional ambulation classification grade in the FES group; however, there was a tendency toward improved receptivity to gait. The authors concluded that the use of FES did not show efficacy in the convalescent treatment of Japanese participants with stroke and foot drop.

Sannyasi et al. (2022) conducted a single-center, prospective, crossover study to compare the gait parameters in participants with foot drop following stroke for at least 3 months using an AFO and FES. The study included 20 participants (19 male participants and one female participant) who had hemiplegia following a CVA. The participants were divided into two groups of 10 each (group A and group B) and were observed to see if the order of use for AFO and FES had any effect on the outcome. All participants received 2 hours of gait training every day for 2 weeks, in addition to their regular physical and occupational therapy. The participants in group A received gait training with AFO for the first week, followed by FES using the WalkAide device during the second week, while group B received gait training with FES using the WalkAide in the first week and AFO during the second week. Participant satisfaction and primary and secondary outcome measures were gathered on day 1 and at the end of each week after training with the AFO or FES device. The authors reported that a statistically significant improvement in gait speed and walking endurance was seen with both AFO and FES compared with baseline and that there was a statistically significant improvement between the groups in favor of FES for gait speed and walking endurance. The authors also reported that there was a statistically significant improvement in time to complete the TUG test (the time it takes to get up from a chair, walk 3 meters, and return to sit on the chair) among users of FES compared with AFO users and that FES exhibited statistically significant improvement in stance-swing ratio and single-limb support on the paretic limb compared with AFO. The order of the trial did not show any effect on outcome measures between groups, except for the 6MWT. Limitations of the study include the single-center design, short duration of the FES intervention, and high predominance of male vs female participants in the study. The authors concluded that the study showed that both AFO and FES had significant improvement in gait parameters compared with barefoot walking and that FES users demonstrated statistically significant improvement in walking speed and endurance compared with AFO users. The authors recommended further trials to evaluate the long-term therapeutic benefits, carryover effects, and cost-effectiveness of FES devices for the management of foot drop.

In their Health Technology Assessment on the effectiveness of rehabilitative FES for foot drop in individuals during the acute or subacute phases of stroke recovery, Hayes (2022a; updated 2025) reviewed 10 studies, including nine RCTs and one crossover RCT. The studies varied in their evaluation of FES relative to no placebo or placebo FES, the use of an AFO, and adjunct use of electromechanical gait training and NMES. The update for 2025 found two newly published RCTs; however, their ratings and conclusions remained unchanged. The Health Technology Assessment stated that there is an overall low-quality body of evidence due to the study limitations (including small sample sizes, attrition, lack of power analysis or blinding, and short-term follow-up), use of different FES devices among the studies, variation in treatment intensity among the studies, limited number of studies for the different comparators, inconsistencies in the evidence of benefit, and insufficient follow-up to assess long-term durability of the benefit of FES. The report concluded that while FES treatment appeared relatively safe, there was particular concern across the studies regarding the lack of consistent evidence that FES improved measures of functional recovery and QOL. They recommended additional RCTs, with better standardization of FES devices and treatment protocols with longer follow-up, to establish whether FES improves

outcomes related to conservative therapies for foot drop due to stroke that has occurred less than 1 year prior to starting treatment with FES.

Hayes (2022b; updated 2025) also published a Health Technology Assessment on the effectiveness of FES for foot drop in the chronic phase of stroke recovery that identified eight RCTs and one crossover RCT, which evaluated FES for the treatment of foot drop in individuals who had experienced a CVA 1 year or more before starting FES. In the most recent update, Hayes has not identified any newly published studies since their 2022 report, so their recommendations remain unchanged. The report stated that the body of evidence for assistive FES with skin-surface electrodes and for rehabilitative FES with skin-surface electrodes was low in quality, while the body of evidence for assistive FES with implanted electrodes was very low in quality. The studies in the Health Technology Assessment were downgraded to fair quality due to limitations in the study designs (small size, dropout rate, incomplete statistical analysis, lack of complication reporting, lack of blinding or blind analysis of data, low intensity or short duration of FES treatment, and/or short follow-up periods). The Health Technology Assessment concluded that FES with skin-surface electrodes did not provide any statistically significant improvements in walking, stroke recovery, or QOL measures compared with AFOs. However, when assistive use of FES with skin-surface electrodes was compared with conservative therapies that included AFOs or with no FES in individuals undergoing PT for gait disorders, the evidence showed limited improvements. The report recommended additional RCTs to demonstrate the benefit of the assistive use of FES relative to AFOs and to the benefit of the rehabilitative use of FES to ascertain the reliability and durability of benefits that may diminish in the long term once FES is discontinued.

A Clinical Evidence Assessment published by ECRI (2022) on the safety and effectiveness of FES for physical rehabilitation in individuals with hand paralysis found that functional neuromuscular stimulation improved hand function when used to supplement rehabilitation in individuals with chronic paresis due to stroke but not in individuals with acute or subacute paresis. The Clinical Evidence Assessment included a systematic review with meta-analysis of 26 RCTs (including the Jonsdottir et al., 2017, study below) and review of an additional seven RCTs that were of a high risk of bias from small sample sizes and a single-center focus. The authors indicated that the meta-analysis reported pooled outcomes, with sufficient precision to support conclusions; however, study heterogeneity was significant, limiting the generalizability of the findings to specific individual populations. They noted that most of the studies in the systematic review and the additional studies involved prototype or research devices, so the findings may not fully generalize to individuals treated with commercial devices in clinical practice.

Loh et al. (2022) completed a meta-analysis of six RCTs published between 2012 and 2020 to evaluate the effectiveness of contralaterally controlled FES (CCFES) compared with that of NMES on upper extremity motor recovery in poststroke individuals. The studies included a combined 267 individuals [137 in the CCFES treatment group and 130 in the cyclic NMES (cNMES) group] during various phases of poststroke recovery, with one that investigated acute-phase stroke, one that studied chronic-phase stroke, three that evaluated subacute-phase stroke, and one that studied both subacute- and chronic-phase stroke. The individuals in both intervention groups in all the RCTs received treatment and background interventions for the same length of time. The risk-of-bias assessment indicated that four studies were identified as low risk, one was identified as having some concerns, and one was identified as high risk. The authors stated that the results of their meta-analysis showed that the CCFES group demonstrated greater improvement than the NMES group in Upper Extremity Fugl-Meyer Assessment (FMA) scores (included in all studies), the Box and Block Test (included in three studies), active ROM (AROM) measurements (included in four studies), and the modified Barthel Index (included in two studies); however, results for the Arm Motor Ability Test (included in three studies) did not differ significantly between stimulation types. Limitations noted by the authors include the lack of blinding in all the studies, small number of RCTs included (half of them originated from the same authors), and variability of the phase of stroke recovery or severity of impairment at baseline; additionally, all the comparison groups included only NMES. The authors concluded that CCFES might be an alternative form of intervention for poststroke treatment that may facilitate upper extremity motor function recovery. They recommended more RCTs to verify the efficacy and effects of CCFES and to compare CCFES with other modalities or interventions.

Hayes published a Health Technology Assessment that provided a comparative effectiveness review on the use of FES in addition to conventional occupational and PT (COPT) compared with COPT alone for upper extremity rehabilitation post stroke. The review included 10 RCTs (including the Jonsdottir et al., 2017, study below) and found that the addition of FES to COPT is at least as effective as COPT alone for improving some outcomes in poststroke individuals undergoing upper extremity rehabilitation, with some studies showing improvement in ADL, motor function, and shoulder subluxation. The results were mixed, the overall body of evidence was of low quality, and there was a lack of clarity regarding clinically meaningful changes. The report also noted that the efficacy of FES with COPT is similar to that of COPT alone regarding spasticity outcomes. The report concluded that additional information is needed to determine (1) whether FES effectiveness varies by the type, location, or chronicity of the stroke, (2) that long-term (> 18 months) efficacy is needed, and (3) that optimal parameters for FES treatment have yet to be established (2021; updated 2022).

A systematic review and meta-analysis by Jaqueline da Cunha et al. (2021) evaluated the effectiveness of FES applied to the paretic peroneal nerve and its influence on gait speed, active ankle dorsiflexion mobility, balance, and functional mobility. Electronic databases were searched for RCTs or crossover trials that focused on the effectiveness of FES with or without other therapies in individuals with foot drop after stroke. The review included 14 studies that provided data for 1,115 individuals who had sustained a stroke between less than 1 month and 108 months prior to their study participation. The study demonstrated that FES alone did not enhance gait speed compared with conventional treatments, although when FES was combined with supervised exercises, gait speed was better than supervised exercises alone. It also showed that FES had no effect when combined with unsupervised exercises on gait speed and that the data were inconclusive when FES was combined with regular activities at home. When FES was compared with conventional treatments, the analysis determined that it improved ankle dorsiflexion, balance, and functional mobility. The authors concluded that the meta-analysis showed that the quality of evidence was low for positive effects of FES on gait speed when combined with PT and that FES can improve ankle dorsiflexion, balance, and functional mobility. They stated that the results of the systematic review and meta-analysis should be interpreted carefully, considering the low quality of evidence and high heterogeneity of the data.

ECRI published a Clinical Evidence Assessment on the MyndMove FES device that has been developed to improve voluntary hand and arm movement in individuals with paralysis after a stroke or SCI. However, the focus of the ECRI report was on the device's safety and efficacy in adults post stroke. The report determined that the evidence is inconclusive due to limited available published evidence that included two very small, single-center, unblinded RCTs and one pre-post study. ECRI concluded that the studies are at too high of a risk of bias to be conclusive and that larger, multicenter RCTs are needed to demonstrate improvement in pain, spasticity, or QOL and to demonstrate that the benefits of the device are sustainable after therapy completion (2020).

Nascimento et al. (2020) conducted a systematic review and meta-analysis to evaluate the efficacy of AFOs and FES to the pre-tibialis muscle applied throughout the day to reduce foot drop after stroke. The review included 11 parallel RCTs that assessed the use of AFOs and FES on walking speed and balance in ambulatory adults who were moderately disabled following their stroke. The RCTs included 1,135 individuals between 47 and 65 years of age who were in both acute and chronic phases of recovery. The authors reported that an AFO with FES significantly increased walking speed compared with no intervention/placebo; however, the results regarding the efficacy of an AFO with FES on balance were inconclusive. The meta-analysis also found that AFOs alone were not superior to FES for improving walking speed or balance after stroke. The authors concluded that the systematic review provided moderate-quality evidence that both AFOs and FES improve walking speed after stroke, but the effects on balance remain unclear. The limitations of the review identified by the authors include the lack of blinding of the therapists, individuals, and assessors; lack of description of whether an intention-to-treat analysis was done; small number of included studies; and variation across trials in the number of individuals per group. There was also a lack of evaluation of the maintenance of effects beyond the intervention period. The authors recommended that future RCTs investigate the effects on clinical outcomes related to social participation and adverse events in people with stroke.

A systematic and meta-analysis by Eraifej et al. aimed to evaluate the effectiveness of poststroke upper limb FES on ADL and motor outcomes. A systematic review of RCTs from MEDLINE, PsycINFO, Embase, CENTRAL, ISRCTN (International Standard Randomised Controlled Trial Number), ICTRP (International Clinical Trials Registry Platform), and ClinicalTrials.gov was performed. Overall, 20 studies met the inclusion criteria. The outcomes were ADL (primary), functional motor ability (secondary), and other motor outcomes (tertiary). Quality assessment was determined using GRADE (Grading of Recommendations Assessment, Development, and Evaluation) criteria. In six studies, no significant benefit of FES was found for objective ADL measures (67 individuals in the FES group). A significant benefit on ADL was demonstrated in an analysis of three studies, in which FES was initiated, on average, within 2 months post stroke (n = 32). No significant ADL improvements were seen in three studies, in which FES was initiated more than 1 year after stroke (n = 35). Quality assessment using GRADE found very low-quality evidence in all analyses due to heterogeneity, the low numbers of individuals, and the lack of blinding. Meta-analyses gave rise to certain limitations, including but not limited to the use of many different measurement instruments; additionally, only a minority were used by more than a few studies, and blinding of individuals was inadequate in most studies. The authors concluded that FES is a promising therapy that could play a part in future stroke rehabilitation. There is a need for high-quality, large-scale RCTs of upper limb FES after stroke to draw firm conclusions regarding its efficacy or its optimum therapeutic window (2017).

Multiple Sclerosis

Máté et al. (2024) conducted a pilot study to investigate the cardiorespiratory, power, and participant-reported perceptions during acute sessions of FES cycling, voluntary cycling, and FES cycling combined with voluntary cycling (FES assist cycling). The study included 10 people (nine female; mean age, 52.4 ±9.9 years) with severe MS who undertook three exercise trials on a leg cycle ergometer, with trial 1 including 30 minutes of FES cycling, trial 2 including two 10-minute sessions of voluntary cycling separated by 10 minutes of rest, and trial 3 including a combination of trial 1 and trial 2.

Outcome measures included VO_2, cycle power output, heart rate, rate of perceived exertion, and postexercise perceptions of pain and fatigue. The authors reported that the average VO_2 during the 30-minute trials was significantly higher with FES assist cycling than with voluntary cycling, with a large effect size. The authors also reported that participants had similar rates of perceived exertion at the end of FES cycling, voluntary cycling, and FES assist cycling, while self-reported pain was higher during both FES cycling and FES assist cycling than voluntary cycling, both with large effect sizes; however, there was no difference in self-reported fatigue at the end of each trial. The authors concluded that the study found that FES assist cycling produced significantly higher VO_2 values than voluntary cycling, although the clinical significance of the differences was unknown. Limitations of the study include the small sample size, inclusion of only one male participant, lack of randomization of the order of trials, and lack of regression analysis between disability levels.

Hayes (2021; updated 2024) published a Health Technology Assessment focusing on the use of FES for the treatment of foot drop in individuals with MS. In the eight studies reviewed, the goals were to improve gait, walking speed, QOL, and overall functional mobility. The studies consisted of three RCTs, two randomized crossover trials, two case-control studies, and one pretest-posttest study. Six of the studies used the Odstock FES device, and three studies used the WalkAide FES device. The 2023 update stated that no newly published studies were found. The assessment stated that FES poses little risk of serious adverse events because it is noninvasive and involves low levels of electrical stimulation. Minor complications included pain, muscle spasms, weakness and pain, temporary paresthesia, lightheadedness, increased falls, skin irritation, and knee hyperextension. The authors noted that the body of evidence for FES and its efficacy to treat foot drop in individuals with MS was low in quality due to the individual study limitations, use of different FES devices, and limited number of studies for comparisons. The studies individually were found to be of low quality due to the small size, observational design, high dropout rates, incomplete statistical analysis, potential bias from previous experience with the therapy being evaluated, and short follow-up times. The report concluded that (1) a low-quality body of evidence shows that FES improves walking speed and duration, with reduced exertion at approximately the same benefit level as AFOs, and that (2) FES improves psychological outcomes and perceived but not actual exertion. The update in 2024 did not identify any relevant, newly published studies that met the initial inclusion criteria set out in the report. There was no change in the Hayes rating (C) and no new or updated position statements or guidelines. The authors recommended additional RCTs of FES vs AFOs to validate the psychological and perceived exertion benefits and to determine the durability of benefits over time.

In a systematic review investigating the effect of FES used for foot drop on health-related QOL (HRQOL) in adults with MS, Miller et al. (2019) evaluated the results of eight studies that included one RCT, one randomized crossover trial, three experimental nonrandomized studies, and three observational studies. The total number of individuals was 168, with 63% being female, and the sample sizes in the study groups varied from two to 64. Individuals in these studies were older than 18 years, had a diagnosis of MS, presented with foot drop (unilateral or bilateral), and had used FES. Selected studies required at least one validated HRQOL outcome measure that assessed the effect of FES to be reported. The authors found that seven of the studies demonstrated significant positive effects of FES on different aspects of HRQOL, as measured by the 29-item Multiple Sclerosis Impact Scale, 36-item Short Form Health Status Survey, Canadian Occupational Performance Measure, and Psychosocial Impact of Assistive Devices Scale. The authors concluded that the review showed that FES had a positive effect on aspects of HRQOL in people with MS; however, the variety of HRQOL outcomes used made it difficult to determine definitive conclusions. Future larger-scale RCTs, with long-term follow-up, are recommended to better understand the effect of FES on HRQOL. Limitations that the authors noted include the small number of studies, small number of individuals, lack of control comparators, and broad variety of HRQOL outcomes used in the studies, which made it difficult to determine definitive conclusions from this review. They recommended further qualitative studies to understand how FES affects HRQOL before the most appropriate HRQOL measures can be identified to determine the effectiveness of FES on HRQOL in people with MS; additionally, they recommended that future high-quality research should aim to capture the effect of FES on clinically meaningful aspects of HRQOL in longer-term studies.

Circulatory System Conditions

Zeng et al. (2024) conducted a systematic review and meta-analysis of RCTs to compare the efficacy of FES vs that of conventional exercise training or placebo in individuals with CHF. The study included 18 RCTs (including the Kadoglou et al., 2017, study below) that compared the effects of FES and control treatment on individuals with CHF and were included in both qualitative and quantitative analyses. Six of the studies were based on comparing FES with cycle (including aerobic exercise and cycling training, etc), and 10 studies were based on comparing FES with control (including normal care and sham FES). A total of 777 adult, predominantly male, individuals with CHF were included in the studies. The authors reported that FES significantly improved peak oxygen consumption, increased 6-minute walking distance, and improved QOL compared with the control but that traditional exercise rehabilitation therapy was more successful than FES in improving peak oxygen consumption, 6-minute walking distance, and QOL. The subgroup analysis that was completed by the authors showed that outcomes significantly improved under FES in both individuals with CHF with reduced ejection fraction and individuals with CHF with preserved ejection fraction but that the difference was insignificant

between groups of aerobic exercise and FES on individuals with CHF with reduced ejection fraction. Limitations of the study include the small study populations and short follow-up periods of the included RCTs, heterogeneity of the study designs, and lack of data and inclusion of individuals with higher New York Heart Association (NYHA) classifications. The authors concluded that the study demonstrated that FES improved cardiopulmonary function and QOL in individuals with CHF and that individuals with CHF with reduced ejection fraction benefited more from FES than individuals with CHF with preserved ejection fraction.

In a systematic review and meta-analysis of 14 RCTs, Wang et al. (2022a) evaluated the effectiveness of FES of the legs in 518 study individuals with heart failure. The authors stated that the pooled estimates demonstrated that FES significantly improved peak oxygen consumption (measure included in eight of the reviewed RCTs, n = 321), the 6MWT (10 RCTs, n = 380), and Minnesota Living with Heart Failure Questionnaire QOL score (nine RCTs, n = 383), while muscle strength of the lower extremities was not significantly improved in the FES treatment group compared with the control group (five RCTs, n = 218). They also stated that a subgroup analysis showed that FES significantly improved peak oxygen consumption, the 6MWT, and Minnesota Living with Heart Failure Questionnaire QOL score in the heart failure with reduced ejection fraction and the heart failure with preserved ejection fraction subgroups. The authors assessed the quality of the RCTs as fair for six of the studies and good for the other eight studies. The conclusion reached by the authors was that FES can effectively improve cardiopulmonary function and QOL in individuals with heart failure but does not significantly improve muscle strength in the legs. Limitations that were acknowledged by the authors include the potential bias risks in most of the included studies, which limited the strength of the results; limited availability of studies for inclusion; and heterogeneity of the studies, FES treatments, and muscles stimulated. Additionally, seven of the RCTs used sham FES with sensory input or low-intensity stimulation of the control group, which might have influenced outcomes.

Kadoglou et al. (2017) performed a randomized placebo-controlled study to investigate the effects of FES on the lower limbs as an alternative method of training in participants with CHF. Participants who were deemed stable (n = 120; defined by NYHA class II/III and mean left ventricular ejection fraction of 28% ±5%) were randomly selected for either a 6-week FES training program or placebo. Participants were followed up for up to 19 months for death and/or hospitalization due to heart failure decompensation. At baseline, there were no significant differences in demographic parameters, heart failure severity, or medications between groups. During a median follow-up of 383 days, 14 participants died (11 cardiac and three noncardiac deaths), while 40 participants were hospitalized for heart failure decompensation. Mortality did not differ between groups, although the heart failure–related hospitalization rate was significantly lower in the FES group. The latter difference remained significant after adjustment for prognostic factors: age, gender, baseline NYHA class, and left ventricular ejection fraction. Compared with placebo, FES training was associated with a lower occurrence of the composite end point (death or heart failure–related hospitalization) after adjustment for the above-mentioned prognostic factors. The authors concluded that 6 weeks of FES training in participants with CHF reduced the risk of heart failure–related hospitalizations, without affecting the mortality rate. The beneficial long-term effects of this alternative method of training require further investigation.

Clinical Practice Guidelines

National Institute for Health and Care Excellence (NICE)

In the NICE guideline regarding rehabilitation after traumatic injury, NICE states that for rehabilitation after SCI, additional techniques and specialized equipment (such as FES, gait orthoses, body weight–supported gait training, and robotic devices) should be considered to promote mobility, upper limb function, and independent walking (2022).

Neuromuscular Electrical Stimulation for Muscle Rehabilitation

Although the evidence is limited, NMES for the treatment of disuse atrophy in individuals in whom the nerve supply to the muscle is intact is supported by evidence. There is some evidence that the use of NMES may be an effective rehabilitative regimen for swallowing disorders or to prevent muscle atrophy associated with intensive care unit acquired weakness and prolonged knee immobilization following ligament reconstruction surgery or injury; however, controlled clinical trials are necessary to determine if the addition of NMES to the current standard rehabilitation programs will improve health outcomes.

NMES has shown beneficial effects in improving muscle strength, functional recovery, and pain reduction across a range of MSK and neurological conditions, including joint replacement, anterior cruciate ligament (ACL) reconstruction, CP, stroke, cystic fibrosis (CF), and chronic obstructive pulmonary disease (COPD). Studies indicate that NMES can enhance quadriceps strength, reduce edema, improve gait and mobility, and support rehabilitation when used alongside conventional PT. However, its impact on ROM and long-term outcomes is mixed, and effectiveness may vary depending on timing, dosage, and individuals' characteristics. Limitations include small sample sizes, inconsistent protocols, a lack of

blinding, and heterogeneity in study designs. Further high-quality, large-scale RCTs are needed to confirm its efficacy, optimize treatment parameters, and establish its role in clinical practice.

Musculoskeletal System Conditions

In their article published in 2025, Sun et al. conducted a meta-analysis and systematic review of 10 RCTs from 2009 to 2024 using the PubMed, Wiley Library, Embase, Web of Science, Cochrane Central, and PEDro databases. The study's objective was to evaluate the effectiveness of NMES in improving rehabilitation outcomes after joint replacement surgery. Only RCTs in individuals (n = 549) who had joint replacement surgery and underwent conventional rehabilitation or those who received NMES and conventional rehabilitation were included in this study. Studies on animals, academic reports, conference proceedings, and review articles as well as studies without full text, no required data, or inclusion of other combinations of rehabilitation therapies were excluded. R Studio software was used to conduct the meta-analysis using SMDs, with a 95% CI, and a statistical significance set at $p < 0.05$ as the effect measures to analyze. The I2 statistic was assessed for heterogeneity. When no significant heterogeneity existed, a fixed-effects model or random-effects model was used. NMES plus conventional rehabilitation was compared with just conventional rehabilitation alone. Pain (high heterogeneity SMDs; I2 = 82%), functional recovery, ROM, and muscle strength were the assessed outcomes. Their findings indicated a significant improvement in the reduction in pain scores and the Stair Climb Test for NMES. There was improvement in pain scores, functional scores, and quadriceps strength (I2 = 95%). There was mixed improvement for TUG before standardization indicated a small positive effect ($p < 0.01$), but after standardization, there was a significant positive effect ($p < 0.01$) in the NMES group, limited impact on extension ROM ($p = 0.04$), and minimal impact to the knee score (SMD, 0.10; 95% CI, -0.23 to 0.44), with no heterogeneity (I2 = 0%). Flexion ROM (I2 = 33%) showed no significant improvement. This study was limited by small study sizes, high heterogeneity, bias potential in some trials, and the need for more high-quality RCTs to confirm findings. The authors concluded that NMES can reduce pain, enhance muscle strength, and improve functional recovery after joint replacement surgery. However, its impact on ROM is limited, and further research is needed to optimize its use.

A systematic review was conducted by Li et al. (2025) using PubMed, the Cochrane Library, Embase, and Web of Science from database inception through August 2023 to study the effects of NMES on quadriceps strength and knee function recovery after ACL surgery. Individuals (13 years of age or older) who had ACL repair or reconstruction, with NMES as their postoperative rehabilitation with conventional PT as the control intervention, were included in this study. Animal or cadaveric testing studies, quasiexperimental or observation studies, and studies in which NMES was not the primary intervention were excluded. Each included study's quality was assessed using the Cochrane Collaboration Risk of Bias Tool. SMDs in Lysholm scores and muscle strength were quantitatively analyzed, along with qualitative assessments of the lower limb. Both quantitative and qualitative assessments were then pooled using a random-effects model. This resulted in a collection of 11 studies (n = 202 individuals) meeting the inclusion criteria. Nine of the 11 studies showed that in short-term and long-term follow-up, those who had physical rehabilitation with NMES had better improvement and recovery with quadriceps muscle strength compared with the conventional PT group (SMD, 0.53, 95% CI, 0.27-0.79 vs > 6 weeks: SMD, 0.59, 95% CI, 0.18-0.99; $p < 0.001$). Earlier physical rehabilitation with NMES in the subgroup analyses also resulted in better muscle strength recovery (≤ 1 week: SMD, 1.48, 95% CI, 0.80-2.17 vs > 1 week: SMD, 0.44, 95% CI, 0.21-0.67; $p < 0.001$). The Lysholm scores meta-analysis (three studies) showed no indication of significant differences between physical rehabilitation with NMES or without NMES. Limitations of the study identified include the levels of adherence; heterogeneity in nonexplicit original study quality assessments for which the authors could not be contacted to clarify inaccuracies; studies with multiple intervention groups in which only one group was selected for analysis; and publication dates that were not restricted, leading to studies with multiple updates, with only one study being chosen. The authors concluded that in both short- and long-term follow-up studies, compared with conventional rehabilitation alone, NMES in postoperative rehabilitation, after ACL surgery, significantly increased quadriceps muscle strength.

Zhao et al. (2022) conducted an RCT to evaluate the feasibility of using NMES for enhanced recovery after total hip replacement (THR). The single-center open-label study included 60 participants who were randomized into a treatment group (n = 30; 12 male participants; age, 53.1 ±5.7 years) that received NMES via the geko™ device and a control group (n = 30; nine male participants; age, 53.4 ±5.5 years) that did not receive NMES following their THR by the same surgeon. The NMES group participants were required to wear the NMES device for a minimum of 30 minutes each session, added up to 20 sessions over 5 days. Data were collected prior to surgery (day 0) and postoperative days 1, 3, and 5. The authors reported that there was a significant difference between the two groups with respect to pain on postoperative days 1 and 3 during mobilization but that there was no significant difference between the two groups regarding pain values on postoperative day 5. The authors also reported that there was no significant difference in the mean swelling measured of the calf or thigh circumference before THR surgery but that the between-group differences in mean change of calf circumference were significant on postoperative days 3 and 5, while the postoperative change in thigh circumference in the two groups showed very little significance on any of the postoperative days. Limitations of the study include the short follow-up period; open-label, single-center design; and small sample size. The authors concluded that the results of the

study suggested that NMES is partly useful for enhanced recovery after THR surgery, and they recommended a larger study be conducted to determine its effectiveness on compelling data. The visual analog scale (VAS) pain score was used to quantify postoperative pain while moving on postoperative days 1, 3, and 5, and lower limb swelling was examined in the supine position by taking measures of the circumference of both the thigh (10 cm above the patella) and the calf (10 cm below the tibial tubercle) at baseline and on postoperative days 1, 3, and 5.

