07.01.61 Spinal Cord and Dorsal Root Ganglion Stimulation

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Related Policies:

- 07.01.59 Deep Brain Stimulation

Summary

Description

Spinal cord stimulation (SCS) delivers low-voltage electrical stimulation to the dorsal columns of the spinal cord to block the sensation of pain; this is achieved through a surgically implanted spinal cord stimulation device, which comes equipped with a radiofrequency receiver. The neurostimulator device is also issued with a standard power source (battery) that can be implanted or worn externally. Other neurostimulators target the dorsal root ganglion.

Summary of Evidence

Treatment Refractory Chronic Pain

For individuals who have treatment-refractory chronic pain of the trunk or limbs who receive standard spinal cord stimulation (SCS), the evidence includes systematic reviews and randomized controlled trials (RCTs). Relevant outcomes are symptoms, functional outcomes, quality of life (QOL), medication use, and treatment-related morbidity. Available RCTs are heterogeneous regarding underlying diagnoses in select patient populations. However, the trials including individuals with underlying neuropathic pain processes have shown a significant benefit with SCS. Systematic reviews have supported the use of SCS to treat refractory trunk or limb pain, and patients who have failed all other treatment modalities have few options. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have treatment-refractory chronic pain of the trunk or limbs who receive high-frequency SCS, the evidence includes a systematic review and RCTs. Relevant outcomes are symptoms, functional outcomes, QOL, medication use, and treatment-related morbidity. Two RCTs that enrolled participants not previously treated with SCS reported clinically and statistically significant benefits associated with high-frequency SCS. Another RCT in individuals who had chronic pain despite previous treatment with standard SCS found no benefit for those receiving high-frequency stimulation compared with sham-control; however, it is difficult to compare these findings with other trials of SCS due to the different patient populations, short treatment periods, and the crossover period effect. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have treatment-refractory chronic pain of the trunk or limbs who receive dorsal root ganglion stimulation (DRGS), the evidence includes a systematic review, an RCT, and case series. Relevant outcomes are symptoms, functional outcomes, QOL, medication use, and treatment-related morbidity. The unblinded RCT found that individuals receiving DRGS had significantly higher rates of treatment success (physical functioning score and QOL measures), at 3 and 12 months compared with those receiving standard SCS devices. DRGS was found to be noninferior to SCS in the percentage achieving $\geq$50% pain reduction, emotional functioning score, and 36-Item Short-Form Health Survey scores. Both groups experienced paresthesia's but individuals in the dorsal root ganglion group reported less postural variation in paresthesia and reduced extraneous stimulation in nonpainful areas. Rates of serious adverse events were similar between the 2 study arms. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Critical Limb Ischemia

For individuals who have critical limb ischemia who receive SCS, the evidence includes systematic reviews of several small RCTs. Relevant outcomes are overall survival, symptoms, functional outcomes, QOL, morbid events, hospitalizations, and treatment-related morbidity. In pooled analyses, SCS was associated with a lower risk of amputation versus control, but results were not consistently statistically significant due to differences in methodologies. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Treatment-Refractory Angina Pectoris

For individuals who have treatment-refractory angina pectoris who receive SCS, the evidence includes systematic reviews and RCTs. Relevant outcomes are overall survival, symptoms, functional outcomes, QOL, morbid events, hospitalizations, and treatment-related morbidity. Numerous small RCTs have evaluated SCS as a treatment for refractory angina. While some have reported benefits, most have not.

In 2 recent RCTs, there was no significant benefit in the primary outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Heart Failure

For individuals who have heart failure who receive SCS, the evidence includes a systematic review. Relevant outcomes are overall survival, symptoms, functional outcomes, QOL, morbid events, hospitalizations, and treatment-related morbidity. Four studies (including 2 RCTs) with a total of 125 patients were selected. Two studies reported improvements in New York Heart Association classification, and quality of life parameters, while only one study showed positive changes in left ventricular ejection function and VO2 max. No studies found significant changes in NT-proBNP (N-terminal Pro-Brain Natriuretic Peptide) following SCS therapy. Discrepancies in results could be due to methodological variations and induction technique diversity. Further studies are needed to develop a solid approach for employing SCS in heart failure patients.

Cancer-Related Pain

For individuals who have cancer-related pain who receive SCS, the evidence includes case series. Relevant outcomes are symptoms, functional outcomes, medication use, and treatment-related morbidity. No RCTs evaluating spinal cord stimulation in this population were identified. The evidence is insufficient to determine that the technology results in an improvement in the net health outcomes.

Post-Herpetic Neuralgia

For individuals who have postherpetic neuralgia pain (PHN) who receive SCS or DRGS, the evidence includes systematic review, observation and case series. Relevant outcomes are symptoms, functional outcomes, QOL, medication use, and treatment-related morbidity. In a systematic review (Isagulyan et. al. 2023) which evaluated the effectiveness of various types of electrical stimulation (traditional, burst, high-frequency and DRGS) in 134 individuals with PHN. Pain relief was achieved in 91 individuals (68.9%). The mean VAS score improvement was 61.4% with a mean follow-up time of 12.85 months. Even though there were a limited number of individuals that utilized alternative SCS almost all individuals showed a good response to therapy with more than 50% VAS improvement and reduction of analgesic dosage. Despite promising results demonstrating a decrease in pain intensity there was conflicting evidence regarding efficacy in the alternative electrical stimulation types. RCTs are needed with larger sample sizes, comparing alternative and traditional modes of SCS to conventional therapies to establish the safety and effectiveness of SCS in the treatment of PHN. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Multiple Sclerosis

For individuals with multiple sclerosis neuropathic pain who receive SCS, the evidence includes systematic review. Relevant outcomes are symptoms, functional outcomes, QOL, medication use, and treatment-related morbidity. In a systematic review (Rapisard et. al. 2021) evaluated the use of SCS in the management of individuals with MS. Seven studies were included with 373 MS individuals who were submitted for SCS trial in which 285/372 (76.4%) were enrolled for permanent stimulation with a mean follow-up 44.40 ± 25.00 months. Overall improvement was observed in 193 out 346 (55.8%) of individuals with motor disorders, 90 out of 134 (67.13%) individuals with urinary dysfunction and in 28 out of 34 (82.35%) individuals with neuropathic pain. The efficacy of SCS was higher for urinary dysfunction (p=0.0144) and neuropathic pain (