In a prospective, single-blinded, single-center RCT that investigated the role of NMES in increasing femoral venous blood flow after THR surgery and evaluated the potential effects of NMES on preventing postoperative deep vein thrombosis (DVT), Calbiyik and Yilmaz (2022) concluded that there was a significant increase in femoral vein peak velocity (VPV) in the study group that received NMES, which may indicate a potential effect of NMES in preventing postoperative DVT. Their study included 64 participants who were over 60 years old and who were randomly divided into two groups, with one group receiving NMES and low-molecular-weight heparin (n = 32) and the second group (n = 32) receiving a low-molecular-weight heparin plus a compression bandage. All participants had the same surgeon and the same surgical approach (modified Gibson incision) and were operated on in the same position (lateral Sim's position). The length of hospital stays and frequency of leg edema before and after surgery were similar in both groups. The authors reported that there was no difference between the groups in terms of the presence of preoperative and postoperative leg edema but that the calf diameter was significantly lower in the NMES group than in the non-NMES group in both the preoperative and postoperative periods. The authors also reported that the femoral VPV was similar between the two groups in the preoperative period but was significantly higher in the NMES group than in the non-NMES group post operation. They reported that the femoral VPV after total hip prosthesis increased more in the NMES group (43.2%) than the non-NMES group (16.3%). The D-dimer value in the preoperative period was reported to be lower than that on postoperative days 1 and 5 in the non-NMES group, while in the NMES group, a statistically significant difference was found between the preoperative and postoperative test results, as the D-dimer values were significantly lower on the fifth postoperative day than on the first postoperative day, and the preoperative value was significantly lower than the fifth postoperative day value. The authors recommended further research to evaluate the potential of NMES to prevent DVTs in combination with other thromboprophylaxis modalities and to evaluate optimal parameters of NMES and stimulation location.

Wellauer et al. (2022) conducted an RCT to compare the effectiveness of a home-based NMES program applied to the quadriceps of the nonoperative side against sham-NMES as a complement to standard rehabilitation on knee extensor neuromuscular function in participants following ACL reconstruction. Overall, 24 participants completed the 6-week NMES (n = 12) or sham-NMES (n = 12) postoperative interventions and were tested at different time points for neuromuscular function and self-reported knee function. Isometric, concentric, and eccentric strength deficits (muscle weakness) increased from prior to surgery to 24 weeks post surgery in the sham-NMES group ($p < 0.05$), while no changes were observed in the NMES group. On the stimulated (nonoperative) side, quadriceps voluntary activation and muscle thickness were respectively maintained ($p > 0.05$) and increased ($p < 0.001$) because of the NMES intervention, contrary to sham-NMES. Self-reported knee function improved progressively during the postoperative phase ($p < 0.05$), with no difference between the two groups. Compared with a sham-NMES intervention, a 6-week home-based NMES program applied to the quadriceps of the nonoperative side early after ACL reconstruction prevented the occurrence of knee extensor muscle weakness 6 months after surgery. The authors concluded that nonoperative-side NMES may help counteract muscle weakness after ACL reconstruction. Limitations include the small sample size and NMES use that was not fully controlled due to home-based administration of both interventions. Further research is needed to determine the clinical relevance of these findings.

In a single-center, open-label feasibility RCT by Wainwright et al. (2018), the potential role of NMES in preventing the formation of edema following THR was investigated. The study included 40 adults who were scheduled to undergo elective THR and who were randomized to wear either the geko NMES device (n = 20; 14 female participants; age, 67.2 ±9.2 years) or Saphena® antiembolism compression stockings (n = 20; five female participants; age, 67.8 ±11.9 years) continually from post surgery until discharge. The primary outcome measure was the presence of lower limb edema, which was assessed by taking measurements of the circumference of the ankle, knee, and thigh on the operated leg and the nonoperated leg prior to surgery, post operation, at 2 days post operation, and every day until discharge. The authors reported that there were no significant differences between the preoperative swelling measurements at the ankle, knee, or thigh between the operated and nonoperated legs or between the pre- and postoperative swelling measurements at the ankle, knee, or thigh in the nonoperated leg in either group. The authors reported that the NMES group had significantly less edema at the knee and thigh, while the ankle circumference increased more in the compression group than the NMES group, but it was not statistically significant. Limitations of the study include the single-center design, small sample size, and heterogeneity between the two study groups. The authors concluded that the study suggests that NMES is a safe and well-tolerated alternative to compression stockings and that NMES should be considered as part of a DVT prophylaxis.

Talbot et al. (2017) conducted a pilot RCT (NCT00942890) to compare the effects of a home-based NMES rehabilitation program plus the traditional military amputee rehabilitation program (TMARP) vs the effects of TMARP alone on quadriceps muscle strength, functional mobility, and pain in military service members after a combat-related lower extremity amputation. In total, 44 participants with a unilateral transtibial amputation were randomly assigned to TMARP plus NMES (n = 23) or to TMARP alone (n = 21). Both groups received 12 weeks of traditional amputee rehabilitation, including pre- and postprosthetic training. Those in the NMES group also received 12 weeks of NMES. Participants were tested at 3-week intervals during the study for muscle strength and pain. For functional measures, they were tested after receiving their prosthesis and at study completion (weeks 6 and 12). In both groups, residual limb quadriceps muscle strength and pain severity improved from baseline to 12 weeks. The NMES plus TMARP group showed greater strength than the TMARP-alone group at 3 weeks, before receiving the prosthesis. However, 6 weeks post prosthesis, there was no group difference in the residual limb strength. Functional mobility improved in both groups between weeks 6 and 12, with no difference between the two treatment groups. The authors concluded that a home-based NMES intervention with TMARP worked at improving residual limb strength, pain, and mobility. While NMES seemed most effective in minimizing strength loss in the amputated leg prior to prosthesis, further research on amputation rehabilitation is warranted, as NMES may accelerate recovery.

Nervous System Conditions

Cerebral Palsy

Abd Elmonem et al. (2024) conducted a randomized comparative trial to compare the effects of NMES combined with interrupted serial casting (SC) vs SC alone on various aspects of lower limb function in children with diplegic CP. The study included 33 children who were randomly assigned at recruitment to receive SC with a customized PT program (group A) or who received the same SC and customized PT program, along with NMES applied through cast windows during casting. Evaluations conducted before and after 8 weeks of intervention were based on ROM, the Modified Tardieu Scale, handheld dynamometer measurements, and the Observational Gait Scale. The authors reported that both groups showed significant improvements in dorsiflexion ROM, popliteal angle, gastrocnemius dynamic spasticity, and hamstring dynamic spasticity after the intervention; however, significant differences were seen in dorsiflexor strength, knee extensor strength, and observational gait scale score between groups after the intervention, favoring group B. The authors concluded that the use of NMES during SC in children with diplegic CP may help overcome the substantial decrease in strength resulting from casting and may lead to less reduction of tone, improvement in ROM, without significantly decreasing strength, and achievement of greater improvements in gait function.

In a scoping review of 26 interventional studies and seven review articles, Greve et al. (2022) assessed the application of NMES to augment lower extremity exercises and the effects of NMES on neuromuscular impairments and function in people with spastic CP. The 26 intervention publications included a total of 558 individuals who were aged 3 to 57 years with CP. The review included studies on three NMES applications, including NMES-assisted strengthening (14 studies), NMES-assisted gait (11 studies), and NMES for spasticity reduction (seven studies). NMES-assisted strengthening included the use of therapeutic exercises and cycling, while NMES-assisted gait included the use of NMES to improve gait patterns. NMES spasticity reduction included the use of transcutaneous electrical stimulation or NMES to decrease tone. The authors stated that the findings of their scoping review indicated that NMES applied to strengthening exercise, gait, and spasticity reduction demonstrated potential benefits for improving muscle physiology, neuromuscular impairments, gait patterns, and functional mobility in individuals with spastic CP. The authors noted that the dosage of NMES intervention varied by study, as did the exercise activities, NMES devices used, and frequency and intensity parameters; they recommended further research to determine optimal protocols and dosage for NMES. The authors concluded that (1) NMES was found to improve muscle structure, strength, gross motor skills, gait kinematics, and walking speed and distance and reduced spasticity and that (2) the use of NMES-assisted strengthening with therapeutic exercise and cycling, NMES-assisted gait, and NMES for spasticity reduction supports the use of NMES to improve mobility in people with spastic CP.

Rocha et al. (2022) conducted a systematic review of randomized clinical trials to evaluate the safety and efficacy of nonsurgical interventions for the treatment of masticatory muscle spasticity in individuals with CP. The authors conducted a comprehensive search in the following databases: MEDLINE, Embase, the Cochrane Library, Latin American and Caribbean Health Sciences Literature, Brazilian Library of Odontology, PEDro, ClinicalTrials.gov, and World Health Organization(WHO)/ICTRP, without date and language restrictions. Randomized clinical trials evaluating nonsurgical interventions were considered. Primary outcomes such as masticatory function and adverse events were planned to be assessed. The risk-of-bias assessment was performed using the Cochrane Risk of Bias Tool. The certainty of the evidence was assessed using the GRADE approach. Three randomized clinical trials assessing the effects of botulinum toxin, functional masticatory training, and NMES were included. Evidence, with a very low certainty, showed (1) no difference between botulinum toxin and placebo regarding maximum chewing strength, chewing efficiency, and global oral health scale; (2) improvement in masticatory function in favor of functional masticatory training vs conventional exercises;

and (3) favorability toward strengthening exercises plus NMES vs placebo. All studies reported the blinding of the outcome assessors and were of low risk of bias for this domain. No losses were reported from individuals in any of the included studies. The authors concluded that there is insufficient evidence to support the use of botulinum toxin and masticatory muscle strengthening programs alone and associated with NMES for the treatment of masticatory muscle in individuals with CP. The clinical decision must be individualized, and further studies are needed to support or refute the use of different nonsurgical interventions for CP. This systematic review is limited by its small sample size (three randomized clinical trials), heterogeneous groups, and lack of a controlled comparator group. Further research, with randomized clinical trials, is needed to validate these findings.

Cobo-Vicente et al. (2021) performed a systematic review and meta-analysis to analyze the effect of NMES on skeletal muscle and biomechanics of movement, functional mobility, strength, spasticity, muscle architecture, and body composition in children and adolescents with chronic neurological disorders (CNDs) and chronic diseases. Their review consisted of 18 studies (including the Pool et al., 2016, study below), of which 15 were RCTs, two were non-RCTs, and one was a cross-sectional study. There were 595 individuals between 3 and 14 years of age, of whom 49% were female. Most of the studies (88.9%) included in the review were about CP (16 articles). There was also one study on spinal muscular atrophy and one study about obstetric brachial plexus injury. All the studies used NMES as their main intervention, with the NMES programs lasting from 4 to 48 weeks in duration and an average application of 14 weeks. Half of the programs were home-based programs, and half of the cases indicated that the NMES was applied by professionals. The authors concluded that the use of NMES programs for children with CNDs, specifically CP, appears to be effective in improving strength, biomechanics of movement, and functional mobility; however, they noted that there are not enough studies to confirm that NMES produces benefits on spasticity, muscle architecture, and body composition. This study noted that there is little agreement in the variables analyzed in the different studies, which made it difficult to compare results and perform the statistical analysis of some variables. It also identified that there are small sample sizes in most of the studies and that since most of the studies were focused on CP, the conclusions would be difficult to expand to other types of CNDs. The authors recommended that future RCTs focus on analysis of the effect of NMES on spasticity, muscle architecture, and body composition in children with CNDs and that further research is needed to evaluate the effectiveness of NMES in pediatric individuals with other chronic diseases.

An RCT by Pool et al. (2016) evaluated whether NMES applied to the ankle dorsiflexors during gait improves muscle volume and strength in children with unilateral spastic CP. The study involved 32 children (mean age, 10.5 years) and a Gross Motor Function Classification System of I or II. Participants were randomly assigned to either the 8-week daily NMES treatment group or control group (usual or conventional treatments). Outcomes at week 8 (post NMES) and week 14 (carryover) included MRI for muscle volumes (tibialis anterior, anterior compartment, and gastrocnemius), strength (handheld dynamometry for isometric dorsiflexion strength and heel raises for functional strength), and clinical measures for lower limb selective motor control. At week 8, the treatment group demonstrated significantly increased muscle volumes and dorsiflexion strength, not only when compared with their baseline values but also when compared with the control group at week 8. At week 14, both tibialis anterior and lateral gastrocnemius volumes in the treatment group remained significantly increased compared with their baseline values. However, only lateral gastrocnemius volumes had significantly greater values compared with the control group at week 14. There were no between-group differences in the clinical measures for lower limb selective motor control at weeks 8 and 14. The authors concluded that 8 weeks of daily NMES-assisted gait increases muscle volume and strength of the stimulated ankle dorsiflexors in children with unilateral spastic CP. These changes are use dependent and do not carry over after the 8-week treatment period. Gastrocnemius volume also increased post treatment, with carryover at week 14.

Cerebral Vascular Accident

Oh et al. (2023) conducted a systematic review and meta-analysis to examine the effectiveness of mirror therapy (MT) and NMES therapy on lower extremity motor function recovery, including walking speed, spasticity, balance, and other gait parameters, in individuals recovering from CVAs. The study included six RCTs (five parallel studies and one crossover study) that evaluated the use of a combination of MT and NMES therapy in individuals who had experienced a CVA and that assessed the outcomes of lower extremity motor function and impairment. There was a total of 181 individuals (52% male) who had experienced hemiplegia at any stage of stroke and exhibited various degrees of impairment in the motor function of the lower extremities (91 in the treatment group who received MT plus NMES and 90 in the control group who underwent conventional therapy with or without sham therapy). The authors reported that MT combined with NMES resulted in greater improvement relative to the control group in walking speed, cadence, step length, and stride length but not in spasticity. The quality of evidence was reported by the authors to be moderate for the assessment of walking speed; low quality for balance and gait parameters; and very low quality for spasticity. Limitations of the study include the small number of individuals in the included RCTs, small number of individuals in the subanalysis groups, inclusion of individuals from multiple levels of recovery, and short follow-up periods for the included studies. The authors concluded that MT combined with NMES may be a suitable supplemental intervention to conventional therapy in individuals who survive CVAs.

Wang et al. (2023) conducted a systematic review and meta-analysis to evaluate the clinical efficacy of NMES in individuals with poststroke dysphagia. Their study included 46 RCTs, with a total of 3,346 individuals with poststroke dysphagia. There were 1,679 individuals who received NMES plus swallowing therapy, and the other 1,667 individuals received just swallowing therapy. The treatment course range was from 2 to 12 weeks. The authors stated that the meta-analysis showed that NMES combined with routine swallowing therapy could effectively improve swallowing function and QOL, increase the upward and forward movement distances of the hyoid bone, reduce the rate of complications, and improve the swallowing function in individuals with poststroke dysphagia. The authors also stated that subgroup analyses found that individuals with an onset of less than 20 days and who were older than 60 years of age appeared to have more positive effects after treatment and that a course of 4 weeks or less might achieve more satisfactory clinical efficacy than a course of more than 4 weeks. Limitations of the study include the predominance of studies being from one country (China), heterogeneity of the NMES treatment protocols, lack of clarity in most of the RCTs of the blinding method, and lack of reporting of adverse events in most of the studies. The authors recommended more large-sample, high-quality, multicenter studies to strengthen the data on adverse events and to prove the clinical efficacy of NMES and swallowing therapy in the treatment of poststroke dysphagia.

In a single-center, randomized, self-controlled, crossover study in 35 participants with poststroke dysphagia, Zhang et al. (2022) reported that participants demonstrated improved Modified Barium Swallow Impairment Profile and Penetration-Aspiration Scale scores when NMES was applied. Participants were considered eligible for inclusion if they were adults between 18 and 80 years of age who had been diagnosed with stroke with dysphagia and scored below level 3 on the Modified Barium Swallow Impairment Profile-6. To eliminate order effects, 17 participants received NMES first, while the remaining 18 participants received sham stimulation first. A video fluoroscopic swallowing study procedure was initiated 30 seconds after each participant had fully adapted to real-NMES while the participant was fed three mouthfuls of mildly thick food over the 5-minute stimulation period. The sham stimulation period was done with the same electrode placement and video fluoroscopic swallowing study process, without the application of NMES. The authors reported that NMES significantly shortened oral transit time and improved initiation of the pharyngeal swallow while decreasing the risk of penetration and aspiration, which may aid in early feeding training for individuals with dysphagia following stroke. Limitations of the study include the small sample size, single-center design, and lack of blinding. The authors concluded that the results of this study suggest that NMES may aid in promoting early therapeutic feeding following stroke.

Miller et al. (2022) conducted a systematic review to evaluate the most recent studies regarding the potential effectiveness of NMES as a treatment for oropharyngeal dysphagia. Overall, 18 studies were identified, with varying groups of individuals, stimulation protocols, electrode placements, and therapy settings. However, 16 studies have reported beneficial outcomes in relation to NMES. The authors concluded that there is a considerable amount of level 2 studies that suggest that NMES is an effective treatment option, especially when combined with traditional dysphagia therapy for individuals with dysphagia after stroke and individuals with Parkinson disease or with different kinds of brain injuries. Further research is still necessary to clarify which stimulation protocols, parameters, and therapy settings are most beneficial for certain individual groups and degrees of impairment. Data pooling and statistical analysis could not be conducted due to the inhomogeneity of the study protocols. Further research, with RCTs, is needed to validate these findings.

Ohnishi et al. (2022) conducted an RCT to investigate the effect of combined therapy with repetitive facilitative exercise (RFE) and NMES in participants who had experienced a stroke with severe upper paresis. This study included a total of 99 participants who had very severe paresis and scores of 0 or 1a on the Finger-Function test of the Stroke Impairment Assessment Set. Participants were randomly divided into four groups, namely NMES, RFE, RFE under NMES, and conventional training groups. A total of 20 minutes of group-specific training, in addition to 40 minutes of conventional exercise per day, seven times a week for 4 weeks after admission, was performed. The upper extremity items of the FMA were evaluated before and after the training period. The total score gains of the FMA, FMA wrist item, and FMA finger item were larger in the RFE under NMES group than those in the conventional training group ($p < 0.05$). The authors concluded that the combination of voluntary movement and electrical stimulation may promote the activation of paralyzed muscles and improve distal function for very severely paralyzed upper limbs. A limitation of this study is that the number of joint movement repetitions was arbitrary, although the training period in each group was defined. The authors suggested that additional studies are warranted to verify the effects of treatments with a fixed number of movements.

Xie et al. (2022) conducted a two-arm RCT to investigate the effects of simultaneous use of NMES on the median nerve and language training (m-NMES-LT) on cerebral oscillations and brain connection as well as the effect on clinical efficacy following CVA. A total of 21 right-handed adult participants with aphasia after stroke were randomly assigned to the language training group (n = 10) and m-NMES-LT group (n = 11), and tissue concentration of oxyhemoglobin and deoxyhemoglobin oscillations were measured by functional near-infrared spectroscopy in the resting and treatment state during 3 consecutive weeks. Five characteristic frequency signals (I, 0.6-2.0 Hz; II, 0.145-0.600 Hz; III, 0.052-0.145 Hz; IV, 0.021-0.052 Hz; V, 0.0095-0.021 Hz) were identified using the wavelet method. The wavelet amplitude and wavelet

phase coherence (WPCO) were calculated to describe the frequency-specific cortical activities. The m-NMES-LT induced higher wavelet amplitude values in the contralesional prefrontal cortex in intervals I, II, and V and the ipsilesional motor cortex in intervals I to V than the resting state. The WPCO values between the ipsilesional prefrontal cortex-motor cortex in intervals III to IV and between the bilateral motor cortex in intervals III to IV were higher than the resting state. In addition, there was a positive correlation between WPCO and Western Aphasia Battery in the m-NMES-LT group. The authors concluded that language training combined with NMES on the median nerve could improve and achieve higher clinical efficacy for aphasia. This is attributed to the m-NMES-LT, which could enhance cortical activation and brain functional connectivity in individuals with aphasia, which is derived from myogenic, neurogenic, and endothelial cell metabolic activities. A small sample size makes it difficult to decide whether these conclusions can be generalized to a larger population. Further investigation is needed before the clinical usefulness of this procedure is proven.

An RCT was completed by Huang et al. (2021) to compare the effectiveness of CCFES vs that of NMES on motor recovery of the upper limb in participants with subacute stroke. Overall, 50 participants within 6 months post stroke were randomly assigned to the CCFES group (n = 25) and the NMES group (n = 25). Both groups underwent routine rehabilitation plus 20-minute stimulation on wrist extensors per day, 5 days a week for 3 weeks. The FMA of upper extremity (FMA-UE), Action Research Arm Test (ARAT), Barthel Index, and surface electromyography (sEMG) were assessed at baseline and the end of the intervention. After a 3-week intervention, the FMA-UE and Barthel Index increased in both groups ($p < 0.05$). The ARAT increased significantly only in the CCFES group ($p < 0.05$). The changes in the FMA-UE, ARAT, and Barthel Index in the CCFES group were not greater than those in the NMES group. The improvement in sEMG response of the extensor carpi radialis by CCFES was greater than that by NMES ($p = 0.026$). The co-contraction ratio of the flexor carpi radialis did not decrease in both groups. No adverse events were reported during the intervention and follow-up in any of the groups. The authors concluded that CCFES improved upper limb motor function but did not show a better treatment effect than NMES. CCFES enhanced the sEMG response of the paretic extensor carpi radialis compared with NMES but did not decrease the co-contraction of the antagonist. There are multiple limitations to this study. The central plasticity of the participants was not evaluated by electrophysiological or functional imaging investigation at baseline, which could be a confounder of the treatment effect of CCFES. The effect of CCFES on central plasticity was not measured in this study, and the duration of the intervention was short, which may reduce the effect of CCFES. The findings of this study need to be validated by well-designed studies, and further investigation is needed before the clinical usefulness of this procedure is proven.

Kristensen et al. (2021) conducted a systematic review and meta-analysis to elucidate the effectiveness of NMES toward improving ADL and functional motor ability post stroke and to investigate the influence of paresis severity and the timing of treatment initiation for the effectiveness of NMES. The inclusion criteria were RCTs exploring the effect of NMES toward improving ADL or functional motor ability in survivors of stroke. The search identified 6,064 potential articles, with 20 being included. Two independent reviewers conducted the data extraction. Methodological quality was assessed using the PEDro scale and the Cochrane Risk of Bias Tool. Data from 428 and 659 individuals (mean age, 62.4 years; 54% male) for outcomes of ADL and functional motor ability, respectively, were pooled in a random-effects meta-analysis. The analysis revealed a positive effect of NMES toward ADL (SMD, 0.41; 95% CI, 0.14-0.67; $p = 0.003$), whereas no effect on functional motor ability was evident. Subgroup analyses showed that application of NMES in the subacute stage (SMD, 0.44; 95% CI, 0.09-0.78; $p = 0.01$) and in the upper extremity (SMD, 0.34; 95% CI, 0.04-0.64; $p = 0.02$) improved ADL, whereas a beneficial effect was observed for functional motor abilities in individuals with severe paresis (SMD, 0.41; 95% CI, 0.12-0.70; $p = 0.005$). The authors concluded that the results of the meta-analysis are indicative of the potential beneficial effects of NMES toward improving ADL post stroke, whereas the potential for improving functional motor ability appears less clear. Furthermore, subgroup analyses indicated that NMES application in the subacute stage and targeted at the upper extremity is efficacious for ADL rehabilitation and that functional motor abilities can be positively affected in individuals with severe paresis. Limitations include a high risk of blinding and reporting bias. Further investigation is needed before the clinical usefulness of this procedure is proven.

In a systematic review of RCTs, Alamer et al. (2020) evaluated the efficacy of NMES on swallowing function in individuals who experienced a dysphagic stroke. The authors analyzed 11 RCTs that included studies that examined NMES and/or NMES combined with conventional swallowing therapy, irrespective of the duration of the intervention provided or the outcome(s) measured. The studies included a total of 784 individuals, with a mean age of 54 to 66.2 years in the treatment groups and 55.8 to 66.1 years in the control groups. The mean duration since stroke was 15.7 hours to 35.4 weeks in the treatment groups and 16.0 hours to 36.0 weeks in the control groups. The RCTs compared the effectiveness of NMES and/or conventional swallowing therapy with the controlled group; conventional swallowing therapies and/or placebo/sham stimulations were considered. The reviewers used the PEDro scale and determined that the overall methodological quality of the evidence ranged from moderate to high. The authors concluded that NMES, along with traditional swallowing therapy, could be an optional intervention to improve swallowing after stroke; however, they noted that great attention is needed regarding the course of disease duration and its severity when NMES is used for poststroke dysphagia. The authors could not perform a meta-analysis due to the heterogeneity of the interventions. They

recommended that future research be conducted on NMES efficacy in individuals with chronic stroke with swallowing dysfunction.

Knutson et al. (2016) evaluated whether CCFES or cNMES was more effective for poststroke upper limb rehabilitation in an interventional, phase 2, randomized trial conducted at a single institution. Participants who had experienced a stroke (n = 80) with chronic (more than 6 months) moderate to severe upper extremity hemiparesis were randomized into two groups, receiving 10 sessions/week of CCFES- or cNMES-assisted hand-opening exercise at home, plus 20 sessions of functional task practice in the lab over 12 weeks. The primary outcome was improvement in Box and Block Test score at 6 months post treatment, with the FMA-UE and Arm Motor Ability Test also being measured. Evaluation of participants occurred at baseline, every 3 weeks during the treatment period, at the end of treatment, and 2, 4, and 6 months post treatment by a blinded assessor. At 6 months post treatment, the CCFES group had greater improvement than the cNMES group on the Box and Block Test, 4.6 vs 1.8, respectively, and a between-group difference of 2.8. No significant between-group difference was found for the FMA-UE or Arm Motor Ability Test. The authors concluded that 12 weeks of CCFES therapy resulted in improved manual dexterity compared with cNMES in stroke survivors experiencing chronic moderate to severe hand impairment, with advantage given to those whose impairment was moderate and who were less than 2 years post stroke. The translatability of CCFES therapy to other research sites and to clinical practice still has not been established.

In an RCT by Shen et al. (2015), CCFES was compared with NMES as an innovative method to improve upper extremity functions after stroke. Overall, 66 participants were also treated with conventional medical treatment and rehabilitation training and were equally randomized into two groups. The treatments were administered in 20-minute sessions, five times per week for 3 weeks. Tools to assess results included the FMA, Motricity Index, FTHUE-HK (Hong Kong version of the Functional Test for the Hemiplegic Upper Extremity), and AROM of wrist extension. Participant status was measured before and after 3 weeks of treatment. Both groups showed significant improvements in all the measurements after treatment. Participants in the CCFES group showed significantly higher upper extremity FMA, FTHUE-HK scores, and AROM of wrist extension than those in the NMES group. The authors concluded that compared with conventional NMES, CCFES provides better recovery of upper extremity function in individuals with stroke.

Respiratory System Conditions

The therapeutic effects of NMES in combination with respiratory muscle training in individuals with moderate to severe COPD were studied by Jin et al. (2025). There were 135 individuals with COPD divided into a rehabilitation group (RG) with 72 individuals, a control group with 63 individuals, and a blank group with 63 non-COPD individuals. Individuals received 8 weeks of intervention. The RG received NMES of the quadriceps plus pulmonary rehabilitation (cycling, strength, and breathing training), while the control group received conventional muscle training (aerobic and strength training), and the blank group was used for baseline comparison with only routine monitoring and no intervention. There were five key findings in this study: (1) pulmonary function showed significant improvement in predicted forced expiratory volume in 1 second (FEV_1) and FEV_1/FVC in the RG vs the control group, and FEV_1 improved in both the RG and control group, but there was no significant difference between the two; (2) blood gas analysis showed a decrease in partial pressure of oxygen in arterial blood, while partial pressure of carbon dioxide in arterial blood and the saturation of oxygen in arterial blood increased post intervention, and the RG showed better gas exchange improvements than the control group; (3) muscle strength showed an increased peak torque and endurance ratio of the quadriceps in both the RG and control group, and there was no significant difference between the RG and control group for muscle strength gains; (4) QOL (COPD Assessment Test scores) was significantly reduced in the RG compared with the control group, indicating better symptom control and QOL; and (5) mental health hospital anxiety and the depression scale decreased significantly in the RG vs the control group. Limitations of the study include the small sample size; lack of diversity, with all individuals from a single hospital; no long-term follow-up; lack of blinding; limited muscle assessment to only the quadriceps; and lack of confounding factor (e.g., comorbidities, medications used, lifestyle differences) outcomes. The authors concluded that muscle strength improvements were similar between groups, and NMES plus pulmonary rehabilitation is more effective than conventional training in lung function, oxygenation, carbon dioxide exhalation, QOL, and psychological well-being.

In 2024, Liou et al. conducted a meta-analysis and systematic review of 19 RCTs in 589 individuals with moderate to severe COPD who had difficulty with pulmonary rehabilitation due to dyspnea and exercise intolerance. The authors' objective was to determine the muscle stimulation effects of NMES on improving physical function and QOL, without increasing pulmonary workload. The Academic Search Complete, CINAHL, PubMed, Cochrane Library, and Airiti Library databases were searched for RCTs from inception to December 2022. The Cochrane Risk of Bias Tool and GRADE were used in the analysis. A random-effects model was used to calculate pooled estimates. There were three key findings: (1) NMES significantly improved exercise capacity in the 6-minute walk distance and the TUG test results ($p < 0.05$), but no significant improvement in the shuttle walk test or volume of oxygen peak was observed; (2) physical function was improved by NMES in the fat-free mass and quadriceps strength ($p < 0.05$), but no significant effect on volume of oxygen peak was observed; and (3) HRQOL showed a small but significant improvement in Saint George's Respiratory

Questionnaire, London Chest Activity of Life, and modified Medical Research Council scores ($p < 0.05$). Daily activity and dyspnea performance improvements were also noted. The GRADE assessment ratings as low to very low certainty, risk of bias in many studies, and high heterogeneity in NMES protocols were identified limitations of this study. The authors concluded that NMES combined with conventional exercise training can enhance muscle strength, reduce dyspnea, and improve exercise capacity and QOL in individuals with COPD. However, NMES alone may not be sufficient and requires more high-quality research to confirm long-term benefits and standardize protocols.

In a systematic review and meta-analysis on the effectiveness of NMES in individuals with COPD on mechanical ventilation (MV), Gutiérrez-Arias et al. (2022) concluded that NMES may improve functional independence and decrease MV time in adults with COPD. The study included four RCTs, with a total of 144 adults aged 18 years or older with COPD who were hospitalized and received ventilatory support and who received NMES while on MV. Comparator interventions included studies that did not apply any intervention or that included sham electrical stimulation. Three of the studies were conducted in an acute critical care setting, while the fourth study was conducted in a chronic critical care rehabilitation setting. The authors reported that the results of their review showed that NMES can improve functional independence in being able to move from bed to chair more quickly than was seen in individuals with COPD who did not receive NMES and that individuals with COPD who received NMES were on MV for a shorter period of time than was seen in individuals with COPD who did not receive NMES. Limitations of the study include the heterogeneity of the NMES treatment and in the reporting parameters among the studies, small number of studies included, and heterogeneity of the place of service in the included studies. The authors recommended future RCTs, with better methodological design, and for studies to assess the duration of MV weaning, dyspnea, fatigue of the lower limbs, functional exercise capacity at discharge, maximal exercise capacity at discharge, and physical activity level at discharge.

Donadio et al. (2022) conducted an RCT to evaluate the effects of a supervised resistance training program, associated or not with NMES, on muscle strength, aerobic fitness, lung function, and QOL in children with CF presenting with mild to moderate pulmonary impairment. A total of 27 participants, aged between 6 and 17 years, were enrolled in this study. Participants were randomly allocated to control (CON), exercise (EX), or exercise and NMES (EX + NMES) groups and evaluated at baseline and at the end of an 8-week individualized exercise program (3 days per week for 60 minutes per session). NMES was applied in the quadriceps and the interscapular region, simultaneously to the exercises. The CON group followed the CF team recommendations. The main outcome measures were lung function, cardiorespiratory fitness, functional capacity, QOL, and muscle strength. No interactions were found for cardiorespiratory fitness. Functional capacity presented differences, indicating a better performance in both the EX and EX + NMES groups. No changes between groups were seen in QOL and lung function. As for muscle strength, EX and EX + NMES presented large effect sizes and differences compared with CON for quadriceps ($p = 0.004$; $\eta 2p = 0.401$), pectoral ($p = 0.001$; $\eta 2p = 0.487$), dorsal ($p = 0.009$; $\eta 2p = 0.333$), and handgrip ($p = 0.028$; $\eta 2p = 0.278$). The authors concluded that a resistance exercise training program led to improvements in muscle strength and functional capacity in participants with CF with mild to moderate pulmonary impairment. The addition of NMES to the training program resulted in no extra favorable effects. This study has limitations, including the difference in genotyping between groups. Although there is evidence to support that its effect on exercise variables is not substantial, it may have influenced present results. In addition, the mild to moderate impairment of the sample could also affect results, as smaller effects are expected in participants with high aerobic fitness and lower muscular abnormalities. Further investigation is needed before the clinical usefulness of this procedure is proven.

Wu et al. (2020) conducted a systematic review and meta-analysis to determine the effects of NMES on exercise capacity, functional performance, symptoms, and HRQOL in individuals with COPD. They reviewed 13 RCTs, of which seven studies explored the effect of NMES vs usual care, and six studies compared NMES plus conventional exercise vs exercise training alone, with or without sham training for NMES. Study individuals totaled 447 adults, with confirmed diagnosis of severe or very severe stable COPD. The authors noted no statistical increase in HRQOL among individuals allocated with NMES, and NMES had no benefit for the peak rate of oxygen uptake and peak power. The authors stated that the results of the study showed that there is insufficient evidence to support the positive effects exerted by NMES in individuals with COPD. The authors concluded that based on current available data, NMES should not be regarded as a replacement for pulmonary rehabilitation completely, as the combination does not result in further improvement. The fundamental limitation that was noted by the authors is that the quality of the evidence in their meta-analysis is very low and limited by poor methodology, leading to the risk of bias. Other limitations noted include the lack of blinding of the assessors and estimates of random variability that were present in only seven of the 13 studies. The authors recommended that future studies add data describing the intrinsic muscle function or peripheral muscle force and follow up the adverse signs or events, in which NMES is applied alone or in isolation from rehabilitation strategies.

A 2018 Cochrane review by Hill et al. evaluated the effects of NMES, either alone or concurrently with conventional exercise therapy, to determine if this treatment might improve the overall physical condition and HRQOL in people with COPD. Overall, 19 studies met the inclusion criteria, of which 16 contributed data on 267 individuals with COPD. Of these

16 studies, seven explored the effect of NMES vs that of usual care. Nine explored the effect of NMES plus conventional exercise training vs conventional exercise alone. The reviewers concluded that NMES, when applied alone, increased quadriceps force and endurance, 6-minute walking distance, and time to symptom limitation exercising at a submaximal intensity and reduced the severity of leg fatigue on completion of exercise testing. The evidence quality was considered low or very low due to the risk of bias in the studies, imprecision of the estimates, small number of studies, and inconsistency between the studies.

Clinical Practice Guidelines

National Institute for Health and Care Excellence (NICE)

In the NICE guideline on stroke rehabilitation in adults, the recommendation was made for further research to be conducted on the use of NMES for the treatment of dysphagia before it can be recommended due to the potential high cost of the intervention, size of the trials, and low quality of evidence. NICE noted that the current studies indicate that use of NMES for the treatment of dysphagia appeared to improve QOL, reduce dysphagia and chest infections, and help people return to a normal diet. The guideline also stated that the evidence on the effect of NMES on mortality is uncertain because of small trial sizes and short follow-up times (2023).

NICE published a guideline for the management of knee osteoarthritis (OA) in which they concluded that NMES should not be offered to people with OA because there is insufficient evidence of benefit. The guideline stated that although there were many studies on electrotherapy, the findings were inconsistent and mostly showed little benefit. The committee found that most studies were small, with fewer than 100 individuals, and that the evidence from direct comparisons of electrotherapy with other interventions was uncertain (2022).

NICE guidance on transcutaneous NMES for oropharyngeal dysphagia in adults found current evidence on efficacy for adults with dysphagia after a stroke to be limited in quality and quantity although it may have potential benefit. They also noted that, for adults with dysphagia not caused by a stroke, there is insufficient evidence on efficacy to support the use of this procedure. NICE states that this technology should only be used with special arrangements for clinical governance, consent and audit or research; and encourages further research into transcutaneous NMES for this condition, which clearly documents indications for treatment and details of patient selection (2018).

American Heart Association (AHA)/American Stroke Association (ASA)

In its Guidelines for Adult Stroke Rehabilitation and Recovery, the AHA/ASA state that NMES combined with therapy may improve spasticity, but there is insufficient evidence that the addition of NMES improves functional gait or hand use. The AHA/ASA guidelines are endorsed by the American Academy of Physical Medicine and Rehabilitation and the American Society of Neurorehabilitation (Winstein et al., 2016).

Interferential Therapy

There is insufficient evidence to support the safety and efficacy of interferential therapy (IFT) to treat MSK pain or bone fractures or to facilitate healing of nonsurgical soft tissue injuries, as the studies are mostly case series, comparison studies, or RCTs with small sample sizes, heterogeneous study protocols, and short-term results. More robust studies are needed to establish the effectiveness of IFT compared with that of conventional treatment options for these conditions.

Low Back Pain

The Wolfe et al. (2024) systematic review and meta-analysis synthesized evidence from 14 randomized and quasirandomized trials evaluating transcutaneous electrotherapies for chronic low back pain (CLBP) in adults aged 18 to 70 years. Eligible individuals had pain lasting at least 12 weeks, without radicular symptoms or major spinal pathology, and studies required a minimum of eight treatment sessions per group. Interventions included transcutaneous electrical nerve stimulation (TENS), IFT, and electromyostimulation (EMS), delivered either as stand-alone or mixed protocols. Comparators were active controls such as exercise, massage, or cryotherapy and passive controls such as sham stimulation or usual care. Primary outcomes were pain and disability, assessed with validated scales [VAS, Numeric Pain Rating Scale, Oswestry Disability Index (ODI), Roland-Morris Disability Questionnaire], while secondary outcomes included QOL, fear-avoidance beliefs, and depression. Meta-analyses found no significant differences between TENS and either active or passive controls for pain at post intervention (SMD, 0.43, 95% CI, -0.67 to 1.53, $p > 0.05$; SMD, -0.36, 95% CI, -1.21 to 0.49, $p > 0.05$) or for disability (SMD, 0.60, 95% CI, -0.57 to 1.76, $p > 0.05$). In contrast, IFT demonstrated superiority to controls in two studies: pain reduction (MD, -11.34; 95% CI, -20.91 to -1.77; $p = 0.032$) and disability improvement (MD, -13.38; 95% CI, -21.78 to -4.97; $p = 0.002$). EMS showed mixed results; while generally similar to active controls, it was significantly better than passive controls for pain in some trials (e.g., whole-body EMS vs no intervention; MD, 0.67; 95% CI, 0.18-1.21; $p = 0.028$). Subgroup analyses suggested that these effects were largely short term, with limited data beyond 3 months. Psychosocial outcomes and QOL could not be meta-analyzed due to

insufficient data. Across analyses, heterogeneity was high (I^2 often > 80%), and all included studies carried at least some concerns for risk of bias, primarily due to absent protocols and selective reporting. The authors concluded that IFT may provide incremental benefits over active comparators, although evidence remains limited. However, findings should be interpreted cautiously, given the methodological limitations, small sample sizes, and high heterogeneity.

Rampazo et al. (2023) conducted a systematic review and meta-analysis to assess the effectiveness of IFT in people with non-specific CLBP. The review included 13 RCTs, with a pooled sample size of 1,367 individuals. The authors reported that the main results showed moderate-quality evidence and moderate effect sizes that IFT probably reduced pain intensity and disability compared with placebo immediately post treatment but not at the intermediate-term follow-up, while low-quality evidence, with a small effect size, showed that IFT may reduce pain intensity compared with TENS immediately post treatment but not for disability. The authors also reported that there is very low-quality evidence that IFT combined with other interventions may not further reduce pain intensity and disability compared with the other interventions provided in isolation immediately post treatment. Limitations of the review include the variability in treatment protocols and study designs, disproportionate number of female individuals to male individuals, and heterogeneity of the comparison therapies. The authors concluded that moderate-quality evidence showed that IFT was probably better than placebo for reducing pain intensity and disability immediately post treatment in people with non-specific CLBP, and they suggested that future trials were needed to investigate IFT efficacy compared with that of other interventions and when combined with other interventions. This systematic review and meta-analysis included the Espejo-Antúnez et al. (2021) and Franco et al. (2017) RCTs, which were previously included in this policy.

Rajfur et al. (2017) conducted a pilot study to compare the effects of treating LBP using selected electrotherapy methods, assessing the influence of individual electrotherapeutic treatments on reduction of pain, improvement of the range of movement in the lower section of the spine, and improvement of motor functions and mobility. Individuals were assigned to six comparison groups: conventional TENS (A), acupuncture-like TENS (B), high-voltage electrical stimulation (C), IFT stimulation (D), diadynamic current (E), and control group (F). Of the 127 qualified individuals, 123 completed the 3-week study. The authors determined that selected electrical therapies (IFT, TENS, and high-voltage electrical stimulation) appear to be effective in treating CLBP.

Disorders of the Knee

The Chen et al. (2025b) network meta-analysis synthesized data from 139 RCTs, involving 9,644 adults with mild to moderate knee OA that was diagnosed according to American College of Rheumatology criteria and Kellgren-Lawrence grading. Trials were conducted internationally in clinical and rehabilitation settings, with follow-up durations ranging from 2 to 240 weeks. Eligible individuals were aged 18 years or older and had knee pain; studies excluded individuals with prior knee surgery, systemic inflammatory or infectious disease, recent intra-articular injections, or prior PT within 1 year. The analysis compared 12 PT interventions (IFT, low-level and high-intensity laser therapy, TENS, short-wave diathermy, ultrasound, lateral wedged insoles, knee braces, exercise, hydrotherapy, Kinesio taping, and extracorporeal shock wave therapy) against each other and placebo. The outcomes assessed at the last follow-up included Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain, function, stiffness, and total scores as well as VAS scores at rest and during activity. Across all outcomes, knee brace ranked highest for improving WOMAC pain, function, and stiffness, while hydrotherapy was most effective for total WOMAC score and VAS-rest. Exercise consistently performed well, particularly for pain and function. IFT demonstrated moderate efficacy but did not achieve statistically significant superiority over comparators. For example, IFT vs placebo yielded a WOMAC pain effect size of 0.87 (95% CI, 0.00-7786.47), VAS-rest of 1.18 (0.20-6.84), and VAS-activity of 1.78 (0.43-7.36), with none reaching statistical significance. Most included trials were rated at a low risk of bias, although some had unclear allocation concealment or blinding, and wide CIs in several comparisons reflect variability and small sample sizes. Limitations include the language restriction to English, heterogeneity in intervention protocols, and absence of detailed subgroup analyses for IFT. Clinically, these findings suggest that IFT may offer modest benefits but lack strong evidence for superiority over other treatment modalities. (Artuç et al., 2023, previously cited in this policy, is included in this network meta-analysis.)

Chen et al. (2022a) conducted a systematic review and meta-analysis to assess the effectiveness of IFT in individuals with knee OA. The authors searched PubMed, the Cochrane Library, Embase, ClinicalKey, and Scopus for relevant studies from their date of launch to March 22, 2022. They included RCTs in which IFT was applied to individuals with knee OA and the outcomes of pain scores or functional scales were assessed. Ten RCTs, with 493 individuals, met the inclusion criteria. Nine RCTs were included in the meta-analysis. The IFT groups exhibited significant improvements relative to the control groups for short-term pain scores (SMD, -0.64; 95% CI, 1.04 to -0.25; p = 0.001), long-term pain scores (SMD, -0.36; 95% CI, -0.60 to -0.11; p = 0.005), and short-term WOMAC scores (SMD, -0.39; 95% CI, -0.77 to -0.02; p = 0.04). All included studies did not observe any obvious adverse effects of IFT. The authors concluded that IFT can be recommended as a treatment for knee OA because it improves short- and long-term pain and short-term function. However, they recommended large-scale and high-quality RCTs, with longer follow-up, to establish an appropriate standardized treatment. Limitations to this study include the moderate to high heterogeneity for some results, as the IFT

devices, IFT parameter settings, and treatment protocols used by the included studies were inconsistent. In addition, some of the included studies did not implement blinding of therapists and individuals, resulting in risks of bias that may have affected the results of this study. Finally, five of the 10 RCTs reported immediate outcome measurements on treatment completion, thereby limiting the applicability of long-term results. Well-designed, adequately powered, prospective, controlled clinical trials of IFT are needed to further describe safety and clinical efficacy. (Alqualo-Costa et al., 2021, previously cited in this policy, is included in this systematic review and meta-analysis.)

Kadı et al. (2019) conducted a single-center, double-blinded RCT to investigate the effectiveness of IFT following total knee arthroplasty (TKA). Of the 98 people who completed the study, 49 were in the treatment group, in which they received IFT for 30 minutes, twice a day for 5 days post operation, and 49 were in the sham control group, in which the same pads were applied but no IFT stimulation was given. At baseline, there were no statistically significant differences between the groups with respect to demographics and clinical data. The authors concluded that no significant difference was seen between the two groups in pain, ROM, and edema at days 0, 5, and 30 and that IFT was not shown to be an effective modality for pain management in participants who had undergone TKA. They observed that the amount of paracetamol used was significantly lower in the IFT group; however, the authors noted that the difference did not continue after the end of the first month, and they stated that this result cannot be construed as demonstrating the effectiveness of IFT. The main limitations documented by the authors included the relatively short duration of the treatment and lack of preoperative data for the participants. They recommended that high-quality, multicenter RCTs and studies with long-term follow-up be conducted to show the exact effects of IFT on functional recovery when it is added as a supplement to a postoperative rehabilitation program.

Zeng et al. (2015) performed a systematic review and Bayesian network meta-analysis of 27 RCTs over a 30-year period, which compared different electrical stimulation therapies (high-frequency TENS, low-frequency TENS, NMES, IFT, pulsed electrical stimulation, and noninvasive interactive neurostimulation) with the control group (sham or no intervention) for relief of knee pain in 1,253 people with OA. The primary goal was to identify whether the different electrical stimulation modalities offered pain management by measuring the degree of pain intensity and the change pain score at the last follow-up time point. Of the six therapy modalities, IFT was the only significantly effective treatment in both pain intensity and changed pain scores at the last follow-up time point compared with the control group. In addition, IFT was deemed the best probable option for pain relief among the six therapy modalities. The authors' conclusions were that IFT is the most promising for the management of knee pain related to OA. The other electrical stimulation therapies were considered safe for individuals with knee OA, although some were considered inappropriate. The study limitations include the small number of included trials, heterogeneity of the evidence, and indirectness of comparisons inherent to network meta-analyses.

Bone Fractures

Duran et al. (2024) performed a double-blinded, randomized, placebo-controlled trial to evaluate whether adding IFT to a standard orthopedic rehabilitation program would improve shoulder function, pain, and disability in participants with conservatively treated proximal humeral fractures. Conducted at a physical medicine and rehabilitation outpatient clinic, the study enrolled 35 participants aged 40 to 80 years within 2 weeks of fracture occurrence, excluding those with prior shoulder surgery, electrotherapy experience, contraindications to IFT, rheumatic disease, additional fractures, or systemic conditions such as diabetes. Participants were randomized to IFT (n = 18) or sham IFT (n = 17), both receiving identical rehabilitation three times weekly for 4 weeks. IFT was applied for 20 minutes before exercise sessions using medium-frequency currents (4,000-4,100 Hz) to achieve a strong but comfortable tingling sensation, without muscle contraction, while sham therapy involved electrode placement without stimulation. The primary outcome was shoulder function assessed by the Constant-Murley Score (CMS), with secondary outcomes including activity pain (VAS), disability [Disabilities of the Arm, Shoulder, and Hand (DASH)], and weekly paracetamol intake. Measurements were taken post treatment, at 6 weeks, and at 18 weeks. Both groups demonstrated significant intragroup improvements over time in CMS, the VAS, the DASH, and paracetamol use ($p < 0.001$ for all), but no statistically significant differences emerged between the IFT and sham groups for any outcome. For example, CMS increased from 57.0 ±7.7 to 79.6 ±9.4 in the IFT group and from 48.2 ±12.0 to 69.3 ±14.2 in the sham group, with between-group interaction ($p = 0.727$). Similarly, VAS activity pain decreased from 3.9 ±1.5 to 0.7 ±1.1 in the IFT group and from 4.7 ±1.5 to 1.7 ±1.4 in the sham group, and DASH scores improved from 28.0 ±11.0 to 7.7 ±7.3 vs 38.4 ±17.5 to 12.5 ±11.3, respectively, with no significant intergroup differences. No adverse effects were reported. The authors noted that the study's limitations include the absence of a rehabilitation-only group, lack of baseline CMS and DASH score due to initial immobilization, and small sample size. These factors may limit interpretation of placebo effects and generalizability. The findings suggest that IFT does not confer additional benefit over sham therapy when combined with early mobilization and structured rehabilitation.

Nonsurgical Soft Tissue Injuries and Other Musculoskeletal Disorders

A triple-blinded RCT by Hussein et al. (2025), conducted between May and November 2024, enrolled 120 participants aged 17 to 45 years (65% female) with chronic latent trigger points in the upper trapezius muscle, confirmed by Simon criteria. Participants were randomized into four groups: three experimental groups received IFT combined with standard manual techniques using amplitude-modulated frequencies of 4 Hz, 80 Hz, or 130 Hz, while the control group received manual therapy alone. Interventions were delivered three times per week for 4 weeks. Outcomes included pain intensity NRS, cervical lateral flexion ROM, neck disability index, average monthly pain episodes, and sleep quality (Insomnia Severity Index), assessed at baseline, post intervention, and for pain episodes and sleep quality at the 3-month follow-up. Posttreatment analysis showed significant improvements across all outcomes compared with baseline ($p < 0.02$). Between-group comparisons revealed that all IFT groups improved pain, ROM, and function more than the control ($p \leq 0.04$). The 4-Hz group demonstrated superior results for pain reduction compared with the 80-Hz group ($p = 0.002$) and for average pain episodes compared with both the 130-Hz and control groups ($p = 0.003$ and 0.002, respectively). Sleep quality improved most in the 4-Hz group, which was significantly better than all other groups ($p < 0.001$). Effect sizes for between-group differences were large for pain ($\eta^2 = 0.28$) and sleep quality ($\eta^2 = 0.44$). Limitations include the absence of long-term follow-up for pain, ROM, and function and the inability to measure pressure pain thresholds (PPTs). Generalizability is limited, but the results suggest that adding IFT (particularly at 4 Hz) to manual therapy may offer enhanced benefits for pain control, functional improvement, and sleep quality for individuals with chronic trigger points.

Hayes published an Evolving Evidence Review (2023; updated 2025) for the neo-GEN-Series System (product name NEO GeneSys 2k) for the treatment of neuropathic pain. Hayes did not find any relevant clinical studies, relevant systematic reviews, or professional society guidelines or practice statements that included the neo-GEN-Series System for neuropathic pain. They reviewed literature for their 2024 and 2025 updates and again did not find any published studies, systematic reviews, or practice guidelines.

In a single-center, prospective RCT, Tugay and Kul (2023) evaluated the effectiveness of IFT on ROM of joint and shoulder pain, functional status, and QOL in participants with subacromial impingement syndrome and to compare IFT with TENS and sham IFT. The study included 52 participants who were randomized into three groups, with group 1 (n = 17; male participants, 4; mean age, 51.8 years) receiving IFT, group 2 (n = 18; male participants, 3; mean age, 51.8 years) receiving TENS, and group 3 (n = 17; male participants, 2; mean age, 49.1 years) receiving sham IFT, with all participants also receiving hot-pack and exercise treatments. Therapy was provided for 3 weeks, five times a week for 20 minutes for each session. All participants were evaluated before treatment (T0), at the end of the eighth treatment (T1), and at the end of treatment (T2) with the AROM and VAS, DASH questionnaire for functional status, and Short Form-36 for QOL. The authors reported that there was significant improvement in effects on all of the ROM, VAS, and DASH questionnaire scores at T2 and on the scores in some subparameters of the Short Form-36 in all groups; however, there was no statistically significant difference at T2 between the groups. Limitations of the study include the single-center design, short follow-up period, and small number of participants in each arm of the study. The authors concluded that IFT and TENS exhibited equivalent results regarding ROM, pain, function, and QOL in participants with subacromial impingement syndrome, with no significant difference between IFT and TENS, and that adding IFT or TENS to hot-pack and exercise therapy did not result in any extra benefits.

In a systematic review and meta-analysis evaluating the efficacy of IFT in alleviating MSK pain in adults, Hussein et al. (2022) reviewed 35 RCTs of variable methodological quality, from which 19 trials were included in the meta-analysis. The RCTs included 14 studies involving LBP, seven with shoulder issues, six with knee pain, five with neck pain, two with lumbar discogenic pain, and one each for carpal tunnel syndrome and plantar fasciitis. In reviewing the methodologies, the studies included six that were placebo controlled, four that included IFT as part of the control or standard therapy, and 25 that included IFT as part of the experimental arm or compared IFT with another experimental treatment. The results of the critical appraisal for the studies revealed that 16 of the 35 RCTs were of high methodological quality, 16 were of medium quality, and three studies demonstrated low quality. The 19 trials that they included in the meta-analysis provided a total sample size of 1,167 individuals. The other trials were not included in the meta-analysis due to a lack of required data, the inclusion of IFT as part of the standard treatment arm, or because they consisted of more than one experimental IFT or control group. The authors determined that in general, IFT could have a significant pain-relieving effect compared with placebo; however, the low number of studies raised suspicions about this conclusion. The authors also concluded that IFT showed no significant difference when it was added to a standard treatment protocol compared with placebo plus standard treatment or compared with standard treatment alone. They also found that IFT showed no significant difference when compared with other single interventions such as laser, TENS, or cryotherapy. Limitations identified by the authors include the heterogeneity of the population of the trials, exclusion of non–English language publications, subjective nature of the pain measures, and lack of a validation study in the quality assessment method used in the review.

Albornoz-Cabello et al. (2019) conducted a single-blinded, single-center RCT to investigate the effects of adding IFT to usual care after surgery in adults with subacromial pain syndrome (SAPS). The study included 56 adults with SAPS who

underwent acromioplasty in the past 12 weeks. All participants underwent a 2-week intervention, three times a week of either a 15-minute IFT electromassage plus usual care (treatment group; n = 28) or usual care only (control group; n = 28). There were no adverse reactions or dropouts during the study protocol. A blinded evaluator collected outcomes at baseline and after the last treatment session. The authors concluded that IFT plus usual care resulted in significant improvement in shoulder pain intensity, upper limb function, and shoulder flexion, abduction, and internal and external rotation; however, there was no difference between groups for shoulder extension and adduction. The authors stated that the study is limited by the lack of a sham IFT group, that there was a lack of data beyond the immediate results after the last treatment, and that the therapist who provided the interventions was not blinded to the participant allocation group. They recommended further research to investigate if different results would be expected using different IFT current parameters and to identify the medium- and long-term effects of IFT on postoperative pain in adults with SAPS.

Dissanayaka et al. (2016) compared the effectiveness of TENS and IFT in a single-blinded RCT in participants with myofascial pain syndrome. The aim of this study was to compare the effectiveness of these treatment modalities, both in combination with hot pack, myofascial release, AROM exercise, and a home exercise program in participants with myofascial pain syndrome with an upper trapezius myofascial trigger point. A total of 105 participants were randomly allocated among three therapeutic groups of 35 participants each: control/standard care (hot pack, AROM exercises, myofascial release, and a home exercise program with postural advice), TENS/standard care, and IFT/standard care. Therapeutic regimens were administered eight times during 4 weeks at regular intervals. Pain intensity and cervical ROM (cervical extension, lateral flexion to the contralateral side, and rotation to the ipsilateral side) were measured at baseline, immediately after the first treatment, before the eighth treatment, and 1 week after the eighth treatment. Immediate and short-term improvements were marked in the TENS group compared with the IFT group and the control group with respect to pain intensity and cervical ROM. The IFT group showed more significant improvement in these outcome measurements than the control group. The authors concluded that TENS with standard care facilitates recovery better than IFT in the same combination.

Clinical Practice Guidelines

American College of Physicians (ACP)

In their clinical practice guideline addressing noninvasive treatments for acute LBP, subacute LBP, and CLBP, the ACP states that evidence is insufficient to determine the effectiveness, benefits, and harms, if any, of IFT. Clinicians and patients should initially select nonpharmacological treatments, including but not limited to exercise (e.g., tai chi, yoga, motor control exercise) and multidisciplinary rehabilitation (e.g., electrical stimulation therapies) when managing CLBP (Qaseem et al., 2017).

National Institute for Health and Care Excellence (NICE)

NICE published a guideline for the management of knee OA, in which they concluded that IFT should not be offered to people with OA because there is insufficient evidence of benefit. The guideline stated that although there are many studies on electrotherapy, the findings were inconsistent and mostly showed little benefit. The committee found that most studies were small, with less than 100 individuals, and that the evidence from direct comparisons of electrotherapy with other interventions was uncertain (2022).

NICE guidance on the assessment and management of all chronic primary pain included guidance on TENS, ultrasound, and IFT for chronic primary pain and found no evidence for IFT. The committee noted that IFT has been around for some time, so it is unlikely that new research will be done. The committee agreed that IFT should not be offered for chronic primary pain and made a recommendation against its use (2021).

NICE updated their guidance on the use of TENS, percutaneous electrical nerve stimulation (PENS), and IFT for managing LBP with or without sciatica and stated that these modalities should not be offered for the treatment of LBP due to the paucity of evidence available that included mostly small, individual studies of low or very low quality. No difference between interventions was seen when comparing IFT with sham or traction in people with LBP without sciatica or when IFT was combined with education, exercise, and self-management. The committee found that the studies had inconsistencies across domains and in terms of their efficacy in the long or short term. The Guideline Development Group concluded that there is a lack of evidence of clinical benefit to support a recommendation for the use of IFT as a treatment for LBP or sciatica (2016; updated 2020).

Microcurrent Electrical Nerve Stimulation Therapy

Microcurrent electrical nerve stimulation (MENS) therapy has been studied in several small RCTs and case series for conditions such as delayed onset muscle soreness (Curtis et al. 2010) and diabetes, hypertension, and chronic wounds (Lee et al., 2009). None of these studies are large, controlled trials designed to test the effectiveness of MENS therapy against a placebo device. Therefore, due to the limited evidence in the peer reviewed literature, conclusions cannot be

reached regarding the safety, efficacy, or utility of MENS therapy to decrease pain and/or facilitate healing for any condition.

The Maeda et al. (2025) prospective, single-center, three-group, parallel study evaluated the effects of TENS and MENS therapy on pain relief and knee function following TKA. Overall, 35 participants with end-stage knee OA scheduled for primary TKA were enrolled between August and November 2024, with a mean age of 70.9 years. Participants were randomized by envelope method into TENS (n = 13), MENS (n = 11), or control (n = 11) groups, all receiving standard postoperative rehabilitation. Interventions began on postoperative day 3 and were administered five times per week for 2 weeks using standardized electrode placement. Outcomes included pain intensity during walking (w-pain, measured by the VAS), maximum walking speed, TUG, and isometric knee extension strength (IKES), assessed prior to the operation and at 2 and 4 weeks post operation. Pain Catastrophizing Scale score was measured prior to the operation. At 2 weeks, w-pain was significantly lower in the TENS group than both MENS and control groups ($p < 0.05$), with mean VAS scores of 21.5 mm with TENS vs 41.1 mm with MENS and 43.6 mm with the control. Maximum walking speed was significantly faster in the TENS group than in the MENS group at 2 weeks ($p < 0.05$), although the difference between TENS and the control was not statistically significant. No significant between-group differences were observed for the TUG or IKES, which improved gradually over time across all groups. Subgroup analyses did not reveal additional significant findings. Limitations include the small sample size, missing data due to ward closures, and standardized electrode placement that may have reduced MENS efficacy. These results suggest that TENS provides superior early postoperative pain relief and modest improvement in walking speed compared with MENS, while MENS showed no advantage over the control. Threats to validity include limited power and lack of participant-reported outcome measures.

In a systematic review and meta-analysis, Bavarian et al. (2024) assessed the efficacy of MENS therapy in treating myofascial pain of the masticatory muscles. The systematic review included four RCTs, with a pooled population of 159 individuals (age range, 13-60 years; 64.8% female) who had a diagnosis of masticatory myofascial pain disorder. The meta-analysis included three RCTs, with a pooled population of 140 individuals. All studies used pain measured by VAS score as a primary outcome. The duration of therapy ranged from 5 days to 4 weeks, and outcome assessments were completed immediately after each treatment session. The authors reported that treatment with MENS showed an improved mean reduction in pain by an additional -0.57 points compared with the control groups. Limitations of the systematic review and meta-analysis include the limited number of studies available for inclusion, small total sample size, and heterogeneity of the study designs such as inclusion criteria, therapy protocols, control group comparison therapies used, and follow-up periods. The authors concluded that evidence from the meta-analysis showed that MENS therapy was an effective, noninvasive treatment option to reduce pain in individuals with myofascial pain of the masticatory muscle, and they recommended that more robust RCTs, with standardized protocols and larger sample sizes, be conducted.

Jha et al. (2023) conducted a single-center comparative study to compare the effectiveness of TENS and MENS for the relief of masticatory muscle discomfort. The four-arm study included 120 adults with a diagnosis of masticatory muscle pain who were divided into two groups of 60 participants (each having 36 male and 54 female participants; mean age, 32.4 years; range, 18-54 years). Groups I and II were further separated into two subgroups of 30 participants (group I into subgroups A and B and group II into subgroups C and D) based on their VAS scores, with groups 1A and 2C having VAS scores of 1 to 5 and groups 1B and 2D having VAS scores of 6 to 10. VAS scores were also assessed each day and at 1 month following therapy. Group I participants received TENS, and group II received MENS, with each participant receiving electrical stimulation for 5 consecutive days. Participants were instructed not to use any additional medications to manage their masticatory muscle pain for 1 month following the therapy. The authors reported that there was a considerable reduction in pain in subgroup D, which was treated with MENS; however, in subgroups A and C, there was a comparable reduction in VAS score in both groups treated with MENS and TENS therapy. When evaluating the mouth-opening improvement in the MENS and TENS groups, the authors reported that there was an instantaneous and sustained rise at the 1-month recall from day 0 and that for the MENS group, a statistically significant improvement in mouth opening was observed starting on day 3 that persisted through 1-month recall after MENS. The authors concluded that MENS provided quicker and more effective pain relief compared with TENS. The authors also found that paresthesia and tingling were two adverse effects of TENS that were not found with MENS; however, MENS and TENS were equally helpful at treating masticatory muscle discomfort as well as improving mouth opening. Limitations of the study include the single-center design, limited sample size, and short follow-up period.

A systematic review and meta-analysis completed by Iijima and Takahashi (2021) determined that microcurrent therapy (MCT) significantly improved shoulder pain and knee pain compared with sham MCT, without any severe adverse events. Their review included four RCTs and five non-RCTs that studied the effectiveness of MCT for treating neck pain (one non-RCT), shoulder pain (one RCT), elbow pain (one non-RCT), LBP (one RCT and two non-RCTs), and knee pain (including the Lawson et al., 2021, and Ranker et al., 2020, RCTs below and one non-RCT). No serious adverse events requiring medical treatment were reported among the 281 pooled individuals. The authors also stated that placebo response may

be joint- or disease-dependent and that sham MCT may elicit a clinically beneficial response in subacute to chronic knee pain, as was supported by the high quality of evidence established by using GRADE, and with high reproducibility using the TIDieR (Template for Intervention Description and Replication) checklist. The authors noted that (1) their review was limited by only having a single reviewer rather than the preferred independent review by two reviewers; (2) their review did not include studies in which MCT was compared with other treatment approaches; and (3) the small number of included studies limited their analysis, so generalizability could not be addressed. They suggested that future research includes high-quality clinical trials for shoulder pain and LBP as well as the treatment effects of MCT on pain from multiple sites and studies on the mechanism of MCT itself.

Lawson et al. (2021) conducted a double-blinded, placebo-controlled RCT to determine if MENS increased function and decreased pain in people with acute knee pain. The study was conducted in their university laboratory and in the homes of the 52 self-referred study participants. The participants were randomized into the treatment group (n = 26) or placebo-control group (n = 26). Participants wore electrodes with the active or placebo microcurrent treatment for 3 consecutive hours per day and abstained from pain or anti-inflammatory medications throughout the 4-week study. Daily text reminders were sent to use the device. This method demonstrated high adherence, as it required participants to respond affirmatively or repetitive reminder texts would be sent until confirmation of adherence was achieved. The authors reported that the study showed a trend in increased function that correlated well with a decrease in pain, especially in the third week, and decreased effusion on MSK ultrasound imaging over the first 2 weeks in the active MENS group vs the placebo group. Limitations noted by the authors include the small number of participants; use of the Lower Extremity Function Scale, as it appeared to not be sensitive enough in this population to capture changes in function; and lack of long-term follow-up. They concluded that MENS decreased knee pain and increased function and that it may be an alternative or be used with a pharmacological approach for people with acute knee pain. The authors recommended that future studies evaluate the effect that MENS has on edema via MSK ultrasound elastography and the effect that different dosages of MENS have in the perception of specific acute knee pain and function; they recommended that longer-term follow-up should be conducted to observe the posttreatment effect of MENS on pain, function, muscle, or edema and the effect of MENS on chronic knee pain, especially in knee OA.

A retrospective case-control study by Shetty et al. (2020) showed that a higher percentage of adults treated in their facility with adjuvant frequency-specific microcurrent (FSM), in addition to physical rehabilitation for LBP, had significantly improved pain and disability compared with patients in a control group who chose to not receive FSM. In their study, they retrospectively reviewed data from the records of 213 patients (167 with LBP and 46 with neck pain) who received FSM, in addition to a personalized therapy program, along with the records of 78 patients (61 with LBP and 17 with neck pain) who only received a personalized therapy program. Each patient's rehabilitation protocol was varied and personalized based on their severity of pain and response to movement testing. All patients underwent a minimum rehabilitation period of 30 days, with a maximum of 90 days and a minimum of six supervised physiotherapy sessions at the clinic. The authors concluded that the use of adjuvant FSM therapy, along with active rehabilitation, significantly reduced pain and disability compared with patients treated with active rehabilitation alone for LBP; however, the addition of FSM to therapy did not appear to significantly affect clinical outcomes of pain and disability in patients with neck pain. The authors noted that their study was limited by its retrospective design; additionally, they noted that the reporting period for results of 90 days did not reflect medium- and long-term implications of adjuvant FSM therapy, and the study measurements did not consider the effect of neurophysiological and psychosocial factors. They recommended future well-designed, placebo-controlled, randomized trials to confirm the benefits of adjuvant FSM therapy for treating LBP or neck pain.

In a single-center, four-arm, double-controlled pilot RCT, Ranker et al. (2020) evaluated the potential effects of microelectrical therapy (MET) on pain in participants with knee OA to explore the effects of different treatment parameters and to distinguish these effects from placebo effects. The study included 52 participants who were randomized into four groups: MET with 100 µA (n = 14), MET with 25 µA (n = 13), a sham treatment group (n = 12), and a control group with no intervention (n = 13). In the intervention groups, all participants received 10 treatment sessions total, given over a 3-week period. The participants and therapists were blinded to the treatment allocation. The authors observed that evening pain was reduced significantly in the groups that received MET compared with the sham and control groups. They also found that the difference between the sham group and the control group was not significant and that all but the sham group improved in ADL. They concluded that MET has beneficial effects on pain in people with OA that are not explained by a placebo effect; however, they also recognized that further confirmation is needed before recommendations can be given. Limitations of the study that were noted by the authors include the lack of systematic tracking of additional therapies during the study and of self-medication of analgesics that could bias the results.

Kwon et al. (2017) conducted a prospective, double-blinded, sham-controlled RCT to evaluate the effects of short-term MENS on muscle function in elderly participants. A total of 38 healthy participants, aged 65 years and above, were enrolled and randomly divided into a real MENS or a sham MENS stimulation group. Both groups received stimulation to the eight anatomical points of the dominant arm and leg during the course of 40 minutes. The authors reported that their

hypothesis was accurate that real MENS was superior to sham in enhancing muscle function in healthy elderly participants following short-term application. Limitations to this study include the lack of definition of the “healthy elderly,” short application time of the MENS, and lack of follow-up evaluation. Long-term RCTs, with follow-up assessments, are needed to confirm these results.

Gossrau et al. (2011) conducted a single-blinded, placebo-controlled, randomized trial to assess the efficacy of MENS for the reduction of painful diabetic neuropathy (PDN) in 41 participants who were divided into two groups: 22 treated with MENS therapy and 19 with placebo. The treatment plan was three therapy sessions per week for 4 weeks. Primary outcomes measured included pain intensity, pain disability, and QOL at baseline, at the end of treatment, and 4 weeks post treatment using standardized questionnaires. Participants with a minimum of 30% reduction in Neuropathic Pain score were defined as therapy responders. After 4 weeks, only six of 21 participants in the study group (30%) had responded to MENS therapy vs 10 of 19 (53%) in the placebo group. The differences in Pain Disability Index in both groups were not statistically significant. The authors concluded that MENS therapy for PDN is not superior to placebo.

Percutaneous Electrical Nerve Stimulation

While some studies have compared the effectiveness of PENS with that of placebo, the overall quality of the evidence is weak and quite limited as published studies have included small study populations and short-term follow-ups. Further robust studies are needed to evaluate the efficacy of this therapy for chronic pain.

Caballero-López et al. (2025) performed a prospective RCT to evaluate the short-term effects of ultrasound-guided PENS on pain and muscle function in participants undergoing ACL reconstruction. Overall, 70 participants aged 18 to 55 years, within 2 to 6 weeks post surgery who had a VAS pain score of at least 2 out of 10, were randomized into two groups: one received two sessions of femoral nerve PENS combined with a 12-week rehabilitation program (n = 35), and the other underwent rehabilitation alone (n = 35). Exclusion criteria included metabolic or rheumatic disease, chronic illness, prosthesis or osteosynthesis, cardiac or CNS disorders, and contraindications to invasive techniques. Both groups followed standardized rehabilitation protocols, while the PENS group received additional ultrasound-guided stimulation using a 30 × 0.40-mm needle and electrical parameters of 2-Hz frequency and 240-μs pulse duration. The primary outcomes included pain intensity (VAS), PPT at the quadriceps and patellar tendons, IKES, and knee ROM, assessed at baseline, immediately after each intervention, and at 4 and 12 weeks. A post hoc analysis revealed statistically significant short-term reductions in pain intensity in the PENS group compared with the control immediately after the first intervention ($p = 0.00$), after the second intervention ($p = 0.003$), and at 4 weeks ($p = 0.003$). Mean isometric quadriceps strength also improved significantly after the first PENS session ($p = 0.049$), although no sustained group-by-time interaction was observed ($p = 0.695$). Both groups demonstrated significant improvements in knee flexion ($p < 0.001$) and extension ($p = 0.021$) ROM at 12 weeks, and the PENS group showed greater PPT gains at the patellar tendon over time. Limitations include the short follow-up period, inclusion of only two PENS sessions, and lack of psychological factor assessment, which may affect long-term outcomes. Clinically, these findings suggest that PENS may offer immediate benefits in pain reduction and quadriceps activation, potentially facilitating early rehabilitation engagement, although its long-term advantage over standard rehabilitation remains unproven.

Li et al. (2024) performed a multicenter RCT with a 2 × 2 factorial design to evaluate the effectiveness of electroacupuncture (EA) and low-dose carbamazepine (CBZ) for trigeminal neuralgia (TN). Conducted at two tertiary care centers, the study enrolled 120 participants aged 18 to 80 years (mean age, 58.5 years; 62.5% female) who met diagnostic criteria for TN, had a baseline VAS pain score of ≥ 5, and experienced attacks more than three times per day on at least 4 days per week. Participants were randomized equally into four groups: EA plus CBZ (300 mg/day), sham EA plus CBZ, EA plus placebo, and sham EA plus placebo. EA or sham EA was administered for 60 minutes, three times weekly for 4 weeks, while CBZ or placebo was given orally for the same duration. The primary outcome was change in VAS score from baseline to weeks 2, 4, 16, and 28; secondary outcomes included the Pain Rating Index (PRI), present pain intensity, number of pain attacks, QOL measures, and adverse events. Both EA and CBZ produced statistically significant main effects on VAS reduction ($p < 0.001$), and their interaction was significant ($p = 0.041$). Compared with controls, EA alone reduced VAS scores by MDs of -0.3 (95% CI, -0.40 to -0.20) at week 2, -1.6 (-1.70 to -1.50) at week 4, -1.1 (-1.31 to -0.89) at week 16, and -0.8 (-1.01 to -0.59) at week 28. CBZ alone showed reductions of -0.6 (95% CI, -0.70 to -0.50) at week 2 and -0.9 (-1.03 to -0.77) at week 4, but effects were not significant at weeks 16 and 28. The combination of EA and CBZ achieved the greatest benefit, with reductions of -1.8 (95% CI, -1.90 to -1.70) at week 2, -3.7 (-3.83 to -3.57) at week 4, -3.4 (-3.61 to -3.19) at week 16, and -2.9 (-3.11 to -2.69) at week 28. EA also significantly improved the PRI, present pain intensity, and QOL scores, while CBZ showed limited benefit beyond PRI. Adverse events were more frequent with CBZ (25.4%) than EA (10.2%), and all were mild to moderate. Limitations include the use of a fixed EA protocol rather than individualized treatment and absence of comparison with higher CBZ doses. The study’s rigorous design, including successful blinding and standardized interventions, supports the validity of its findings. Clinically, combining EA with low-dose CBZ may offer enhanced pain relief and improved QOL in individuals with TN who cannot tolerate higher CBZ doses.

Rodriguez Lagos et al. (2023) conducted a systematic review and meta-analysis to determine the effects of PENS and TENS on endogenous pain mechanisms in individuals with MSK pain. There were 24 RCTs included in the qualitative analysis and 23 in the meta-analysis. Overall, 14 of the studies used TENS (n = 1,136), 10 used PENS (n = 808), and one used PENS and TENS (n = 133). In the PENS studies, four used EA, four used electrical intramuscular stimulation, and two used electrical dry needling. In total, 16 studies compared with a sham or placebo group, eight added one intervention and compared with that intervention, and two compared with a control group without intervention. Regarding the outcome measures, 23 measured local PPTs. Most studies conducted a single treatment session (n = 15), one included 16 treatment sessions, and the rest of the studies included two to 10 sessions. All studies measured the immediate results, eight studies measured short-term results, two measured mid-term results, and none measured long-term results. The authors reported that the immediate effects of PENS and TENS on local PPTs were significant, with a moderate effect size, and that when the authors analyzed studies only with a lower risk of bias, the heterogeneity decreased and a decrease in the overall effect was also observed. The authors reported that the short-term effects on local PPTs were not significant compared with the control group and that both the mid-term effects on local PPTs and the immediate effects on conditioned pain modulation were significant, with a large effect size. The authors concluded that PENS and TENS have a mild to moderate immediate effect on local mechanical hyperalgesia in individuals with MSK pain and that it appeared that these effects were not sustained over time. The authors also concluded that their analysis suggested an effect on central pain mechanisms that produced moderate increases in remote PPT and an increase in conditioned pain modulation. Further studies are recommended to draw clearer conclusions.

Fernández-de-Las-Peñas et al. (2023) conducted a single-center, randomized, parallel-group trial to compare the outcomes of the application of ultrasound-guided PENS targeting the median nerve vs surgery for improving pain and function in women with unilateral carpal tunnel syndrome. The study included 70 adult women who were randomly assigned to either receive PENS (n = 70; age, 46 ±10 years) once a week for 3 weeks targeting the median nerve or undergo surgical/endoscopic decompression release of the carpal tunnel (n = 70; age, 47 ±7 years). The primary outcome was hand pain intensity, and secondary outcomes included functional status, symptom severity, and self-perceived improvement. Outcomes were assessed at baseline and 1, 3, 6, and 12 months after the end of the intervention. The authors reported that their analysis showed an adjusted advantage for PENS at 1 and 3 months for mean pain and at 1, 3, and 6 months for worst pain intensity and for function. The authors also reported that both groups showed similar changes in symptom severity and reported similar improvement at 12 months for all outcomes. The authors concluded that PENS is as useful as surgery for women with carpal tunnel syndrome without denervation. The study was limited by the single-center design, small sample size, lack of a control group, and lack of control for confounding variables.

Beltran-Alacreu et al. (2022) conducted a systematic review and meta-analysis to determine if the use of PENS is more effective compared with TENS for the reduction of MSK pain intensity in adults. The study included nine RCTs (n = 563) in the qualitative analysis and seven RCTs (n = 527) in the quantitative analysis. All the studies compared the effect of PENS vs TENS, with four of the studies including either a sham or placebo group. Six of the studies had a parallel design, and the other three were crossover studies. While the search period ended on December 31, 2020, the most recent study included in the review and meta-analysis was published in 2012. Individuals' diagnoses included LBP (n = 254), chronic neck and shoulder pain (n = 90), sciatica (n = 64), knee OA (n = 24), and chronic MSK pain (n = 131). Pain was the main outcome assessed (via the VAS and NRS), and the follow-up period ranged from 24 hours to 8 months. Protocols and parameters for PENS and TENS application were heterogeneous among the studies. The authors reported that there was a significant improvement in pain intensity, medication use, and QOL in favor of PENS, with a low recommendation level per GRADE guidelines, while there was a moderate recommendation level supporting no differences when TENS and PENS were used for pain intensity when only the three studies with a lower risk of bias were analyzed. The authors concluded that there was low quality of evidence for more pain intensity reduction with PENS, but the difference was not clinically significant; additionally, based on their findings, the authors did not recommend the use of PENS in a clinical setting as the first treatment step.

A Hayes Evidence Analysis Research Brief (2022) on the use of PENS for the treatment of LBP concluded that there were no relevant, newly published studies that met the inclusion criteria since they published their Health Technology Assessment on PENS in 2017 (archived August 2021). In the Health Technology Assessment, Hayes had identified three clinical studies that evaluated the safety and efficacy of PENS for CLBP and found that the body of evidence was of very low quality and was insufficient to make a definitive conclusion about PENS as monotherapy or in combination with PT in individuals with CLBP. The Health Technology Assessment noted that the results suggested a short-term (3-month) improvement in pain and pain-related disability from baseline; however, these differences were typically statistically but not clinically significant.

To evaluate the effects of PENS alone or as an adjunct intervention on pain and related disability in MSK conditions, Plaza-Manzano et al. (2020) conducted a systematic review and meta-analysis of 19 parallel or crossover RCTs with various MSK conditions, with short- or mid-term follow-ups. They found most studies to be of high methodological quality,

except for three that were considered poor quality; additionally, they found that most of the trials were biased due to the inability to blind the therapists and individuals; however, in general, the risk of bias in the meta-analysis was low. The authors concluded that there was a low level of evidence indicating that PENS, used in isolation, had a large effect compared with sham and a moderate effect compared with other interventions for decreasing pain intensity in the short term. The authors acknowledged that (1) the systematic review and meta-analysis was limited by the paucity of RCTs looking at the effect of PENS on specific MSK pain conditions; (2) the method of evaluation of PENS varied; and (3) the results of some of the RCTs were inconsistent and imprecise. They recommended that well-designed RCTs should be conducted to examine the effect of PENS alone or in combination with other therapeutic interventions, with long-term follow-up, and that the trials should be designed to compare the effect of real vs sham PENS as well as to study the most appropriate treatment parameters and anatomical locations to create reproducible results.

In a single-center, double-blinded RCT, Kong et al. (2020) evaluated the effect of EA on pain severity in adults with CLBP. The study included 121 adults who were randomized into either a treatment group (n = 59) or a sham group (n = 62) and then treated by one of 10 acupuncturists for 12 sessions of real or sham EA, administered twice a week over 6 weeks. Participants were followed up for 2 weeks beyond completion of the 6-week treatment protocol. The authors found no significant difference in CLBP scores between real and sham EA treatment; however, post hoc analyses did find a significant treatment effect of EA in reducing disability associated with CLBP. They stated that the finding of an association between positive coping strategies and functional improvement that was seen on both the univariate and multivariate analyses is unique to the study. The authors also found that White race was associated with worse outcomes in pain and feel that the racial influence may be caused by differences in cultural backgrounds, such as that participants with backgrounds that include traditional Chinese medicine may be more likely to respond to acupuncture. Limitations include that (1) the study does not quantify the specific effect of EA vs manual acupuncture; (2) there were missing blinding data due to implementation imperfections; and (3) the outcome collection spanned a total of only 10 weeks. The authors recommended larger studies, with multicultural samples and testing the interaction between cultural background and treatment allocation, as well as collecting longer-term outcomes.

Rossi et al. (2016) conducted a multicenter, prospective, observational study to evaluate the short- and long-term efficacy of a single-probe and single-shot PENS approach to treat chronic neuropathic pain. Overall, 76 participants affected by neuralgia were enrolled in the study and divided into three groups depending on the etiology of the neuralgia (21 herpes zoster, 31 causalgia, and 24 postoperative pain). In the study, the NRS and Neuropathic Pain Scale were assessed at baseline, 60 minutes after PENS, at 1 week, and 1, 3, and 6 months post therapy. Perceived health outcome was measured with the EQ-5D questionnaire at baseline and at 6 months. Pain assessment ratings decreased significantly after 60 minutes of PENS therapy, and the reduction remained constant throughout the follow-up period. Perceived health outcome measured with EQ-5D increased significantly from baseline. The authors concluded that PENS therapy produced significant and long-lasting pain relief in chronic peripheral neuropathic pain of different etiologies. The study limitations include the small sample size, nonrandomized observational design, short follow-up period, and high prevalence of postherpetic and occipital neuralgias.

Clinical Practice Guidelines

American Academy of Orthopaedic Surgeons (AAOS)

In the updated evidence-based clinical practice guideline on nonarthroplasty management of OA of the knee, the AAOS reviewed one high-quality study and downgraded their recommendation to one level to limited due to feasibility issues. The authors noted that PENS is feasible but requires a practitioner trained in PENS, which may limit access for some patients. The guideline stated that continued research, with larger RCTs that examine the long-term effectiveness of PENS, is needed and that studies that identify responders and nonresponders to PENS would also be important (2021; updated 2022).

National Institute for Health and Care Excellence (NICE)

NICE (National Guideline Center, 2016; updated 2020) recommends against the use of PENS for managing LBP with or without sciatica due to the paucity of evidence available that includes mostly small, individual studies of low or very low quality. No clinical benefit was found for PENS on improving pain and function compared with usual care in a mixed population of people with or without sciatica. Clinical benefit for pain and function was observed at less than 4 months, but no clinical benefit was found after 4 months. NICE noted that although there was evidence in places positive for people with LBP, it was of low quality, with low patient numbers. It was also noted that PENS is not widely used, so a recommendation for its use would be a significant change in practice. NICE concluded that there is insufficient evidence of clinical benefit to support a recommendation for the use of PENS for LBP or sciatica.

American Academy of Neurology (AAN)/American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM)/American Academy of Physical Medicine and Rehabilitation (AAPMR)

In a joint guideline report on the treatment of PDN (Bril et al., 2011), the AAN, AANEM, and AAPMR concluded that PENS should be considered for this indication, stating that it is probably effective in lessening pain and improving QOL (level B recommendation).

Percutaneous Electrical Nerve Field Stimulation

While some studies have compared the effectiveness of percutaneous electrical nerve field stimulation (PENFS) with that of placebo, the overall quality of the evidence is weak and quite limited, as published studies have included small study populations and short-term follow-ups. Further robust studies are needed to evaluate the efficacy of this therapy.

An Evolving Evidence Review by Hayes (2022; updated 2025) on the use of IB-Stim for the treatment of pain associated with irritable bowel syndrome (IBS) in adolescents was updated in 2024 to include a review of abstracts for four newly published, prospective, pretest-posttest studies and stated that there is no change to their no/unclear level of support of the use of this device for this indication. The update indicated that there is longer-term follow-up (up to 1 year) since the initial publication of their 2022 review and that there is a new application of the technology being investigated: the use of IB-Stim for cyclic vomiting syndrome (CVS). In the 2025 update, Hayes identified four newly published clinical studies as well as one new guideline but did not identify any systematic reviews that addressed the use of IB-Stim for this clinical indication. Hayes has not revised its assessment that there is no/unclear evidence-based support for this treatment.

Ilfeld et al. (2025) performed a randomized, double-masked, sham-controlled pilot study to evaluate the feasibility and analgesic effect of percutaneous auricular neuromodulation following primary unilateral TKA. Thirty adults scheduled for surgery at a single academic center between October 2022 and July 2023 were enrolled after receiving a single-injection adductor canal block with ropivacaine and epinephrine. Participants were randomized in the recovery room to five days of active electrical stimulation or sham treatment using the NSS-2 Bridge device, which was applied with three percutaneous leads and one ground electrode and left in situ during discharge. Inclusion criteria required age ≥ 18 years and ability to maintain contact during treatment; exclusions included chronic opioid use, neuromuscular deficits, opioid misuse history, bleeding disorders, anticoagulation, skin abnormalities, pregnancy, and pacemaker use. The dual primary outcomes were cumulative oral oxycodone consumption and mean daily “average” pain scores on the NRS during the first five postoperative days. Active stimulation significantly reduced opioid use [median 4 mg (IQR, 2 mg-12 mg) vs 13 mg (IQR, 5 mg-23 mg); $p = 0.039$] and pain intensity [median 2.5 (IQR, 1.5-3.3) vs 4.0 (IQR, 3.6-4.8); p = 0.014] compared with sham. Awakenings due to pain over eight nights were also lower with active treatment [median 5 (IQR, 3-8) vs 11 (IQR, 4-14); $p < 0.001$]. No device-related adverse events occurred, though three active participants removed devices early due to discomfort. Secondary outcomes, including worst and least pain scores and interference with physical and emotional functioning, favored active treatment but were not consistently statistically significant. The study’s strengths include rigorous randomization, masking, and use of validated pain measures, supporting internal validity. However, limitations include its small sample size, lack of a prespecified analysis plan, and inability to confirm continuous device function, which may affect reliability. The manufacturer donated devices but had no role in design, data analysis, or reporting; no competing interests were declared. Clinically, these findings suggest auricular neuromodulation may offer a simple, opioid-sparing adjunct without systemic side effects, but confirmation in a larger, adequately powered trial is essential before widespread adoption.

Ilfeld et al. (2024) performed a randomized, double-blinded, sham-controlled pilot study to evaluate the feasibility and analgesic effect of percutaneous auricular neuromodulation following ambulatory laparoscopic cholecystectomy or hernia repair. Conducted at the University of California, San Diego, between November 2022 and October 2023, the trial enrolled 30 adults aged 18 years or older who met the inclusion criteria and excluded those with chronic opioid use, opioid misuse history, neuromuscular deficits, bleeding disorders, anticoagulation, pregnancy, or contraindications to electrical stimulation. Participants were randomized in the recovery room to receive either active electrical stimulation or sham treatment using the NSS-2 Bridge device for 5 days. All participants were discharged home with the device in situ and received standard multimodal analgesia, including acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), and oxycodone as needed. The primary outcomes were cumulative oral opioid consumption and mean daily pain scores (NRS) over the first 5 postoperative days, with secondary outcomes that included pain interference, with physical and emotional functioning assessed by the Brief Pain Inventory. The median pain score during the initial 5 days was significantly lower in the active stimulation group at 0.6 (IQR, 0.3-2.4) compared with 2.6 (IQR, 1.1-3.7) in the sham group (p = 0.041). Opioid use did not differ significantly, with both groups reporting a median of 0 mg of oxycodone (active IQR, 0-1 mg; sham IQR, 0-3 mg; p = 0.524), and 67% of participants in each group avoided opioids entirely. Over the 8-day study period, severe pain occurred in only one participant (7%) receiving active stimulation vs seven (47%) in the sham group (p = 0.031). Active treatment also reduced pain interference with physical and emotional functioning on

postoperative days 4 and 6, and 47% of participants in the active group reported no interference throughout the study compared with 7% in the sham group (p = 0.031). No device-related adverse events were observed, although three participants removed devices early due to discomfort. Limitations include the small sample size, absence of a prespecified analysis plan, and inability to confirm continuous device function. These findings suggest that auricular neuromodulation may provide meaningful analgesia, without systemic side effects, warranting further investigation in a larger, adequately powered trial.

ECRI (2024; updated 2025) conducted an Evidence Analysis on the use of PENFS for treating abdominal pain in children with IBS, concluding that the evidence is generally favorable. ECRI considered evidence from eight studies, one of which was a double-blinded, sham-controlled RCT that showed that PENFS was safe and effective as a treatment for abdominal pain in children with IBS and other functional abdominal pain disorders (FAPDs). The analysis also included six pretest-posttest studies that were reported to improve functional disability associated with IBS and FAPDs. ECRI's report stated that the results of the studies were based primarily on 4 weeks of treatment, with most studies reporting outcomes up to the 12-week follow-up; however, long-term efficacy data were scant, and it was not clear whether treatment benefits were sustained long term. ECRI's analysis also included one retrospective study that compared PENFS with cyproheptadine and with amitriptyline that reported no statistical difference in abdominal pain and Functional Disability Inventory (FDI) score between the three treatments at the 3-month follow-up, and ECRI stated that this study provided very low-quality evidence and did not enable conclusions about comparative effectiveness. The Chogle et al. (2023), Chogle et al. (2024), Krasaelap et al. (2020), and Santucci et al. (2023) studies, summarized in this policy, were included in this evidence analysis.

Chogle et al. (2024) conducted a multicenter, prospective, open-label registry of children who underwent PENFS for disorders of the gut-brain interaction (DGBIs) to explore the efficacy of PENFS as a standard therapy for DGBIs. The study included 292 children between 8 and 18 years of age (74% female; median age, 16.3 years) who had functional dyspepsia (68%) and had experienced failure with four or more pharmacological therapies (61%). The Rome IV Diagnostic Questionnaire on Pediatric Functional Gastrointestinal Disorders, Abdominal Pain Index (API), Nausea Severity Scale (NSS), and FDI were completed at baseline and weekly during therapy, with a subset of participants completing follow-up surveys every 3 months up to 1 year post therapy. All participants were managed per standard practice conditions, and data were collected for up to 12 weeks of consecutive PENFS therapy. The authors reported that the API scores improved significantly from a baseline of 2.88 to 1.99 at 3 weeks, and further reductions were observed at 3 months and 6 months; the NSS scores similarly improved from a baseline of 2.53 to 1.65 at 3 weeks and stayed significantly reduced at 3 and 6 months, and the FDI scores decreased across time from a baseline of 20 to 12.0 at 3 weeks, with scores staying persistently low at 3 months but not at 6 months. Limitations of the study include the lack of a control group, inconsistent completion of the surveys, high dropout rate during the first few weeks, lack of long-term follow-up, lack of control for any other interventions during the study, and heterogeneity of the types of DGBIs included in the study. The authors concluded that the study demonstrated the efficacy of PENFS for gastrointestinal symptoms and functionality for pediatric DGBIs in a real-world setting. [This study is included in the Hayes Evolving Evidence Review for IB-Stim (2022; updated 2025).]

In a prospective observational study of the effect of auricular PENFS on QOL in children with DGBIs, Chogle et al. (2023) included 31 children aged 11 to 18 years (80.6% female) with DGBIs from a single-center institution. DGBIs included IBS (n = 13) and functional dyspepsia (n = 9). Participants were evaluated for changes in gastrointestinal symptoms, QOL, functional disability, somatization, global health, anxiety, and depression using the API, NSS, FDI, Children's Somatization Inventory, and PROMIS (Patient-Reported Outcomes Measurement Information System) Global Health Anxiety and Depression assessment tools. Medication use was reported by 83.9% of participants, with a median number of medications of five. Each participant received PENFS therapy once a week for 4 consecutive weeks. Participants reported significant reductions in abdominal pain, nausea severity, functional disability, somatization, and anxiety from baseline to week 4 after receiving PENFS therapy, while self-reported QOL and depression did not significantly change from baseline to week 4; however, parents reported significant improvement in average QOL for their child in terms of physical function, psychosocial disability, abdominal pain, and somatization. The authors also reported that the number of medications participants were taking influenced several outcomes, as those participants who were on three or more medications experienced significant decreases in anxiety and nausea severity and improved QOL and physical functioning. Limitations of the study include the small sample size, single-center design, lack of objective measurement tools, lack of long-term follow-up, and absence of a sham control group. The authors concluded that PENFS is a promising nonpharmacological treatment for children with DGBIs, potentially leading to improvements in both symptom severity and QOL, and recommended future research that includes larger sample sizes, placebo-controlled study designs, and long-term follow-up. [This study is included in the Hayes Evolving Evidence Review for IB-Stim (2022; updated 2025).]

Santucci et al. (2023) conducted a retrospective study to examine changes in abdominal pain, nausea, and disability before and after treatment and to compare outcomes between treatments in children who met the Rome IV criteria for

FAPDs. The study included 101 patients between 11 and 21 years old who were treated with 4 weeks of PENFS (n = 49; median age, 17 years; 75% female; 98% Caucasian), cyproheptadine (n = 31; median age, 16 years; 90% female; 87% Caucasian), or amitriptyline (n = 21; median age, 15 years; 52% female; 95% Caucasian). Outcomes were evaluated using the API, NSS, and FDI at baseline and follow-up within 3 months. In the PENFS group, 29 patients (59%) had been on medications but experienced treatment failure and thus received PENFS. These patients remained on a stable medication dose for the duration of treatment with PENFS. The authors reported that (1) patients in the PENFS group had significantly lower scores on the API, NSS, and FDI at follow-up; (2) the patients in the amitriptyline group had a significantly decreased API at follow-up but not the NSS and FDI; and (3) the patients in the cyproheptadine group did not change significantly on any of the three assessments. The authors concluded that therapy with PENFS showed improvements in abdominal pain, nausea, and disability, while amitriptyline showed improvements in abdominal pain within 3 months of treatment, and that PENFS was more effective than cyproheptadine in improving abdominal pain and may be a good nonpharmacological alternative for FAPDs. The study is limited by the homogeneity of the study population, small sample size, short follow-up period, and lack of objective measurement tools.

In a single-center, open-label, prospective clinical trial, Karrento et al. (2023) evaluated the effects of PENFS on pain, common comorbidities, and QOL in children with CVS. The study included 30 children (60% female) who were 8 to 18 years old and had drug-refractory CVS. Each participant completed surveys at the beginning, at week 6, and at the extended follow-up approximately 4 to 6 months later. Surveys included the API, State-Trait Anxiety Inventory for Children, Pittsburgh Sleep Quality Index, and PROMIS Pediatric Profile-37. Each participant wore the PENFS device for 5 days (24 hours/day) for 6 consecutive weeks. The authors reported that the frequency of episodes per month decreased from a median of 2.0 episodes per month at baseline to 0.5 episodes per month at the extended follow-up. The authors also reported that the median API scores and State-Trait Anxiety Inventory for Children scores decreased from baseline to week 6 and to the extended follow-up, while short-term improvements in sleep were seen at 6 weeks but not at the extended follow-up. QOL measures, including physical function, anxiety, fatigue, and pain interference, were also reported by the authors to have improved in the short term, with long-term benefits noted only for anxiety. Limitations of the study include the single-center design, lack of randomization and blinding, small sample size, and lack of objective assessment tools. The authors concluded that auricular neurostimulation using PENFS is effective for pain and several disabling comorbidities, including anxiety, sleep, and several aspects of QOL in children with CVS.

In a subanalysis of a cohort of participants from a single-center, double-blinded RCT, Krasaelap et al. (2020) evaluated the efficacy of PENFS in adolescents with IBS. The study included 50 participants who met Rome III criteria for IBS and were randomly assigned to groups that either received PENFS (n = 27; median age, 15.3 years; 89% female) or a sham stimulation (n = 23; median age, 15.6 years; 91% female) 5 days per week for 4 weeks. Both groups were comparable in age, gender, BMI, ethnicity, baseline pain (Pain Frequency-Severity-Duration Scale), and functioning FDI scores. Questionnaires were completed at baseline, after each week of therapy for weeks 1 to 3, and during an extended clinic follow-up visit 8 to 12 weeks after the end of therapy. Stool consistency was extracted from the Questionnaire on Pediatric Gastrointestinal Symptoms, and participants kept a daily diary during week 4 of therapy, noting if they had a bowel movement or not. The authors reported that reductions of 30% or more in worst abdominal pain were observed in 59% of participants who received PENFS vs 26% of participants who received sham stimulation and that participants who received PENFS had a composite pain median score of 7.5 vs 14.4 in the sham group and a usual pain median score of 3.0 vs 5.0 in the sham group. The authors also reported that a symptom response scale score of ≥ 2 was observed in 82% of participants who received PENFS vs only 26% of participants in the sham group. The authors concluded that auricular neurostimulation reduced abdominal pain scores and improved overall well-being in adolescents with IBS and that PENFS is a noninvasive treatment option for children with functional bowel disorders. Limitations of the study include the small sample size, retrospective design, short-term follow-up, and incomplete assessment of stool frequency and consistency.

Kovacic et al. (2017) conducted a single-center, blinded, sham RCT evaluating the efficacy of the Neuro-Stim (Innovative Health Solutions, Versailles, IN) PENFS device in adolescents with FAPDs. Adolescents (aged 11-18 years) who met Rome III criteria with FAPDs were enrolled and assigned to PENFS (n = 60) with either an active device or sham (n = 55). After exclusion of participants who discontinued treatment (one in the study group and seven in the sham group) and those who were excluded after randomization because they had organic disease (two and one in the study and sham groups, respectively), 57 participants in the PENFS group and 47 participants in the sham group were included in the primary analysis. The primary efficacy end point was change in abdominal pain scores measured via the Pain Frequency-Severity-Duration Scale. Participants in the PENFS group had greater reduction in worst pain compared with sham after 3 weeks of treatment. Three participants discontinued the study due to side effects, none of which were serious. The adverse events included ear discomfort, adhesive allergy, and syncope due to needle phobia. The researchers concluded that PENFS with Neuro-Stim has sustained efficacy for FAPDs in adolescents. Study limitations include a small sample size, a short follow-up period, and exclusions after randomization.

Clinical Practice Guidelines

European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN)/ North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN)

ESPGHAN/NASPGHAN issued guidelines (Groen et al., 2025) for the treatment of IBS and functional abdominal pain in children. PENFS is suggested as a treatment option for patients who have shown considerable difficulty in achieving pain relief (conditional recommendation, moderate certainty evidence).

Percutaneous Peripheral Nerve Stimulation

There is insufficient evidence to support the use of peripheral nerve stimulation (PNS) for the treatment of pain. While some studies have compared the effectiveness of PNS with that of placebo, the overall quality of the evidence is weak and limited. Most of the published studies consist of retrospective reviews, case reports, small case series, and small RCTs. Further large, multicenter, blinded, long-term RCTs are needed to evaluate the efficacy of PNS. Ongoing studies may provide more definitive evidence of the safety and efficacy of PNS.

Hayes (2025) published an Evolving Evidence Review on the SPRINT PNS System and its application for the treatment of chronic pain. The report concluded that based on a review of published clinical studies, there continues to be only minimal support for using this device for the treatment of chronic pain. While Hayes identified three newly published studies in 2025, the impact of these studies after their review of the abstracts is unlikely to change the current minimal level of support for the use of the SPRINT PNS System for the treatment of chronic pain.

ECRI (2018; revised 2025) published a Clinical Evidence Assessment for the SPRINT PNS System. ECRI concluded that current evidence indicates that SPRINT PNS is safe, delivers clinically meaningful pain reduction, and improves QOL and physical function in individuals with chronic pain for up to 5 years post treatment. However, data are insufficient to draw definitive conclusions about its comparative safety and effectiveness vs those of other pain management interventions. While available studies suggest that SPRINT may outperform standard interventional management, PT, cuff-type slings, permanent PNS, and sham treatment in reducing pain and enhancing function, these findings are limited by small sample sizes and heterogeneity in study populations and comparators across RCTs.

ECRI (2024) performed a Clinical Evidence Assessment of the Freedom PNS System. ECRI found that evidence from three small before-and-after studies suggests that Freedom may be safe and reduce chronic pain in adults; however, the evidence is limited in both quantity and quality. No published studies compare Freedom with other PNS systems. All available studies carry a high risk of bias due to small sample sizes, a lack of control groups, and retrospective designs. RCTs comparing Freedom with other PNS systems or alternative pain management interventions, with long-term outcomes, are needed to establish its comparative safety and effectiveness.

ECRI (2024) performed a Clinical Evidence Assessment of the Nalu PNS System, with the intent to evaluate its safety and effectiveness for treating chronic pain compared with those of other chronic pain management methods. ECRI did not identify any relevant studies to inform clinical decision-making related to these topics.

An Ontario Health (2024) Health Technology Assessment systematically reviewed the clinical effectiveness, safety, and cost-effectiveness of minimally invasive percutaneous PNS for adults with chronic neuropathic pain refractory to conventional medical management (CMM). The review included 17 studies: two RCTs and 12 nonrandomized studies evaluating both permanent (StimRouter, Freedom, and Nalu) and temporary (SPRINT) PNS systems. The population comprised adults with chronic neuropathic pain in the trunk, extremities, or postamputation sites, with sample sizes ranging from 11 to over 6,000 and follow-up durations of 1 to 24 months. Interventions were compared with placebo, standard care (e.g., PT, nonopioid and opioid medications), or no intervention. The primary outcomes included pain response (≥ 30% or ≥ 50% reduction), pain scores, opioid use, functional outcomes, HRQOL, and adverse events. In the RCT of permanent PNS (StimRouter), 38% of individuals achieved a ≥ 30% reduction in pain, without increased medication use, compared with 10% in the control group ($p = 0.005$), with a mean pain score reduction of 27.2% vs 2.3% (MD, 24.9%; $p < 0.001$). The RCT of temporary PNS (SPRINT) showed that 67% of individuals achieved ≥ 50% pain relief at 12 months compared with 0% in the control group ($p = 0.001$). Nonrandomized studies reported 60% to 76% of individuals achieving ≥ 50% pain reduction, with sustained improvements in pain, function, and HRQOL up to 12 months. Adverse events were generally mild and localized, with lead migration and skin irritation being the most common. Serious adverse events were rare and not device related. The study design and methodology support moderate validity for RCT findings, although limitations include small sample sizes, high attrition, and selective reporting. Nonrandomized studies were limited by confounding, selection and reporting bias, and lack of control groups, resulting in low certainty of evidence. No meta-analysis was conducted due to heterogeneity in populations and outcomes. This assessment suggests that PNS provides clinically meaningful improvements in pain, function, and QOL in individuals with chronic neuropathic

pain unresponsive to standard treatments. However, the evidence base is limited by methodological weaknesses, and the cost-effectiveness of PNS remains uncertain. Careful selection of individuals and further high-quality research are needed to clarify long-term benefits. (Gilmore et al., 2019a, Gilmore et al., 2019b, and Gilmore et al., 2021, previously cited in this policy, are included in this systematic review.)

The Lin et al. (2024) systematic review and meta-analysis evaluated the efficacy of PNS for postoperative recovery in adults undergoing lower limb orthopedic surgery. The authors searched PubMed, Embase, and the Cochrane Library for RCTs up to September 29, 2023, and included eight trials enrolling 633 individuals (321 in experimental groups and 312 in controls) across five countries. Eligible studies involved individuals aged 18 years or older who received PNS within 24 hours after surgery compared with sham stimulation or placebo. The primary outcomes were pain intensity and analgesic consumption, and the secondary outcomes included ROM and length of hospitalization (LOH). Pain intensity was assessed using validated scales such as the VAS and NRS, while analgesic use served as an objective measure. Functional outcomes were measured by goniometer for ROM and hospital records for LOH. Meta-analysis showed no significant effect of PNS on pain intensity (SMD, 0.17; 95% CI, -0.50 to 0.84; p = 0.618). Analgesic consumption demonstrated a marginally significant reduction favoring PNS (SMD, -2.37; 95% CI, -4.85 to -0.12; p = 0.062). Functional improvements were not significant: ROM (SMD, 0.52; 95% CI, -0.17 to 1.22; p = 0.140) and LOH (SMD, 0.41; 95% CI, -0.12 to 0.93; p = 0.129). Subgroup analyses revealed high heterogeneity across studies, and sensitivity analysis indicated that removal of one influential trial altered pooled estimates by more than 10%. The evidence quality was graded very low for pain intensity, low for analgesic consumption, and moderate for ROM and LOH. A risk-of-bias assessment found four studies at low risk, one with some concerns, and three at high risk, primarily due to missing data and selective reporting. The findings suggest that PNS does not significantly improve pain intensity or functional recovery but may modestly reduce analgesic use. However, small sample sizes, short treatment durations, inconsistent outcome measures, and high heterogeneity limit the reliability of these results. This systematic review indicates that PNS cannot yet be recommended as a standard adjunct for postoperative rehabilitation, and larger, well-designed trials, with standardized protocols and longer follow-up, are needed to clarify its role.

Hatheway et al. (2024) conducted an industry-sponsored, multicenter, unblinded RCT to evaluate the use of a micro-implantable pulse generator (IPG), the Nalu Neurostimulation System, for the treatment of chronic pain via PNS therapy. The study included 89 adults who were between 18 and 80 years of age and had a diagnosis of chronic pain of peripheral nerve origin in the low back (49.4% of participants), shoulder (13%), knee (20.8%), or foot/ankle (16.9%); they were randomized to either the active arm (n = 58), which received PNS and CMM, or the control arm (n = 31), which received only CMM. There were 24 participants in the control arm who crossed over to the active arm after 3 months. Therapy responders were participants who achieved at least a 50% reduction in pain scores compared with baseline. Participants were followed up at 1, 3, 6, 9, and 12 months to gather the participant-reported outcomes and safety data, with 61 of the 82 participants who underwent implant completing the 12-month follow-up. Primary reasons for not completing the 12-month follow-up included withdrawal from the study (n = 10), explantation for infection or inadequate response (n = 7), and nonadherence (n = 2). This study was expected to continue through 36 months of follow-up. The authors reported that the responder rate was 87% at 12 months, with a 69% average reduction in pain compared with baseline and that statistical significance was achieved for all participant-reported outcomes, with mean pain scores on the NRS showing improvement from 7.5 ±1.20 at baseline to 2.3 ±1.7 at 12 months. The authors also reported that there was an excellent safety profile, with no serious adverse device effects or reports of pocket pain, and that a majority of participants used unique programming options and found that the PNS device was easy to use and comfortable to wear. The authors concluded that the 12-month results were consistent with their previously reported 6-month outcomes. Limitations of the study include the lack of blinding; small sample size; allowance for crossover, which reduced the number of control participants available for comparison; use of subjective measurement tools; heterogeneity of the CMM available to participants and of the anatomical locations of the neuropathic pain; and allowance for continued use of medications for treatment of pain. Multiple investigators reported competing interests, including with the device manufacturer, Nalu Medical.

Hayes (2024) published an Evidence Analysis Research Brief that addresses PNS for the treatment of superior cluneal neuralgia (SCN). The Brief stated that there is not enough published, peer-reviewed literature to evaluate the evidence related to PNS for the treatment of SCN and that no clinical studies, professional position statements or guidelines were found that addressed PNS for the treatment of SCN.

Goree et al. (2024) conducted a multicenter, double-blinded, randomized, placebo-controlled crossover trial to evaluate the effect of 60-day PNS treatment for addressing persistent postoperative pain after TKA. The study included 52 adults who were randomized to receive either active PNS (n = 28; 89.2% female; mean age, 63.3 years) or placebo (n = 24; 75% female; mean age, 62.2 years) stimulation. All study participants underwent placement of percutaneous leads targeting the femoral and sciatic nerves on the leg with postoperative pain. Leads were left in for 8 weeks, with the primary outcome comparing the proportion of participants in each group that reported a ≥ 50% reduction in average pain compared with

baseline during weeks 5 to 8 post implantation. Participants had weekly follow-up visits to evaluate outcomes and progress and were observed until 1 month after lead removal (i.e., 3 months after the start of treatment). Participants who received PNS were observed for another 9 months, with visits at 6, 9, and 12 months after the start of treatment. Placebo group participants were allowed to cross over to receive PNS treatment or exit the study. If they elected to cross over, the placebo group participants underwent the same procedure as PNS participants, had follow-up visits at 2, 4, and 8 weeks after the start of treatment, with leads removed at 8 weeks, and underwent observation for 12 months after the start of active treatment, with follow-up visits at 3, 6, 9, and 12 months. The authors reported that 60% of participants in the PNS treatment group responded with ≥ 50% pain relief relative to baseline, while the placebo group had 24% respond with ≥ 50% pain relief relative to baseline; participants in the PNS group also walked a significantly greater distance at the end of treatment than did the participants in the placebo group, with a mean percentage improvement in walking ability at the end of treatment of 47% in the PNS group, while the placebo group experienced a decrease in walking ability of -9%. The authors also reported that participants in the PNS group improved to 16 percentage points above the threshold and into the range of healthy individuals, whereas the walking ability of participants in the placebo group further decreased to 22 percentage points below the threshold. Limitations of the study include the small study population and inclusion of participants with partial knee replacements, revision knee replacements, and bilateral knee replacements only in the placebo group. The authors concluded that the study provided evidence that percutaneous PNS decreased persistent pain, which led to improved functional outcomes after TKA. Multiple investigators reported financial and nonfinancial support from SPR Therapeutics and other medical device manufacturers, including honoraria, stock/stock options, and employment or consulting relationships. [This study is included in the ECRI Clinical Evidence Assessment of the SPRINT PNS System (2025) and the Hayes Evolving Evidence Review for the SPRINT PNS system (2025).]

Parikh et al. (2024) conducted a systematic review to summarize the literature involving the efficacy of PNS in orthopedic surgery. The review included 16 studies [knee pain in eight studies (n = 31), shoulder joint pain in six studies (n = 23), and foot pain in two studies (n = 11)], with 69 adult individuals. The studies evaluating knee pain applied PNS leads targeting the femoral nerve, sciatic nerve, auricular nerve, and/or saphenous nerve, while the studies on the use of PNS for shoulder pain included the axillary nerve and suprascapular nerves. The authors reported that all the studies demonstrated that PNS is effective in reducing pain, with one study reporting statistically significant results. The authors also reported that some studies also showed reduced opioid consumption; however, conclusions regarding opioid consumption in the setting of PNS could not be made. The studies included were subject to selection bias and placebo effect, according to the authors, which can lead to confounding, and the absence of randomization and comparative methodologies with controls also hindered the formulation of conclusive findings. The authors concluded that PNS can be effective in managing postoperative or chronic pain in individuals with orthopedic pathology. Limitations of the study include the lack of control groups or randomization, small sample sizes in the included studies, heterogeneity of the included studies, and low number of studies available for inclusion.

In an Evidence Analysis Research Brief on the efficacy of PNS for the treatment of shoulder subluxation post stroke, Hayes (2023) did not find any published clinical studies, position statements, or guidelines that met their criteria (studies evaluating the clinical utility of whether PNS improves health outcomes) that addressed the use of PNS for this indication. Hayes concluded that the lack of evidence appears to confer no or unclear support for PNS for the treatment of shoulder subluxation post stroke.

Hayes published a Clinical Research Response (2023) on the StimRouter Neuromodulation System for the treatment of chronic pain that included a review of abstracts of two studies, including one RCT and one single-arm study, that met the inclusion criteria (studies that reported the effect of StimRouter on pain perception and validation scores, changes in opioid usage, or adverse events and that were a clinical study of any design). Hayes did not find any systematic reviews meeting the inclusion criteria, and based on their review of full-text clinical practice guidelines and position statements, there was no or unclear practice guidance support for PNS for managing chronic pain with a peripheral nerve origin.

Früh et al. (2023) conducted a multicenter retrospective study to investigate the safety and efficacy of externally powered PNS systems targeting the saphenous nerve for the treatment of chronic, intractable, postsurgical knee pain refractory to a multimodal pain management paradigm. The primary diagnosis for knee pain that led to knee arthroplasty was OA (76%), meniscus/cruciate ligament injuries (12%), fractures (8%), and injury of the nervus saphenous after stripping of the vena saphenous (4%). Outcomes were measured using a 10-point pain scale measuring pain intensity at rest and in motion, QOL with the 12-Item Short Form Survey, quality of sleep with the Pittsburgh Sleep Quality Index, and mood states with the short form of the General Depression Scale. Overall, 33 patients (median age, 58 years; 45.5% female) were implanted with a PNS device targeting the saphenous nerve branches; however, six (18.2%) were explanted due to nonsufficient initial benefit from the therapy, and two patients were explanted due to wound infections. The authors included the remaining 25 patients in the study and reported that all of them had significant improvements in knee pain, both during motion and at rest, QOL, mood quality, and quality of sleep through the 6-month follow-ups. The authors also reported that nine patients underwent an additional 12-month follow-up visit and reported a significant decrease in knee

pain at rest and in motion. The patients also reported a significant reduction in opioid medication intake from a median of 80 morphine milligram equivalents (MMEs) prior to the operation to 20 MMEs at 3 months and 6 months post permanent implant. When the authors included the patients who initially did not benefit from the PNS system (trial phase) and those who had system explantations due to wound infections, their intention-to-treat analysis showed an overall success rate with a minimum pain improvement of 50% in 75.8% of all patients. Limitations of the study include the retrospective design, small sample size, and short-term follow-up. The authors concluded that externally powered PNS at the saphenous nerve branches is safe and effective for individuals with chronic knee pain, as the short-term results were promising and showed considerable reductions in pain scores and opioid intake. [This study is included in the systematic review by Ontario Health (2024) and in the ECRI Clinical Evidence Assessment of the Freedom PNS System (2024).]

Gilmore et al. (2023) completed a prospective multicenter case series of participants with CLBP recalcitrant to multiple nonsurgical treatments to illustrate the durability of responses to medial branch PNS. The study included 74 adults (average age, 56.3 years; 53% female) who completed their treatment with implanted percutaneous PNS for 60 days. Participants were implanted with the PNS device and were instructed to use percutaneous PNS for at least 6 hours per day and up to 12 hours per day for 60 days. They were then followed up through 14 months (12 months after the treatment period) to assess responses to pain intensity, disability, pain interference, HRQOL, depression, and Patient Global Impression of Change. The authors reported that 91% of participants experienced clinically meaningful improvement in at least one outcome after 2 months, with 79% at 5 months, 73% at 8 months, 75% at 11 months, and 77% at 14 months; 77% of participants experienced clinically meaningful improvement in two or more outcomes at 2 months, 63% at 5 months, 60% at 8 months, 59% at 11 months, and 58% at 14 months. Opioid use was also noted to be reduced in 15 of the 20 participants who reported taking them at baseline, and the reductions in opioid consumption were sustained over the 12-month follow-up period, with the average consumption reduced from 28.5 MMEs at baseline to 13.4 MMEs after 2 months of PNS; it was further reduced to 5.4 MMEs at 14 months. Limitations of the study include the lack of randomization to treatment vs the placebo intervention, lack of control of supplemental treatments (such as medications or other therapies), and heterogeneity of CLBP diagnoses and previous treatments. The authors concluded that treatment of CLBP with 60 days of percutaneous PNS treatment produced clinically meaningful improvements in average pain intensity, disability, and/or pain interference for a majority of participants through the entire 14-month follow-up period. [This study is included in the systematic review by Ontario Health (2024) and the Hayes Evolving Evidence Review for the SPRINT PNS system (2025).]

Hayes published an Evidence Analysis Research Brief on the Nalu Neurostimulation System for the treatment of chronic pain of peripheral nerve origin (2023), which indicated that they did not find any published, peer-reviewed studies related to the Nalu Neurostimulation System and that while they did identify two clinical practice guidelines and position statements, neither supported the use of implantable PNS devices for the treatment of chronic pain.

In their Health Technology Assessment on percutaneous PNS for the treatment of intractable chronic pain in adults, Hayes (2022; revised 2025) identified and reviewed four studies (two RCTs and two prospective pretest-posttest studies) and found that the quality of evidence was very low, with two studies deemed fair quality, one poor quality, and one very poor quality. The report concluded that these studies suggest that percutaneous PNS may be associated with pain reduction and improvement of QOL, ADL, and medication use rates and appears to be safe; however, the available evidence was insufficient to draw definitive conclusions regarding efficacy and safety. They noted that none of the four studies included subgroup analysis or regression analyses to inform selection criteria for individuals, and the report recommended additional well-designed studies, with larger populations and comparisons with treatment alternatives, to strengthen the reliability of the evidence base and to provide greater confidence in the observed trends. Hayes noted in their 2025 update that three relevant, newly published studies (one RCT and two single-arm studies) may meet their inclusion criteria, with a possible upgrade to their current rating of this technology.

Char et al. (2022) completed a systematic review of 14 prospective studies on the efficacy of PNS for neuropathic pain as it relates to pain intensity, neurological deficits, neuropathy, and other secondary outcomes. Three of the studies were RCTs, and 11 studies were prospective observational studies/case series. The studies addressed various types of peripheral pain, including complex regional pain syndrome (three studies), phantom limb pain (three studies), shoulder pain (two studies), postsurgical pain (two studies), and mononeuropathies (five studies). The authors stated that the pooled results demonstrated very low quality or low quality of evidence supporting reduced pain intensity of peripheral neuropathic pain after treatment with PNS for upper or lower extremity neuropathic pain. The authors reported that the majority of individuals experienced at least a 30% reduction in pain and that it was common for individuals to report > 50% pain relief. They also reported that this reduction in pain was consistent across all types of peripheral neuropathic pain syndromes. The authors recommended future prospective, well-powered studies to assess the efficacy of PNS for peripheral neuropathic pain. Two investigators reported industry grants, resulting in conflicts of interest. (Gilmore et al., 2019a, and Gilmore et al., 2019b, previously cited in this policy, are included in this systematic review. This study is included in the ECRI Clinical Evidence Assessment of implantable PNS devices, 2023.)

ECRI published a Clinical Evidence Assessment on implantable PNS devices for treating chronic pain (2021; revised 2023) that focused on safety and efficacy for PNS's ability to treat chronic pain and how it compared with other chronic pain management conditions. The 2023 update included three systematic reviews (that included mostly small RCTs and case series) and four additional low-quality case series. ECRI stated that larger RCTs are needed that include comparisons of PNS with other chronic pain management methods, as the current studies have high heterogeneity, which makes it difficult to permit firm conclusions.

Clinical Practice Guidelines

American Society of Interventional Pain Physicians (ASIPP)

ASIPP evidence-based guidelines (Manchikanti et al., 2024) support the use of implantable PNS leads and neurostimulators in patients with moderate to severe chronic pain refractory to two or more conservative treatments.

- The evidence of effectiveness of PNS in managing chronic pain, for implantable PNS systems following a trial or selective lumbar medial branch stimulation without a trial, is level III or fair, with moderate certainty using GRADE criteria. (Evidence level: fair; strength of recommendation: moderate)
- The evidence of effectiveness of PNS in managing chronic pain, for implantable stimulation systems following temporary PNS for 60 days, is level III or fair, with moderate certainty using GRADE criteria. (Evidence level: fair; strength of recommendation: moderate)
- Based on the evidence and recommendations, indications may be expanded from present CMS guidance, with the addition of craniofacial pain, phantom limb pain, and LBP, either nociceptive or neuropathic, with present evidence showing level III or fair, with moderate certainty using GRADE criteria. (Evidence level: fair; strength of recommendation: moderate)

Peripheral Nerve Field Stimulation

Evidence on peripheral nerve field stimulation (PNFS), also known as peripheral subcutaneous field stimulation, is limited, consisting of small trials and case studies. More robust, prospective controlled trials comparing PNFS with placebo or alternative treatment modalities are needed to evaluate the efficacy of this treatment for chronic pain.

van Heteren et al. (2023) performed a comparative study of the efficacy of spinal cord stimulation (SCS) with the addition of PNFS on pain and QOL in individuals with persistent spinal pain syndrome or failed back surgery syndrome (FBSS) for at least 6 months and who had a pain score on the VAS of at least 50 mm for both leg and back pain. The study was based on data from a multicenter RCT and included 100 adults between 18 and 75 years of age. All individuals received lead placement and underwent trial stimulation for 1 week. In those individuals who responded to SCS alone, with a reduction of back and leg pain by at least 50%, an IPG was implanted (SCS-only group). In individuals with a pain reduction of at least 50% only in their legs, subcutaneous leads were additionally implanted (SCS + PNFS group) and connected to one single IPG. Both groups received optimal pain treatment and were consequently followed up per protocol for 12 months after implantation. There were no significant differences in baseline characteristics between the two groups. The outcome measures included pain, QOL, anxiety and depression, overall health, and disability. Data were reviewed for the 75 individuals who completed the 12-month follow-up visit, which included 21 from the SCS-only group and 54 from the SCS + PNFS group. The authors reported that both groups showed a significant reduction in back and leg pain at 12 months compared with baseline measurements and that the SCS + PNFS group showed improvements in the affective pain ranking index, sensitive pain ranking index, and total pain ranking index, whereas there was no significant improvement in these outcomes reported by individuals in the SCS-only group. Limitations include the small size of the control group, retrospective design, and lack of blinding. The authors concluded that PNFS, in addition to SCS, provided equal beneficial long-term pain relief and QOL improvements in individuals with chronic back and leg pain that was refractory to SCS alone. The authors recommended future research to identify differences in characteristics to identify individuals who need SCS alone and those who need SCS with PNFS.

Rigoard et al. (2021) conducted an RCT, with a 12-month follow-up, to assess the potential added value of PNFS as a salvage therapy in participants with persistent spinal pain syndrome type 2 experiencing failed SCS syndrome in the back pain component. Overall, 14 participants between February 2013 and April 2017 were enrolled in this study (NCT02110888) and randomized into two groups: SCS + PNFS (n = 6) and SCS only (n = 8). The primary objective of the study was to compare the percentage of back pain surface decrease after 3 months using a computerized interface to obtain quantitative pain mappings, combined with multidimensional SCS outcomes. The authors concluded that back pain surface decreased over a 12-month period from baseline in the SCS + PNFS group (80.2% ±21.3%) compared with the SCS-only group (13.2% ±94.8%) (p = 0.012), highlighting the clinical interest of SCS + PNFS in cases in which SCS fails to address back pain. With paresthesia generated under tonic stimulation, the authors were unable to blind the SCS + PNFS combination. In addition, a small sample size (14 participants) makes it difficult to decide whether these conclusions can be generalized to a larger population. Further investigation is needed before the clinical usefulness of this procedure is proven.

In a follow-up to their 2016 multicenter RCT, included below, van Gorp et al. (2019) continued with an open-phase part of the study in which all participants received optimal SCS and PNFS simultaneously for the treatment of LBP due to FBSS. Outcome data were collected from the 50 participants by analyzing their questionnaires using multilevel regression models at 12 months and compared with the data collected at baseline. The authors found improvement in all secondary measurements, including functional capacity and overall QOL, to be statistically significant. They noted that more than 40% of the participants reported a reduction in back pain of ≥ 50%. The authors concluded that PNFS, in addition to SCS, provides a statistically significant and relevant relief of LBP in individuals with FBSS for whom SCS alone is only effective for relief of leg pain. They noted that (1) the study is limited due to the controlled part of the study only lasting for 3 months; (2) the study could not be blinded; and (3) the study combined participants from both arms into the analysis. They recommended future studies to target optimization of the technique and pattern analysis.

Eldabe et al. (2019) conducted the SubQStim study, which was a prospective multicenter RCT, to compare the effectiveness of PNFS (referred to as subcutaneous nerve stimulation in this study) plus optimized medical management (OMM) with that of OMM alone in participants with back pain due to FBSS. There were 116 participants recruited from 21 centers, which was short of the goal of 314 participants due to the sponsor ending the study because of prolonged recruitment challenges. In the first phase of the trial, 56 participants were randomized to receive PNFS plus OMM, and 60 received OMM only for 9 months. Due to early study termination, participants were not able to complete the study and attend all visits, as they were discontinued at various time points; in all, 74 participants were able to complete the 9-month primary end point visit. The authors recognized that the study had a few potential limitations. First, there was a lack of blinding because insertion of the PNFS was a surgical intervention. Second, participants in the study could be considered as having already experienced failure of OMM by definition of FBSS, which may predispose those in the OMM-alone arm to not experience significant improvement. Third, the decision to end the study early resulted in a smaller number of participants contributing to the data analysis and affected the study's ability to inform on the long-term effectiveness of PNFS. The authors concluded that despite early termination of the study, the addition of PNFS to OMM was clinically and statistically more effective than OMM alone in relieving LBP at up to 9 months.

The study by van Gorp et al. (2016) was a multicenter RCT investigating the efficacy of subcutaneous stimulation (SubQ) as add-on therapy to traditional SCS in treating back pain in participants with FBSS. Participants with a minimal pain score of 50 on a 100-mm VAS for both leg and back pain were eligible. If pain reduction after trial SCS was ≥ 50% for the leg but < 50% for the back, participants received additional SubQ leads and were randomized in a 1:1 ratio in a study arm with subcutaneous leads switched on (SubQ add-on) and an arm with subcutaneous leads switched off (control). The primary outcome was the percentage of the participants, at 3 months post implantation, with ≥ 50% reduction in back pain. A total of 97 participants were treated with SCS for leg and back pain. Of them, 52 participants were randomized and allocated to the control group (n = 24) or to the SubQ add-on group (n = 28). The percentage of participants with a ≥ 50% reduction in back pain was significantly higher in the SubQ add-on group (42.9%) compared with the control group (4.2%). Mean VAS score for back pain at 3 months was a statistically significant 28.1 mm lower in the SubQ add-on group compared with the control group. The authors concluded that SubQ as an add-on therapy to SCS is effective in treating back pain in individuals with FBSS for which SCS is only effective for pain in the leg.

McRoberts et al. (2013) conducted a multisite, two-phase, crossover RCT evaluating the safety and efficacy of PNFS in 44 participants with localized, chronic, intractable pain of the back. During phase 1, participants rotated through four stimulation groups (minimal, subthreshold, low frequency, and standard stimulation). If a 50% reduction in pain was achieved during any of the three active stimulation groups (responder), the participant proceeded to phase 2, which began with implant of the permanent system that remained in place for 52 weeks. The primary end point was a reduction in pain, assessed by the VAS. Of the 44 participants enrolled, 30 completed phase 1. Overall, 24 participants were classified as responders in phase 1, and 23 received permanent system placement. Significant differences in VAS scores were observed between baseline and all follow-up visits during phase 2. The authors concluded that PNFS is safe and effective as an aid in the management of chronic, localized back pain. A limitation to this trial is the small study group size.

Pulsed Electromagnetic Field Stimulation

Evidence on pulsed electromagnetic field (PEMF) stimulation is insufficient to support its use for the treatment of pain. More robust prospective controlled trials comparing PEMF stimulation with placebo or alternative treatment modalities are needed to evaluate the efficacy of this treatment for chronic pain.

The Kull et al. (2025) systematic review evaluated the efficacy of PEMF therapy for pain reduction and improvement of physical function in adults with non-specific LBP. The authors searched PubMed, MEDLINE, Embase, the Cochrane Library, and PEDro through May 15, 2023, and included nine RCTs comprising 420 individuals (50.9% female; mean age, 44.6 years). All individuals had non-specific LBP of varying duration, and studies excluded individuals with specific spinal pathologies, prior major lumbar surgery, malignancy, neurological deficits, or contraindications such as pacemakers. Interventions compared PEMF therapy alone or combined with conventional PT to placebo-PEMF therapy, conventional

therapy alone, high-intensity laser therapy, or osteopathic manipulative treatment. Treatment regimens varied widely in frequency (2-7 sessions/week), duration (10-30 minutes), and PEMF stimulation parameters (3-50 Hz, 2-150 mT), with follow-up periods ranging from 2 to 12 weeks. Pain was assessed using the VAS or NRS, and physical function was assessed with the ODI or Roland-Morris Disability Questionnaire. All studies reported pain reduction in the intervention groups, but statistically significant differences compared with controls occurred in five of 9 trials ($p < 0.05$). Similarly, five studies demonstrated significant functional improvement with PEMF therapy ($p < 0.05$), although some effects were limited to specific time points. For example, one trial found that PEMF therapy plus conventional therapy significantly improved pain and ODI scores at 6 and 12 weeks compared with conventional therapy alone ($p < 0.05$), while another found significant ODI improvement at both time points but pain reduction only at 6 weeks ($p < 0.05$). Another reported significant benefits across all outcomes for PEMF therapy vs placebo ($p < 0.05$), whereas two trials reported no significant differences between groups. No serious adverse events were reported. Methodological quality was generally high (mean PEDro score, 7.2/10), although blinding was inconsistent, and heterogeneity in the protocols precluded meta-analysis. The authors concluded that PEMF stimulation appears safe and may enhance pain relief and functional outcomes, particularly as an adjunct to conventional PT. However, substantial variability in treatment parameters, small sample sizes, short follow-up, and lack of standardized protocols limit the certainty of these findings. The authors disclosed no conflicts of interest and recommended further high-quality trials to define optimal PEMF stimulation settings and confirm long-term efficacy.

A systematic review by Picelli et al. (2024) evaluated the effects of PEMF therapy on the healing of acute bone fractures. The review included RCTs published in English between January 2014 and December 2022. Studies were selected based on a PICOS (Population, Intervention, Comparison, Outcomes, and Study) framework, focusing on adults with radiologically confirmed acute fractures, comparing PEMF treatment (alone or with standard care) with placebo and assessing outcomes related to bone healing, pain, ROM, and strength. After screening 692 records, only three RCTs met the inclusion criteria, encompassing a total of 197 individuals. Across the three trials, no statistically significant effects of PEMF therapy on fracture healing were observed. Results of one trial reported fracture union rates of 75% in the intervention group vs 58% in the placebo group at 12 weeks ($p = 0.10$) and 94% vs 87% at 24 weeks ($p = 0.43$), indicating no significant difference. Another RCT found no significant differences in scaphoid fracture union at multiple time points up to 52 weeks (p values ranging from 0.23 to 1.00). The third selected trial reported no significant difference in mean bone density but did observe a statistically significant increase in bone density percentage change at 4 weeks post surgery in the PEMF therapy group ($p < 0.05$). Regarding secondary outcomes, pain relief results were inconsistent: one RCT found significant reductions in pain at 7 and 14 days ($p < 0.05$), while the other two studies reported no significant effects. Functional outcomes also varied, with one study reporting significant improvements in wrist movement at 24 weeks ($p = 0.04$) and grip strength at 12 weeks ($p = 0.03$), but these effects were not sustained at other time points. This systematic review's validity is supported by its adherence to rigorous methodology, including predefined eligibility criteria, independent study selection, and standardized bias assessment. However, reliability is limited by the small number of included studies, heterogeneity in fracture types and treatment protocols, and lack of meta-analysis due to insufficient data. Clinically, the findings suggest that PEMF stimulation should not be routinely used to enhance bone healing in acute fractures, although its potential role in pain and functional recovery remains uncertain and warrants further investigation through high-quality trials.

The Xu et al. (2024) RCT evaluated the efficacy of PEMF stimulation, platelet-rich plasma (PRP), and their combined application in treating early-stage knee OA. Overall, 48 participants, who were aged 40 years or older and had Kellgren-Lawrence grades I to III knee OA, knee pain for at least 3 months, a BMI of < 30 kg/m², and platelet counts of ≥ 150,000/μL, were enrolled from a single orthopedic department between September 2020 and September 2023. Exclusion criteria included bleeding disorders, cancer, prior knee surgery, recent intra-articular injections, and inflammatory arthritis. Participants were randomized into three equal groups: intra-articular PRP injections (4-6 mL leukocyte-poor PRP once monthly for 3 months), PEMF therapy (30 Hz, 1.5 mT, 20 minutes per session, five times weekly for 12 weeks), or combined treatment (PRP plus PEMF stimulation starting 1 week after the first injection). Outcomes were assessed at baseline and weeks 4, 8, and 12 using the VAS for pain, WOMAC, Lequesne Index, and knee joint mobility. All groups showed significant improvement from baseline in pain and function over 12 weeks ($p < 0.001$). At week 12, the combined group achieved the greatest benefit: mean VAS decreased from 8.44 ±0.81 to 2.75 ±0.58, WOMAC from 35.94 ±4.6 to 14.56 ±2.07, and Lequesne Index from 9.97 ±3.72 to 3.63 ±0.81, while knee mobility increased from 99.06° ±5.84° to 105.63° ±5.56° (all $p < 0.001$). Between-group comparisons confirmed superior outcomes with the combined therapy at all posttreatment time points ($p < 0.05$). Adverse events were mild and transient, including swelling, low-grade fever, and temporary pain exacerbation, with no significant difference in incidence among groups ($p = 0.67$). Limitations include a small sample size, restriction to Kellgren-Lawrence grades I to III, absence of radiological follow-up, and single-center design, which may limit generalizability. These findings suggest that combining PRP and PEMF stimulation offers greater pain relief and functional improvement than either modality alone, although larger trials are needed to confirm durability and applicability.

Yabroudi et al. (2024) performed a single-blinded RCT trial to evaluate whether adding PEMF therapy to progressive resistance exercise (PRE) improves outcomes in participants with knee OA. Overall, 34 participants aged 40 years or older with mild to moderate unilateral or bilateral knee OA, confirmed by radiographic evidence and American College of Rheumatology criteria, were recruited from a tertiary care center between April and October 2019. Exclusion criteria included prior knee surgery, inflammatory arthritis, neurodegenerative disease, inability to walk unaided for 6 months, and recent exposure to PEMF stimulation or PRE. Participants were randomized into two groups: one received 24 sessions over 8 weeks of combined PEMF therapy and PRE, and the other received PRE alone. PEMF stimulation was applied for 30 minutes per session at 50 Hz and 50-G intensity, followed by 45 minutes of PRE. Outcomes included the Knee Injury and Osteoarthritis Outcome Score, NRS, 4-meter walking speed, and the Five-Times Chair Stand Test, assessed at baseline, post treatment (2 months), and the 3- and 6-month follow-ups. Results showed no significant group-by-time interaction for any outcome ($p > 0.05$). Both groups demonstrated statistically significant improvements from baseline across all time points in total Knee Injury and Osteoarthritis Outcome Score ($p < 0.001$), NRS ($p < 0.001$), walking speed ($p < 0.001$), and chair stand performance ($p < 0.001$). No statistically significant differences were observed between groups at any time point. Subscale analyses revealed similar patterns, with transient declines in sport subscale scores at later follow-ups. Limitations include a small sample size and inability to stratify by disease severity. These findings suggest that PRE alone is as effective as PRE combined with PEMF stimulation for reducing pain and improving function in knee OA, raising questions about the added value and cost-effectiveness of PEMF stimulation when used alongside exercise therapy.

Öztürk et al. (2024) conducted a single-center, retrospective comparative study to investigate the effect of PEMF therapy added to routine PT on pain and functional status in patients with CLBP. The study included 69 adults (mean age, 49.2 years; 61.8% female) with CLBP who were divided into two groups, with 34 in the group that received a standard regimen of lumbar TENS, infrared, and ultrasound treatments and 35 in the group that received the standard regimen in addition to PEMF stimulation. Patients were evaluated using the Quebec Back Pain Disability Scale (QBPDS) in terms of functional capacity and effects of CLBP and the VAS for pain, both before and after treatment. There was no significant difference detected between the two groups' pretreatment VAS and QBPDS scores. The assessments were conducted by the same physiatrist before therapy, the third week after treatment, and the twelfth week after treatment. The authors reported that while the second and third measurement scores in both groups were significantly lower than their first-measurement VAS and QBPDS scores, the second and third measurement scores in the PEMF therapy group were significantly lower than those in the control group, and the effect size of the difference was large. Limitations of the study include the small sample size, single-center design, short follow-up period, retrospective study design, and use of self-reported assessment tools. The authors concluded that PEMF stimulation appeared to be able to alleviate pain intensity and ameliorate disability in patients with CLBP and that it can be considered an effective and safe option that can be added to routine PT modalities; however, the authors recommended further prospective randomized studies to validate the effectiveness of PEMF stimulation.

In their systematic review of systematic reviews, Markovic et al. (2022) sought to provide an overview of application modalities and of the effectiveness of PEMF therapy in individuals with OA to summarize the current state of knowledge and to provide guidance to improve the quality of future studies. Their analysis consisted of 10 studies (including Yang et al., 2020, and Chen et al., 2019, summarized below), with a total of 6,274 adult individuals. All 10 of the included systematic reviews focused on knee OA, while four also reported on cervical OA, two reported on hand OA, and one reported on ankle OA. The WOMAC was used in all 10 studies as a measurement for physical function or disability, and the VAS was used in all 10 studies to assess pain. The authors reported that most studies were of low or medium quality. According to the authors, five of 10 studies reported positive outcomes associated with the application of PEMF stimulation in individuals with OA in terms of outcomes on disability or physical function; five of the studies reported that PEMF stimulation had significant effects on pain reduction in individuals with OA. The most consensus was observed by the authors for pain reduction, with other end points such as stiffness and physical function showing greater variability in outcomes. The authors noted that treatment protocols were very heterogeneous with the various levels of intensity, duration, and frequency of PEMF therapy used in the studies. The authors concluded that PEMF therapy appears to be effective in the short term to relieve pain and improve function in individuals with OA, even though the existing studies used very heterogeneous treatment regimens, had low sample sizes, and had suboptimal study designs.

Granja-Dominguez et al. (2022) conducted a single-center, randomized, placebo-controlled trial to investigate the effect of low-frequency PEMF therapy on the level of fatigue, walking performance, symptoms of depression, and QOL in participants with relapsing-remitting MS (RRMS). The study included 44 adults (84.4% female; mean age, 41 $\pm$9.9 years) with RRMS who were randomly assigned to either the treatment group (n = 22) or the placebo group (n = 22) using a computer-generated random number sequence, with the participants, outcome assessors, and therapist blinded as to which study arm the participants were assigned. Each participant underwent a 4-week treatment protocol that comprised five sessions per week for 45 minutes. The primary outcome was fatigue, which was assessed with the Fatigue Severity Scale and Modified Fatigue Impact Scale. The secondary outcomes included walking function (evaluated using the

GAITRite system and Timed 25-Foot Walk Test), the Beck Depression Inventory-II, and the MusiQoL Questionnaire. Data were collected at baseline, after the 4-week protocol period, and at 3 months post intervention. The authors reported that there were no changes from baseline for both fatigue measures between the PEMF treatment group and the placebo group at the end of treatment nor were there any differences between groups for any of the secondary outcomes at post intervention or at the 3-month follow-up. The authors concluded that low-frequency PEMF therapy is no more effective than placebo to produce changes in fatigue, walking performance, severity of depression, and QOL in people with RRMS.

D'Ambrosi et al. (2022) conducted an RCT to assess pain relief and clinical outcomes in participants undergoing medial unicompartmental knee arthroplasty (UKA) stimulated with PEMF compared with a control group. A total of 72 participants were randomized into a control group (n = 36) or an experimental PEMF stimulation group (n = 36). The participants allocated to the experimental group were instructed to use PEMF stimulation for 4 hours per day for 60 days. They were evaluated before surgery and then at 1 month, 2 months, 6 months, 12 months, and 36 months after the surgery. No placebo group was included in the RCT. Clinical assessment included the VAS for pain, Oxford Knee Score, the 36-Item Short Form Survey, and joint swelling. During each follow-up visit, the consumption of NSAIDs was recorded. The VAS decreased on follow-up visits in both groups; a statistical difference between the groups was observed during the 6- ($p = 0.0297$), 12- ($p = 0.0003$), and 36-month ($p = 0.0333$) follow-ups in favor of the PEMF stimulation group. One month after UKA, the percentages of participants using NSAIDs in the PEMF stimulation and control groups were 71% and 92%, respectively ($p = 0.0320$). At 2 months, 15% of the participants in the PEMF stimulation group used NSAIDs compared with 39% in the control group ($p = 0.0317$). The objective knee girth evaluation showed a statistically significant difference at 6 ($p = 0.0204$), 12 ($p = 0.0005$), and 36 ($p = 0.0005$) months, with improved values observed in the PEMF stimulation group. The subjective assessment of the swelling demonstrated a statistically significant difference at 2 ($p = 0.0073$), 6 ($p = 0.0006$), 12 ($p = 0.0001$), and 36 ($p = 0.0011$) months, with better values noted in the PEMF stimulation group. The Oxford Knee Score result was higher in the experimental group during all the follow-ups (1 month: $p = 0.0295$; 2 months: $p = 0.0012$; 6 months: $p = 0.0001$; 12 months: $p < 0.0001$; 36 months: $p = 0.0061$). The authors concluded that the use of PEMF stimulation leads to pain relief, clinical improvement, and lower NSAID consumption after medial UKA compared with the control group. Limitations to this study include a lack of placebo group, a small sample size, and use of a modified Cincinnati Rating System Questionnaire to assess participant satisfaction. Further research, with additional RCTs, is needed.

In a double-blinded, prospective RCT, Karakaş and Gök (2020) studied the efficacy of PEMF therapy when added to a conventional PT program in reducing pain and functional limitation in participants with chronic, nonspecific neck pain. The study included 63 participants (15 male participants, 48 female participants; age range, 25-59 years) who were divided into either a PEMF therapy group (n = 33) that received 20 minutes of PEMF stimulation, in addition to a PT, or a control group (n = 30) that received only the PT program. The groups were similar in terms of demographic and clinical characteristics, and both showed improvement in pain and functionality. The authors noted that the study limitations included the use of the conventional PT program in both study groups, lack of monitoring of the use of paracetamol for pain control in the study participants, lack of long-term measurements, subjective measurement tools used, and heterogeneity of the etiology of neck pain among the participants. They concluded that PEMF stimulation is safe for individuals with nonspecific neck pain, but it is not superior in improving pain and functional limitation; they suggested that further large-scale, prospective RCTs using a standard dose of PEMF stimulation, with a more specific clinical population, are needed to demonstrate evidence for the effectiveness of PEMF stimulation.

Yang et al. (2020) completed a systematic review of 16 RCTs and a meta-analysis of 15 RCTs to evaluate the effects of PEMF therapy and PEMF stimulation parameters on symptoms and QOL in people with OA. The total population in the 16 studies was 1,078, with 554 in treatment groups and 524 in placebo-controlled groups. Treatment time varied between 10 days and 6 weeks, so two different treatment durations (< 4 weeks and 4-6 weeks) were used in the subgroup analysis. The longest follow-up time was 12 weeks. Included studies evaluated OA of the knee (n = 14), ankle (n = 1), hand (n = 2), and cervical spine (n = 2). The authors determined that compared with placebo, there was a beneficial effect of PEMF therapy on pain and stiffness, regardless of the treatment duration, while benefit in physical function in people with OA was only seen if the therapy regimen lasted for 4 to 6 weeks. They did not observe any association between PEMF therapy and QOL in people with OA, regardless of the length of the treatment program. Limitations noted by the authors include the high levels of heterogeneity across outcome measures, small number of studies included, and short length of time for the treatment phases (≤ 6 weeks) and follow-up (maximum of 12 weeks). They recommended further studies to explore efficacy, with long-term follow-up, and to assess the effects of this modality on QOL.

ECRI published a Custom Product Brief (2019) on the SofPulse targeted PEMF stimulation device that is intended to reduce pain and swelling post operation. Based on the limited evidence from three very small RCTs on the use of SofPulse following breast surgeries, they concluded that the device may relieve short-term pain and may reduce (but not eliminate) narcotic use when compared with a sham (placebo) device. The report stated that the evidence is inconclusive,

as the studies assessed too few individuals, and the results need to be confirmed in larger, longer-term RCTs examining different surgery types and comparing the device with other pain control methods.

Chen et al. (2019) completed a systematic review and meta-analysis evaluating the efficacy of PEMF therapy on pain, stiffness, and physical function in individuals with knee OA. The review included eight RCTs that compared PEMF stimulation of various parameters and treatment regimens with placebo. The studies involved 421 individuals of similar age, sex ratio, and BMI. All the included studies were determined by the reviewers to have a low or moderate risk of bias. The limitations noted by the authors included the small number of RCTs and sample size available for review, inclusion of only articles published in English, and significant heterogeneity in the meta-analysis of the VAS for pain. The authors concluded that PEMF stimulation is beneficial for improving physical function of the knee joint, despite not having any advantage in treating pain or stiffness. They recommended further RCTs to confirm their findings and to determine the optimal frequency, intensity, treatment regimen, and duration of PEMF therapy.

Newberry et al. (2017) conducted a systematic review to assess the efficacy of a variety of noninvasive interventions [including but not limited to electrical stimulation techniques (including TENS), NMES, and PEMF stimulation] for OA treatment of the knee. A search was conducted using PubMed, Embase, the Cochrane Collection, Web of Science, PEDro, ClinicalTrials.gov, and abstracts from professional practice society annual meetings (e.g., American College of Rheumatology, AAOS). Eligible studies were those that were RCTs that enrolled adults 18 years or over who were diagnosed with OA of the knee and compared any of the interventions of interest with placebo (sham) or any other intervention of interest that reported a clinical outcome (including pain, function, and QOL). The investigators also included single-arm and prospective observational studies that analyzed the effects of weight loss in individuals with OA of the knee on clinical outcomes. Findings were stratified according to duration of interventions and outcomes: short term (4-12 weeks), medium term (12-26 weeks), and long term (> 26 weeks). A total of 107 studies were included in the review, and of those, three studies evaluated treatment with PEMF compared with sham treatment. Based on a pooled analysis, PEMF stimulation had a nonsignificant beneficial effect on short-term pain. In addition, the investigators reported that the evidence is insufficient to assess the effects of PEMF stimulation on short-term or other outcomes and that larger RCTs are needed.

Clinical Practice Guidelines

American Academy of Orthopaedic Surgeons (AAOS)

In its 2021 clinical practice guideline on nonarthroplasty management of OA of the knee, the AAOS reviewed one high-quality study on the use of a wearable PEMF device for pain management in patients with knee OA. The society downgraded their recommendation one level to “limited” due to feasibility issues in that PEMF stimulation is not widely used in practice settings in which patients are treated for knee OA, which may limit access for some patients. They recommended continued research, with larger RCTs that examine the long-term effectiveness of PEMF stimulation and studies that identify factors that distinguish between patients who respond and those who do not respond to PEMF stimulation. The American Physical Therapy Association and American Association of Hip and Knee Surgeons have endorsed this AAOS clinical practice guideline.

Restorative Neurostimulation

There is insufficient evidence in the published, peer-reviewed scientific literature to support the efficacy of restorative neurostimulation for the treatment of CLBP. Additional larger studies comparing restorative neurostimulation with standard of care and current alternative treatments are needed to demonstrate the safety and efficacy for this modality.

Schwab et al. (2025) reported results from the RESTORE trial, a multicenter, open-label RCT that was conducted at 25 US sites between July 2021 and July 2023, to evaluate restorative neurostimulation vs OMM for mechanical CLBP associated with multifidus dysfunction. A total of 203 participants (mean age, 47 years; 62% female), with an average 11-year pain history, were enrolled after experiencing failure of conservative and interventional therapies and meeting strict inclusion criteria, including ODI scores of 30 to 60 and NRS ratings of 6 to 9. Participants were randomized 1:1 to receive either the ReActiv8 Neurostimulation System plus OMM or OMM alone. The primary outcome was change in ODI at 1 year, with secondary outcomes including pain intensity (NRS) and HRQOL (EQ-5D-5L). At 1 year, restorative neurostimulation produced significantly greater improvements than OMM across all end points. The mean ODI change was -19.7 ±1.4 vs -2.9 ±1.4 (between-group difference, -16.8; 95% CI, -20.6 to -13.0; $p < 0.001$), while the NRS improved by -3.6 ±0.2 vs -0.6 ±0.2 (difference, -3.0; 95% CI, -3.6 to -2.5; $p < 0.001$). EQ-5D-5L scores increased by 0.155 ±0.012 compared with 0.008 ±0.012 (difference, 0.147; 95% CI, 0.112-0.182; $p < 0.001$). Clinically meaningful composite response (≥ 15-point ODI and/or ≥ 50% pain reduction) occurred in 72% of the treatment group vs 11% of controls ($p < 0.001$). Device-related adverse events were infrequent and mostly minor, with no lead migrations reported. The trial’s limitations include its open-label design and potential placebo or nocebo effects, although the 1-year end point was chosen to mitigate these influences. The RESTORE trial was funded by Mainstay Medical, the device manufacturer.

Multiple investigators and committee members reported financial and nonfinancial support from Mainstay Medical and other medical device manufacturers, including direct consultant fees, travel expenses, royalties, honoraria, stock options, medical writing support, and research grants. (This study is included in the Hayes Evolving Evidence Review of the ReActiv8 Implantable Neurostimulation System, 2025.)

Gilligan et al. (2024) conducted a prospective, 5-year, longitudinal follow-up of the ReActiv8-B pivotal trial (included below, Gilligan et al., 2021) to evaluate the long-term outcomes of the use of restorative neurostimulation for the treatment of moderate to severe, disabling, refractory, predominantly mechanical CLBP by comparing their baseline data from the VAS, ODI, and EQ-5D-5L index with their data collected at 5 years post implantation. Five-year data were available for 126 of the 204 participants (mean age, 47 years; 54% female) in the original RCT with a crossover study. The authors reported that (1) LBP VAS had improved from 7.3 to 2.4 cm, while 89 of 124 participants (71.8%) had a reduction in pain of at least 50%; (2) the ODI improved from 39.1 to 16.5, with 77 of 126 participants (61.1%) having a reduction of at least 20 points; and (3) the EQ-5D-5L index improved from 0.585 to 0.807. The authors also reported that 46% of the 52 participants discontinued use of opioids, and 23% decreased their intake of opioids over the 5-year follow-up period. Limitations of this follow-up study include the lack of a sham control group (due to crossover), loss of participants to follow-up, and number of explants (62/30%) since the study began. The authors concluded that restorative neurostimulation safely provided clinically substantial and durable benefits in participants with refractory CLBP associated with multifidus muscle dysfunction. The ReActiv8-B trial was funded by Mainstay Medical, the device manufacturer. Multiple investigators reported financial and nonfinancial support from Mainstay Medical and other medical device manufacturers, including grants, royalties, honoraria, stock options, personal and professional fees, and travel expenses. (This study is included in the Hayes Evolving Evidence Review of the ReActiv8 Implantable Neurostimulation System, 2025.)

Thomson et al. (2023) conducted a 3-year, open-label, prospective follow-up for the treatment of CLBP of nociceptive origin with restorative neurostimulation. The study participants completed assessments for pain (NRS), disability (ODI), and HRQOL (EQ-5D-5L), with outcomes collected at 45, 90, and 180 days and at 1, 2, and 3 years after the activation visit, with 33 (79%; mean age, 47.7 years; 36.4% female) of the original 42 (mean age, 47.2 years; 40% female) available at the 3-year appointment. The authors reported that baseline data included a mean NRS of 7.0, mean ODI of 46.6, and EQ-5D-5L of 0.426 and that changes in pain, disability, and QOL at the 3-year follow-up demonstrated a statistically significant improvement, with reductions in NRS scores (by a mean of 2.7) and ODI (to a mean score of 26.0) and an improved EQ-5D-5L index to 0.707. The authors concluded that the ongoing follow-up of this cohort continued to demonstrate that restorative neurostimulation provided a statistically significant, clinically meaningful, and durable response across pain, disability, and QOL scores in participants with mechanical CLBP refractory to conventional management. Limitations of the study include the small sample size, lack of a control group and blinding, and heterogeneity of the study population. This work was supported by Mainstay Medical, including editorial assistance, statistical and data management support, and trial management. Multiple authors reported financial support from Mainstay Medical and other medical device manufacturers, including research grants and consulting fees. (This study is included in the Hayes Evolving Evidence Review of the ReActiv8 Implantable Neurostimulation System, 2025.)

In a follow-up study to Ardeshiri et al. (2022), Ardeshiri et al. (2025) combined data from three clinical trials (ReActiv8-B, ReActiv8-C, and ReActiv8-PMCF), with a combined 261 of the 333 participants who were involved in the original studies and had completed the 2-year follow-up, to examine the effect of restorative neurostimulation in an older demographic. The combined study population was divided into four cohorts of 65 participants based on age quartiles. Each cohort was classified by change in disability (ODI) or change in pain score (NRS/VAS) and assessed as a proportion of participants per group at each time point, while HRQOL and EQ5D-5L were longitudinally compared with baseline. The authors reported that 62% of the oldest quartile (median age, 60 years) had an improvement of 50% in pain and that 48% had a 15-point improvement in ODI, while the entire population (median age, 49 years) had an improvement of 50% in pain in 65% of participants, and 60% of the participants had a 15-point improvement in the ODI. The authors also reported that HRQOL improved in the oldest quartile and the entire population and that all age quartiles improved statistically and clinically over baseline. The authors concluded that their aggregate analysis of the three studies provided an insight into the performance of restorative neurostimulation in an older population and that when compared with a similar cohort of younger participants, there were not statistically or clinically significant differences. Limitations include the heterogeneity of the three included studies and their designs, small cohort of participants in the older quartile, and retrospective design of the study. The ReActiv8-B, ReActiv8-C, and ReActiv8-PMCF trials were funded by Mainstay Medical, the device manufacturer. Multiple authors reported financial and nonfinancial support from Mainstay Medical and other medical device manufacturers, including honoraria, stock options, and professional and consulting fees.

In a prospective, observational follow-up study in 204 implanted trial participants of the ReActiv8-B trial, Gilligan et al. (2023) evaluated the 3-year effectiveness and safety of the ReActiv8 Implantable Neurostimulation System in participants with refractory, disabling CLBP. Data were collected using the LBP VAS, ODI, EQ-5D, and through assessment of the

participant's opioid intake at baseline, 6 months, and 1, 2, and 3 years after activation. There were 45 participants who were withdrawn from the study after device removal (22%) and another 10 participants who were withdrawn due to loss to follow-up (5%). The authors collected data from 133 of the participants and noted that 16 of the participants were not able to keep their 3-year follow-up due to coronavirus disease restrictions but remain available for future follow-up. They reported that a total of 62% of participants had a ≥ 70% VAS reduction, and 67% reported CLBP resolution (VAS ≤ 2.5 cm); 63% had a reduction in the ODI of ≥ 20 points, 83% had improvements of ≥ 50% in the VAS and/or ≥ 20 points in the ODI, and 56% had substantial improvements in both the VAS and ODI. A total of 71% participants (36/51) on opioids at baseline had voluntarily discontinued (49%) or reduced (22%) opioid intake. The authors concluded that 83% of participants experienced clinically substantial improvements in pain, disability, or both at 3 years and that the results of their study showed durable, statistically significant, and clinically substantial benefits in a cohort of participants with severe, disabling CLBP and multifidus muscle dysfunction that were refractory to conservative care. Limitations of the study include the small sample size, high attrition rate, and lack of follow-up in those participants who underwent removal of the device. The study was funded by Mainstay Medical, the device manufacturer. Multiple authors reported financial and nonfinancial support from Mainstay Medical and other medical device manufacturers, including grants, salaries, stock options, and service and personal fees. (This study is included in the Hayes Evolving Evidence Review of the ReActiv8 Implantable Neurostimulation System, 2025.)

Ardeshiri et al. (2022) recruited 44 participants with refractory, predominantly nociceptive, axial CLBP to participate in a single-center, consecutive cohort study to evaluate the effectiveness of restorative neurostimulation to improve pain, disability, and QOL. The median age of the participants was 54 years; the median duration of CLBP was 5.8 years. The study participants had no history of surgical intervention for CLBP prior to being implanted with a neurostimulation device. All surgeries were performed by a single surgeon. Data from 1 year of clinical follow-up were obtained from the ReActiv8 Post Market Surveillance Registry (ReActiv8-C). Outcome measures for pain (NRS), disability (ODI), and QOL (EQ-5D-5L) were collected at baseline and 3, 6, and 12 months after activation. Overall, 40 of the 44 participants (91%) completed follow-up after 1 year of therapy; two participants withdrew from the study before completing 1 year of therapy; and two participants were unable to attend follow-up appointments due to the COVID-19 pandemic. The authors reported that 68% of participants had moderate (≥ 30%) reductions in pain, 52% had substantial (≥ 50%) reductions in pain, and 48% were remitters and had a pain score of ≤ 3 out of 10, which is considered to be mild pain or pain free after 1 year of therapy. No lead migrations were reported; however, one participant required revision due to lead fracture. The authors concluded that clinically meaningful improvements in pain, disability, and QOL were achieved with restorative neurostimulation and that this therapy is a new treatment option for well-selected individuals with refractory CLBP. The study was sponsored by Mainstay Medical, the device manufacturer. Multiple authors reported support from Mainstay Medical and other medical device manufacturers, including research support, salaries, stock ownership, royalties, and speaking fees. (This study is included in the Hayes Evolving Evidence Review of the ReActiv8 Implantable Neurostimulation System, 2025.)

In an Evolving Evidence Review focusing on the ReActiv8 Implantable Neurostimulation System, Hayes (2022; updated 2025) completed a review of full-text clinical studies, clinical practice guidelines, and systematic reviews. Hayes' review of clinical practice guidelines identified weak support for this intervention. They found four poor-/very poor-quality prospective pretest-posttest studies, one fair-quality RCT that compared ReActiv8 treatment to sham, and one good-quality study that compared ReActiv8 to OMM, finding clinically and statistically significant improvements in pain, function/disability, and QOL in individuals with CLBP. Hayes did not find any studies that compared ReActiv8 with an active comparator. They identified a single systematic review evaluating the body of evidence for PNS as a whole, with only one of its included studies assessing the ReActiv8 system. Hayes found two professional society guidelines that specifically addressed multifidus activation and four that addressed unspecified PNS of the lumbar medial branches. Hayes stated that there is weak support for restorative neurostimulation based on these guidelines. Hayes concluded that the evidence suggests that ReActiv8 is a promising treatment for CLBP and that data from two active trials may provide additional insight into the safety and efficacy of the ReActiv8 system.

ECRI (2021; updated 2025) published a Clinical Evidence Assessment focused on the safety and effectiveness of the ReActiv8 Implantable Neurostimulation System for the treatment of CLBP that does not respond to conservative treatment in individuals who are not surgical candidates for spinal procedures. The assessment included studies of any design that reported on clinical outcomes of multifidus stimulation with ReActiv8 in individuals with CLBP. In the initial review, the researchers found two studies to review, including one randomized, double-blinded, sham-controlled clinical trial (Gilligan et al., 2021) and one prospective, multicenter pre-post study. They found that each of the studies had three or more of the following limitations, which resulted in a high risk of bias: a small sample size, no control group, a lack of data on comparisons of interest such as other pain management techniques, short follow-up times, and/or use of an active sham in the study. There were five additional studies identified in the 2023 update, including one RCT and four before-and-after studies. The RCT studied pain relief at the 120-day follow-up, and the researchers found that the between-group difference in pain relief between the treated group and the sham group at the 120-day follow-up was too small to determine if it was clinically important and did not permit conclusions. The review of the four before-and-after studies

suggested that there was pain relief and functional status benefits with the use of ReActiv8 treatment, but the studies were found by ECRI to be at a high risk of bias due to the lack of control groups and small study populations. In the 2024 update, four before-and-after studies were identified, including a 5-year follow-up to the Gilligan et al. (2021) study (Gilligan et al., 2024). The other three studies were found to have enrolled few individuals (n = 44, n = 53, and n = 42); however, the studies were found to be at a high risk of bias due to the lack of independent control groups and/or single-center focus. ECRI also noted that the population of individuals in the Gilligan et al. (2024) follow-up study may have had a different population of individuals than the original group selected for the RCT because of attrition and the lack of continued randomization. ECRI recommended additional independent studies, with outcome reporting that includes broader populations that are intended to receive treatment with ReActiv8. The authors concluded that the evidence remains inconclusive due to too few data on outcomes. In the 2025 update, ECRI's overall assessment of the evidence did not change after review of a newly identified multicenter, open-label RCT (Schwab et al., 2025), funded by the device manufacturer. This study indicated the superiority of ReActiv8 over OMM but had a high risk of bias and lacked blinding.

Four-year outcomes from the ReActiv8-A clinical trial were published by Mitchell et al. (2021) to document the longitudinal benefits of long-term restorative neurostimulation in participants with intractable CLBP. This clinical trial was a prospective, single-arm study at nine sites in the UK, Belgium, and Australia that followed up 53 participants with disabling CLBP with no indications for spine surgery or SCS and failed conventional management, including at least PT and medications. The study population had an average age of 44 ±10 years and had experienced back pain for an average of 14 ±11 years. Stimulation parameters were programmed 14 days post implantation. Participants were given instructions to activate the device for 30 minutes twice each day. The participants were then followed up at 45, 90, 180, and 270 days, and then annually for 48 months. Over the 4 years, one participant was lost to follow-up, 11 exited the study following explant without clinical benefit, four exited following explant with clinical benefit, and one exited because of a device migration that could not be repositioned. Of the initial 53 participants, 34 completed the 48-month follow-up. The authors reported that initially, participant adherence was relatively high, with 84.5% ±22.6% of the maximum number of therapy sessions being completed; however, 4 years after implantation, adherence was at 48.8% ±34.0% (i.e., completion of approximately half of the maximum number of stimulation sessions). The authors reported that mean improvements in LBP from baseline were statistically significant and clinically meaningful for all follow-ups. They concluded that participants with disabling, intractable CLBP who received long-term restorative neurostimulation retained treatment satisfaction and improvement in pain, disability, and QOL through 4 years. Limitations of this study include the small number of participants, high attrition rate, single-arm design, and lack of follow-up in the participants who exited the study. The ReActiv8-A study was sponsored by the device manufacturer, Mainstay Medical. Multiple investigators reported financial and nonfinancial support from Mainstay Medical and other medical device manufacturers, including grants and personal and consultation fees.

Gilligan et al. (2021) conducted a randomized, double-blinded, sham-controlled clinical trial at 26 specialist pain centers to determine the safety and efficacy of an implantable restorative neurostimulator, the ReActiv8 Implantable Neurostimulation System. This study included 204 participants with refractory mechanical CLBP with impaired multifidus control who continued to experience LBP despite > 90 days of medical management and at least one attempt of PT. The participants were randomized after implant surgery using a permuted block scheme for each investigational site to the therapeutic-level stimulation treatment group (n = 102) or the sham low-level stimulation control group (n = 102). All participants participated in two stimulation sessions per day for 120 days. After the primary end point, all reported outcomes were unblinded, and all participants received therapeutic stimulation. All study participants were evaluated for 1 year for long-term outcomes and adverse events. The authors reported that 64% of participants had a ≥ 50% improvement in their LBP. Mean disability improved by 51% (from borderline severe to minimal), and 18 of the 65 participants who were on opioids at baseline discontinued their use. They also reported a 4% serious adverse events rate, including six pocket infections requiring system removal. The authors concluded that this study provided important insights and design considerations for future neuromodulation trials. The study was funded as a regulatory trial by Mainstay Medical, the device manufacturer. Multiple investigators and committee members reported financial and nonfinancial support from Mainstay Medical and other medical device manufacturers, including grants, salaries, stock options, personal fees, and travel expenses. (This study is included in the Hayes Evolving Evidence Review of the ReActiv8 Implantable Neurostimulation System, 2025.)

Scrambler Therapy

There is insufficient evidence in the published, peer-reviewed scientific literature to support the efficacy of scrambler therapy. Studies comparing scrambler therapy with conventional treatment options and with sham therapy are lacking.

The Stowell-Campos et al. (2024) single-center, randomized, single-blinded, sham-controlled pilot study evaluated the efficacy of scrambler therapy for treating poststroke contralesional pain. Overall, 20 participants over age 18 years with ischemic or hemorrhagic stroke confirmed by neuroimaging and persistent pain in the affected area were enrolled. Exclusion criteria included transient ischemic attack, without imaging evidence; implantable devices; recent myocardial

infarction; uncontrolled epilepsy; and symptomatic brain metastases. Participants were randomized to receive either scrambler therapy or sham therapy. Each underwent five consecutive, daily 40-minute sessions, with pain scores recorded at baseline, before and after each session, and at a 4-week follow-up. The primary outcome was change in pain score on the NRS. The secondary outcomes included the proportion of participants achieving > 50% pain reduction. Immediately after the fifth session, the scrambler therapy group showed a statistically significant mean pain score reduction of 3.73 points (SD, 2.85) compared with 0.94 points (SD, 1.36) in the sham group (p = 0.012). At 4 weeks, the scrambler therapy group maintained a mean reduction of 2.57 points (SD, 2.07) vs 0.25 points (SD, 0.84) in the sham group (p = 0.004). Notably, 70% of scrambler therapy–treated participants achieved > 50% pain reduction post treatment compared with 10% in the sham group (p = 0.006), although this difference was not significant at the follow-up (30% vs 10%, p = ns). Limitations include the small sample size, lack of masking of the investigator, and lack of stratification by stroke characteristics. Clinically, scrambler therapy may offer a promising nonpharmacological option for poststroke pain, particularly for individuals who have not responded to conventional medications, although booster sessions may be needed for sustained relief.

Chung et al. (2024) conducted a single-arm pilot study to assess the efficacy of scrambler therapy for the treatment of symptoms of chemotherapy-induced peripheral neuropathy (CIPN). The study included 10 participants (mean age, 60.8 years; 50% male; 70% Caucasian) with moderate to severe CIPN symptoms for more than 3 months who were treated for six different cancer diagnoses. The participants were regularly taking a variety of pain medications for their CIPN-related pain at the time of study enrollment. Each participant underwent scrambler therapy for 45 minutes per treatment for 10 consecutive weekdays over 2 weeks and were evaluated weekly for 1 month, then monthly for 5 more months. One participant stopped treatment after the fifth day due to a family emergency but completed the full 6 months of follow-up. The authors reported that the worst pain was reduced by the 6-month point. By the end of the treatment, there was an improvement from baseline in balance (64%), gait (62%), and activity (64%), with continual improvement at 6 months from baseline in balance (38%), gait (43%), and activity (45%). The authors also reported that symptoms of numbness, tingling, trouble walking, and disturbed sleep had significant improvements, while pain medication use decreased by 70% at the end of treatment and by 42% at 6 months. Participant satisfaction was also reported to be high (82%), and the authors did not report any adverse events. Limitations of the study include the lack of a control group, small sample size, single-center design, heterogeneity of cancer diagnoses, and use of multiple questionnaires that may have been a source of reporting bias. The authors concluded that the results of the pilot study supported the use of scrambler therapy by demonstrating improvement in multiple domains of QOL in participants with CIPN during an extended follow-up of 6 months. They recommended further large-scale, prospective studies to confirm their findings.

Yoo et al. (2023) conducted a single-arm, prospective pilot study to explore the long-term effects of scrambler therapy in managing PDN. The study included nine participants (mean age, 58 years; 34% female) who received 10 consecutive scrambler therapy treatments of 45 minutes every 1 to 2 days. The primary outcome was pain score measured with the VAS at baseline, during scrambler therapy, immediately after the treatment, and at 1, 2, 3, and 6 months after scrambler therapy. The secondary outcomes were the Michigan Neuropathy Screening Instrument (MNSI), Semmes-Weinstein Monofilament Test, and Leeds Assessment of Neuropathic Symptoms and Signs pain scores, which were measured at baseline, immediately after treatment, and at 1, 2, 3, and 6 months after treatment. The authors reported that the VAS scores showed significant improvement at the eighth, ninth, and tenth sessions during the treatment and 1 month after treatment but not at 2, 3, and 6 months post treatment. The authors also reported that the MNSI self-report component score was decreased 1 month after the scrambler therapy, but there was no significant change thereafter. No significant changes in the MNSI examination component, Semmes-Weinstein Monofilament Test, and Leeds Assessment of Neuropathic Symptoms and Signs pain scores were observed during the study period. Limitations include the small sample size, lack of a control group, and lack of more objective measurement tools. The authors concluded that their preliminary data suggested that scrambler therapy may have short-term effects and limited long-term effects on painful PDN, and they recommended further research to investigate the mechanism of action of scrambler therapy.

The aim of the meta-analysis done by Jin et al. (2022) was to investigate the efficacy of scrambler therapy for the management of chronic pain. The study included seven RCTs, with 287 adults (142 were in the intervention group, and 145 were in the control group) who experienced chronic pain for more than 3 months. Pain conditions included in the studies were CIPN in four trials, postsurgical neuropathic pain, postherpetic neuralgia, and pain due to spinal stenosis, each in two trials, and cancer pain and persistent nonspecific LBP in one trial each. Comparison groups received various other treatments, including sham stimulation, conventional medicine, an active comparator, or no treatment. Treatment sessions were 30 to 50 minutes each over 10 working days, and the follow-up periods ranged from 10 days to 3 months from baseline. The authors reported that scrambler therapy marginally decreased pain scores at the end of the treatment period compared with the control group. A subgroup analysis found that the use of scrambler therapy significantly reduced analgesic consumption compared with the control group. The authors noted that there was no significant efficacy observed in the subgroup meta-analyses by methodological quality, type of diseases causing pain, and follow-up period. Limitations include the small sample sizes of the RCTs, low methodological quality, heterogeneity of the devices used

(first generation vs second generation), heterogeneity of the study designs, and inclusion of multiple causes of chronic pain. The authors concluded that scrambler therapy appeared to be effective in the management of individuals with chronic pain; however, they recommended further large RCTs to confirm their findings.

Kashyap et al. (2022) conducted an RCT to evaluate the efficacy of scrambler therapy for enhancing QOL in people with cancer through minimizing pain and opioid intake. A total of 80 participants with head, neck, and thoracic cancer were included in the study. In both arms, participants were given pain management drugs following the WHO analgesic ladder for 10 consecutive days. Scrambler therapy was given each day in the intervention arm. Pain, morphine intake, and QOL (WHOQOL-BREF) were assessed. All domains of QOL improved in the intervention arm compared with the control arm. In comparison to baseline, pain improved in both the intervention and the control arm on day 10 and at follow-up. However, QOL significantly improved in the intervention arm, while morphine intake decreased. In the control arm, QOL deteriorated, while morphine intake increased. The authors concluded that scrambler therapy improved QOL. Since the increase in QOL took place with a lower morphine intake, the improvement in QOL may not only be explained by lower pain scores but also by a reduced intake of morphine because the lower dosages of morphine will decrease the likelihood of side effects associated with the drug. Further research, with RCTs, is needed to validate these findings

Lee et al. (2022) conducted a prospective, double-blinded RCT to evaluate the clinical usefulness of scrambler therapy and identify the pain network alterations associated with scrambler therapy for chronic neuropathic pain caused by burns. This study (NCT03865693) included 43 participants who were experiencing chronic neuropathic pain after unilateral burn injuries. The participants had moderate or greater chronic pain (a VAS score of ≥ 5), despite treatment using gabapentin and other physical modalities. They were randomized 1:1 to receive real or sham scrambler therapy sessions. The scrambler therapy was performed using the MC5-A Calmare device for ten 45-minute sessions (Monday to Friday for 2 weeks). Baseline and posttreatment parameters were evaluated subjectively using the VAS score for pain and the Hamilton Depression Rating Scale. MRI was performed to identify objective CNS changes by measuring the cerebral blood volume (CBV). After 10 scrambler therapy sessions (2 weeks), the treatment group exhibited a reduction in pain relative to the sham group. Relative to the pre–scrambler therapy findings, the post–scrambler therapy MRI evaluations revealed decreased CBV in the orbitofrontal gyrus, middle frontal gyrus, superior frontal gyrus, and gyrus rectus. In addition, the CBV was increased in the precentral gyrus and postcentral gyrus of the hemisphere associated with the burned limb in the scrambler therapy group, as compared with the CBV in the sham group. Thus, a clinical effect from scrambler therapy on burn pain was observed after 2 weeks, and a potential mechanism for the treatment effect was identified. The authors concluded that scrambler therapy may be an alternative strategy for managing chronic pain in individuals with a history of burns. Limitations include a small sample size and short duration of follow-up.

Wang et al. (2022b) conducted a systematic review to evaluate the best available evidence regarding the use of noninvasive neuromodulation techniques for managing CIPN. A systematic literature search of the following databases, from their inception to October 17, 2021, was performed and was updated on March 2, 2022: AMED via Ovid, CINAHL via EBSCOhost, the Cochrane Library, Embase, PEDro, PubMed, and Web of Science. RCTs and quasiexperimental studies examining the safety, feasibility, and efficacy of noninvasive neuromodulation techniques for managing established CIPN were identified. Narrative synthesis was used to analyze data collected from the included studies. Nine RCTs and nine quasiexperimental studies were included. A variety of noninvasive peripheral and central neuromodulation techniques were investigated in those studies, including scrambler therapy, electrical stimulations, photobiomodulation, magnetic field therapy, therapeutic ultrasound, neurofeedback, and repetitive transcranial magnetic stimulation. The authors stated that noninvasive neuromodulation techniques for the management of established CIPN were generally safe and feasible. The efficacy of peripheral neuromodulation techniques such as scrambler therapy and TENS was mostly unsatisfactory, while central neuromodulation techniques such as neurofeedback and repetitive transcranial magnetic stimulation were promising. The authors concluded that the use of noninvasive neuromodulation techniques for managing CIPN, such as scrambler therapy, was still in its early stages. They stated that noninvasive central neuromodulation techniques have significant potential for relieving chronic pain and neuropathic symptoms related to CIPN, meriting further exploration. The heterogeneity of the included studies prevented the conduction of a pooled analysis of data from those studies. Therefore, the overall effect of the neuromodulation techniques for managing CIPN could not be estimated. Further research, with RCTs, is needed to validate these findings.

A systematic review was conducted by Karri et al. (2023) to summarize the available evidence regarding the use of scrambler therapy in treating chronic pain syndromes as well as its analgesic benefits, adverse effects, procedure-specific variables, and other metrics such as sensorimotor tests, medication reduction, and effect on circulation neuropeptides. Two review authors, independently and in a standardized, unblinded fashion, conducted a systematic review to identify relevant studies and extract the necessary outcome measures by surveying multiple data sources from January 1950 through October 2021. A conservative search strategy was implemented to identify all scrambler therapy studies for the treatment of chronic pain syndromes. The primary outcome parameters collected were analgesic benefit, adverse effects, and other metrics such as sensorimotor testing. A total of 21 studies met the final criteria for inclusion and included RCTs

(n = 8), prospective observational studies (n = 10), and retrospective cohort studies (n = 3). Nearly all the reported studies explored the use of scrambler therapy for the treatment of neuropathic pain, with chemotherapy-induced peripheral neuropathy being the most studied condition. Most studies were limited by small cohorts but reported scrambler therapy as being safe, being well tolerated, and providing clinically meaningful pain reduction. The duration of posttreatment follow-up ranged from 10 to 14 days (concordant with completion of typical scrambler therapy protocols) to 3 months. Secondary benefits such as medication reduction and improvement of sensory and motor symptoms were noted by some studies. The authors concluded that scrambler therapy was a safe intervention, with a potential for analgesic benefit for neuropathic pain conditions. Although the available evidence was most robust for treating chemotherapy-induced peripheral neuropathy, scrambler therapy was also shown to be effective in treating other neuropathic pain syndromes. Evidence for scrambler therapy use in nociceptive pain conditions is limited but appears promising. The authors concluded that the favorable safety profile and increasing evidence base for scrambler therapy warrant more extensive recognition and consideration for use in clinical care. Limitations to this study include performance and detection biases, and several included studies reported industry affiliations with the manufacturer of the scrambler therapy device. The inventor of the scrambler therapy device was an author of several of the included studies. Further investigation is needed before the clinical usefulness of this procedure is proven. The Kashyap and Bhatnagar (2020) study and the Compagnone and Tagliaferri (2015) study that were previously included in this policy were included in this systematic review.

Hayes (2020; updated 2023) conducted a systematic review to evaluate evidence on the use of scrambler therapy, also referred to as Calmare Pain Therapy and transcutaneous electrical modulation pain reprocessing, for the management of chronic pain related to cancer or cancer treatment. The initial literature search identified 12 clinical studies on the efficacy and safety of scrambler therapy for cancer- or cancer treatment-related pain, including two RCTs and 10 single-arm repeated-measure time series. Hayes assessed the overall body of evidence as being of very low quality, citing limitations such as general lack of follow-up to assess pain relief over time;, small sample sizes;, lack of statistical rigor;, lack of blinding;, and substantial attrition. With their 2023 update, Hayes identified three newly published studies; however, they determined that the studies of cancer-related pain would not result in a change in their finding that the body of evidence, still considered low or very low quality, is insufficient to draw conclusions regarding the efficacy and safety of scrambler therapy for the management of cancer-related pain in adults. Hayes noted that the newly published studies of scrambler therapy for the management of cancer treatment–-related pain in adults would possibly result in a change in their findings, which had been similarly considered to be of low or very low quality at their last assessment.

Hayes (2020; updated 2023) conducted a systematic review to evaluate evidence on the use of scrambler therapy, also referred to as Calmare Pain Therapy and transcutaneous electrical modulation pain reprocessing, for the management of chronic pain not related to cancer or cancer treatment. The initial literature search identified nine relevant clinical studies that met the inclusion criteria: two RCTs, one quasi-RCT, and six single-arm studies, including one repeated-measures time series, three pretest/posttest studies, and two retrospective database reviews. Hayes noted that a majority of these studies had a limited follow-up of ≤ 6 months, making it difficult to evaluate the long-term effects of scrambler therapy, and that the generalizability of the results was unclear because of the varied treatment regimens across studies and heterogeneity of pain etiologies in the evaluated populations. With their 2023 update, Hayes identified two newly published studies; however, they determined that neither of these would result in a change in their findings, including that the body of evidence, which was considered low or very low quality, is insufficient to draw conclusions regarding the efficacy and safety of scrambler therapy for the management of chronic pain not related to cancer or cancer treatment in adults. Hayes continues to recommend additional large, well-designed clinical studies to evaluate the comparative and long-term effectiveness and safety of scrambler therapy and to delineate selection criteria for individuals.

Clinical Practice Guidelines

American Society of Clinical Oncology (ASCO)

In the updated evidence-based clinical practice guideline by Loprinzi et al. (2020) on the prevention and management of CIPN in survivors of adult cancers, ASCO reviewed two randomized trials evaluating scrambler therapy. The guideline states that outside the context of a clinical trial, no recommendation for its use in the treatment of CIPN could be made due to the low strength of evidence and low benefits. The authors noted that while the evidence suggests a potential for benefit from scrambler therapy, definitive studies, with larger sample sizes, are needed to confirm the efficacy and clarify risks.

European Society for Medical Oncology (ESMO)/European Oncology Nursing Society (EONS)/ European Association of Neuro-Oncology (EANO)

In a joint ESMO/EONS/EANO clinical practice guideline by Jordan et al. (2020) that addresses the diagnosis, prevention, treatment, and follow-up of CIPN, scrambler therapy is not recommended to treat CIPN due to small, randomized trials with inconsistent effectiveness outcomes. The guideline graded scrambler therapy with a D rating, indicating that there is

moderate evidence against efficacy or for adverse outcomes, and that this treatment approach is generally not recommended.

Translingual Stimulation

There is insufficient evidence in the published, peer-reviewed scientific literature to support the efficacy of translingual stimulation (TLS) for gait rehabilitation. Robust studies evaluating the long-term safety and efficacy of TLS to treat gait disorders secondary to MS or other conditions are lacking.

ECRI published a Clinical Evidence Assessment on the Portable Neuromodulation Stimulator™ (PoNS) device and its safety and efficacy for treating chronic balance deficits due to neurological disorders. The PoNS device is a portable, nonimplantable NMES device with a mouthpiece that sends NMES to the dorsal surface of the tongue. The assessment included three RCTs and one nonrandomized controlled study and concluded that the evidence was inconclusive due to too few data on the safety and efficacy of PoNS. The authors noted that the same research center that developed the PoNS device directed the three RCTs. They determined that the RCTs had a low risk of bias, although it was because of the way that the trials blinded the individuals, trainers, and investigators; however, the nonrandomized controlled study had a high risk of bias due to the lack of randomization and blinding. The authors noted that PoNS with PT appeared to improve gait and balance in people with mild to moderate traumatic brain injury (mmTBI) and that it may also benefit those with MS and CP; however, the authors recommended additional studies to confirm the results and to determine how long improvements last (2021).

Multiple Sclerosis

Leonard et al. (2017) completed a pilot study of the effects of noninvasive tongue stimulation using the PoNS device, combined with intensive cognitive and physical rehabilitation, on working memory, gait, balance, and concomitant changes in the brain. Their study included 14 participants with MS who were randomly assigned to a PoNS stimulation group (n = 7) or to a sham PoNS stimulation group (n = 7). At the end of the study, participants in the sham group were offered the opportunity to use the PoNS device, and five participants returned and completed the active training. The authors concluded that there were significant effects of interventions across the wide range of cognitive domains, both in the active and in the sham groups, although there was a trend of greater improvement in the active group. The data demonstrated an improvement over time following PoNS training in both the active and in the rollover group, suggesting that the training can have a positive effect on balance in individuals with MS. The authors noted that a major shortcoming of the study was the low number of participants in each group, and they recognized the need for a larger study that balances disease duration across groups.

In a randomized, double-blinded, controlled pilot trial of PoNS, Tyler et al. (2014) evaluated the effect of targeted PT with and without noninvasive neuromodulation to improve gait in chronic MS. The study included 20 participants with chronic MS and an identified gait disturbance who were randomly assigned by the primary investigator to either an active group (n = 10) that received electrical stimulation on the tongue or to a control group (n = 10) that used a device that did not provide a physiologically significant stimulation on the tongue. The participants and therapists were blinded as to which group the participant was assigned. Both groups completed a 14-week therapy program that included a standardized combination of exercise and the PoNS device that provided electrical stimulation to the tongue. The authors noted that all participants appeared to demonstrate improvements initially, but only the active group continued to improve over the length of the study. Data showed that participants who trained using exercise only, without stimulation (control group), continued to improve for the first month at home and then exhibited a plateau or even a decrease in performance. The authors concluded that the active group showed statistically greater improvement in gait than the control group and that noninvasive electrotactile stimulation, when combined with targeted PT exercises, can significantly reduce the clinical symptoms of gait dysfunction in MS.

Traumatic Brain Injury

In a single-arm pre-post study conducted at an academic medical center, Chu et al. (2025) reanalyzed the same nine-participant cohort reported in Hou et al. (2022) (summarized below) under the same registered trial (NCT02158494). Both participants and behavioral assessors were blinded to stimulation frequency, but there was no sham control, and each participant served as their own comparator. Resting state functional MRI (10 minutes, eyes-closed scans on a 3T GE750) and behavioral assessments [Sensory Organization Test (SOT) for balance and Dynamic Gait Index (DGI) for gait] were obtained immediately before and after the TLS plus therapy program. Whereas the 2022 report used a seed-based approach focused on sensory/somatomotor, visual, and cerebellar seeds and identified one false discovery rate (FDR)–-significant edge plus an uncorrected cerebellar finding, the 2025 paper applied a whole- brain, network- level analysis to the same imaging dataset. Using the Dosenbach 160 node atlas organized by Yeo networks, the authors tested intra- and internetwork functional connectivity as the primary outcome, with SOT and DGI change and brain-behavior correlations as secondary outcomes. All tests used paired statistics with FDR correction; CIs were not reported. Clinically, participants

improved from baseline on both behavioral measures after TLS combined with therapy, mirroring the earlier report. Balance improved on the SOT [t(8) = 2.742;, p = 0.028], and gait improved on the DGI [t(8) = 2.855;, p = 0.024]; CIs were not provided. On imaging, the network- level analysis demonstrated widespread, FDR-corrected increases in intranetwork connectivity across the somatosensory, visual, dorsal attention, default mode, and frontoparietal systems, alongside significant internetwork strengthening between somatosensory and frontoparietal nodes. In contrast to the uncorrected cerebellar edge noted in 2022, the 2025 analysis did not identify significant cerebellar changes after multiple comparison correction. Importantly, the study linked these network effects to function; improvement in gait correlated positively with increased intranetwork somatosensory connectivity (e.g., right precentral/right parietal;, r = 0.728;, p = 0.026), while improvement in balance correlated with reduced coupling between frontoparietal and somatosensory nodes (e.g., right dorsolateral prefrontal/right precentral;, r = -0.784;, p = 0.012), a pattern consistent with more automatic balance control that requires less executive oversight. ; CIs for these correlations were not reported. Taken together, this work extends the 2022 seed-based findings by moving to a comprehensive systems- level account that connects TLS-related network plasticity with clinically meaningful gains in balance and gait. At the same time, key limitations temper interpretation: the sample is small and single -site (n = 9), there was no sham-controlled comparator to isolate the specific effects of TLS vs therapy or nonspecific factors, the stimulation frequency subgroups are underpowered, and all analyses come from the same cohort, rather than an independent replication. This study suggests that a short TLS plus therapy program in chronic mmTBI is associated with measurable improvements in balance and gait and concurrent large- scale connectivity changes that align with plausible neurophysiological mechanisms. However, these findings are preliminary and best viewed as hypothesis generating; larger, sham-controlled trials are needed before routine clinical adoption. Multiple authors disclosed financial interests in Helius Medical Technologies and intellectual property interests in NeuroRehabilitation, LLC's PoNS technology. One author is also a board member of Helius Medical Technologies.

Hou et al. (2022) conducted a clinical investigative study to evaluate the effectiveness of TLNS in patients with mmTBI and related brain connectivity using a resting-state functional connectivity (RSFC) approach. This study was part of a completed long-term clinical trial (NCT02158494) investigating the efficacy of TLS (also referred to as cranial nerve noninvasive neuromodulation). Nine participants with mmTBI were included in the study (ages, 43-62 years; mean age, 53.11 ±6.60 years; three male and six female participants). Their mmTBIs each occurred at least 1 year before enrollment. Participants had previously participated in PT and had reached a plateau in their functional recovery. Their mmTBI diagnoses were made according to the guidelines established by the Veterans Affairs/Department of Defense. All participants could independently walk for at least 20 minutes and had no medication changes for at least 3 months before the experiment. They were without other medical problems such as oral health, diabetes, hypertension, chronic infectious disease, or other potentially confounding neurological disorders. Resting-state images with 5 minutes on the GE750 3T scanner were acquired from all participants with mmTBI. A paired t test was used for calculating changes in RSFC and behavioral scores before and after the TLS intervention. The balance and movement performances related to mmTBI were evaluated by the SOT and DGI. Compared with pre-TLS intervention, behavioral changes in the SOT and DGI were observed. The analysis revealed increased RSFC between the left postcentral gyrus, left inferior parietal lobule, and left Brodmann area 40 as well as increased RSFC between the right culmen and right declive, indicating changes due to translingual neural stimulation treatment. However, there were no correlations between the sensory/somatomotor (or visual or cerebellar) network and SOT/DGI behavioral performance. The authors concluded that this study presents evidence that TLS effectively improves balance and movement in individuals with mmTBI accompanied by increased involvement of neural regions associated with gait, balance, and motor control; therefore, they concluded that TLS is an effective approach to treating the effects of mmTBI. A small sample size makes it difficult to decide whether these conclusions can be generalized to a larger population. Further research is needed to determine the clinical relevance of these findings.

Ptito et al. (2021) conducted a multicenter RCT with 122 adults, who were aged 18 to 65 years, to assess the safety and efficacy of translingual neurostimulation in people with a chronic balance deficit who had received PT following mmTBI and had plateaued in recovery. Translingual neurostimulation was delivered through the PoNS device. Randomized participants received PT plus either high-frequency pulse (HFP; active therapy; n = 59) or low-frequency pulse (LFP; control group; n = 63) translingual neurostimulation during a 5-week treatment program. All participants followed the same translingual neurostimulation and PT regimen, with a customized training intensity that was based on the participant's presentation and abilities. Adherence was monitored and verified through the translingual neurostimulation device automatically by logging usage and showed that overall adherence was a mean of 94% across weeks 2 to 5 of the study. The authors noted that participants in both the active and the control groups had significant and clinically meaningful improvements in SOT composite score and the DGI. They noted that the results of this study are limited by the small sample size; the fact that there were two times more female than male participants, which is not consistent with the incidence of TBI in the general population; and great variability in previous therapy programs, which may have influenced the efficacy of the PT program in the study. The authors concluded that the combination of translingual neurostimulation plus targeted PT resulted in significant improvements in balance, gait, and sleep quality, in addition to reductions in the frequency of headaches and falls.

Tyler et al. (2019) conducted a single-site, double-blinded RCT to compare the efficacy of the dosage of high- and low-frequency noninvasive PoNS plus targeted PT for treating chronic balance and gait deficits in participants with mmTBI. In their study, 44 participants (18-65 years old) were randomized 1:1 into either an HFP group or LFP group. All participants received TLS (HFP or LFP) with PT for a total of 14 weeks (two in clinic, 12 at home), twice daily, followed by another 12 weeks without treatment. The authors found that both groups had a significant improvement in balance, gait, and sleep quality, along with reduction in headache severity and frequency. They also found that the improvements were sustained through the 12 weeks after discontinuing TLS and that results between the groups did not differ significantly. Limitations identified by the authors include the inherent variable presentation of TBI, differences in the nature of mmTBI, participant age, symptom number and severity, time since injury, age at time of injury, and degree of success with prior therapy programs, any or all of which might have influenced the variability seen with each assessment. They also noted that there was variability in each participant's physical, cognitive, and emotional capacity for the training program as well as a placebo effect, Hawthorne effect, and nonspecific attention and care on study outcomes. The authors recommended future research to assess the dosing parameters of TLS as well as the additional and longer-term benefits of this treatment.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Functional Electrical Stimulation Devices

Products used for functional electrical stimulation are extensive. Refer to the following website for more information and search by either product code GZI or product name in the device name section: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed August 14, 2025)

Neuromuscular Electrical Stimulation for Muscle Rehabilitation Devices

Products used for neuromuscular electrical stimulation for muscle rehabilitation are extensive. Refer to the following website for more information and search by either product code IPF or product name in the device name section: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed August 14, 2025)

Interferential Therapy Devices

Products used for interferential therapy are extensive. Refer to the following website for more information and search by either product code LIH or product name in the device name section: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed August 14, 2025)

Pulsed Electromagnetic Field Stimulation

There are several devices used for pulsed electromagnetic field stimulation. Refer to the following website for more information and search by either product code ILX or the product name: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed August 14, 2025)

Percutaneous/Peripheral Nerve Stimulation

There are several devices used for percutaneous/peripheral nerve stimulation such as the StimRouter Neuromodulation System, SPRINT PNS System, and the Freedom Peripheral Nerve Stimulator. Refer to the following website for more information and search by either product codes NHI, GZB, and GZF or the product name in the device name section: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed August 14, 2025)

Peripheral Subcutaneous Field Stimulation or Peripheral Nerve Field Stimulation Devices

No peripheral nerve field stimulation devices have been specifically approved for the treatment of pain or muscle rehabilitation. The devices used in clinical studies typically are implantable pulse generators and supplies approved as Class III devices for spinal cord stimulation, which may be considered an off-label use of these devices. Refer to the following website for more information, and search by product code LGW or product name in the device name section: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm. (Accessed October 13, 2025)

Microcurrent Electrical Nerve Stimulation Therapy Devices

Microcurrent electrical nerve stimulation devices are categorized as transcutaneous electrical nerve stimulation (TENS) devices intended for pain relief. Refer to the following website for more information, and search by product code GZJ with

the specific product name in the device name section:
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed August 14, 2025)

Percutaneous Electrical Nerve Stimulation

The FDA regulates percutaneous electrical nerve stimulators as Class II devices (product codes NHI and BWK). Several percutaneous electrical nerve stimulation devices have been approved by the FDA. The Deepwave Percutaneous Neuromodulation Pain Therapy System received FDA 510K approval on April 27, 2006 (Product Code NHI) as a PENS device used for the treatment of pain. Refer to the following website for more information and search by product name in the device name section: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm.
(Accessed August 14, 2025)

Percutaneous Electrical Nerve Field Stimulation

The IB-Stim, a percutaneous electrical nerve field stimulation system, which is intended for use with functional abdominal pain associated with irritable bowel syndrome in patients 11 to 18 years of age, was FDA approved on June 7, 2019. Refer to the following website for more information, and search by product code QHH or PZR:
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/denovo.cfm?ID = DEN180057.
(Accessed August 14, 2025)

Restorative Neurostimulation

Restorative neurostimulation devices are categorized as implanted neuromuscular stimulators for lower back muscles. The ReActiv8 Implantable Neurostimulation System was granted premarket approval on June 16, 2020. The device is indicated for bilateral stimulation of the L2 medial branch of the dorsal ramus as it crosses the transverse process at L3 as an aid in the management of intractable chronic low back pain that is associated with multifidus muscle dysfunction, as evidenced by imaging or physiological testing in adults who have experienced failure of therapy, including pain medications and physical therapy and are not candidates for spine surgery. Refer to the following website for more information using product code QLK: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm.
(Accessed October 30, 2025)

Scrambler Therapy

The Calmare/ST MC-5A TENS Device was initially approved by the FDA on February 20, 2009. A second 510(k) clearance was issued on May 22, 2015, for the ST MC-5A Device which has also been replaced by the Scrambler Therapy Technology (Model ST-5A) on December 23, 2020 (product code GZJ). Refer to the following website for more information:
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed October 30, 2025)

Transcutaneous Electrical Nerve Stimulators

TENS are regulated by the FDA as Class II devices. Products for TENS are too numerous to list. Refer to the following website for more information (use product codes GZJ, NUH, or NGX). Available at:
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed October 30, 2025)

Translingual Stimulation Devices

Translingual stimulation devices are categorized as neuromuscular tongue stimulators to treat motor deficits. The Portable Neuromodulation Stimulator device was granted De Novo approval on March 25, 2021. The device is indicated for use as a short-term treatment of gait deficit due to mild to moderate symptoms from multiple sclerosis and is to be used as an adjunct to a supervised therapeutic exercise program in patients 22 years of age or over by prescription only. Refer to the following website for more information https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm.
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Policy History/Revision Information

Date	Summary of Changes

05/01/2026	**Coverage Rationale**
	• Revised list of unproven and not medically necessary indications; replaced “pulsed electrical stimulation (PES)” with “*pulsed electromagnetic field stimulation (PEMF)* [*also known as* pulsed electrical stimulation (PES)]
	Medical Records Documentation Used for Reviews
	• Added language to indicate:
	  ○ Benefit coverage for health services is determined by the federal, state, or contractual requirements, and applicable laws that may require coverage for a specific service
	  ○ Medical records documentation may be required to assess whether the member meets the clinical criteria for coverage but does not guarantee coverage of the service requested
	  ○ The patient's medical record must contain documentation that fully supports the medical necessity for the requested services
	  ○ This documentation includes but is not limited to relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures
	  ○ Documentation supporting the medical necessity should be legible, maintained in the patient's medical record, and must be made available upon request
	Applicable Codes
	• Added CPT code 64567
	• Removed CPT code 0720T
	Supporting Information
	• Updated *Description of Services*, *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information
	• Archived previous policy version CS036KY.11

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare uses InterQual® for the primary medical/surgical criteria, and the American Society of Addiction Medicine (ASAM) for substance use, in administering health benefits. If InterQual® does not have applicable criteria, UnitedHealthcare may also use UnitedHealthcare Medical Policies, Coverage Determination Guidelines, and/or Utilization Review Guidelines that have been approved by the Kentucky Department for Medicaid Services. The UnitedHealthcare Medical Policies, Coverage Determination Guidelines, and Utilization Review Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.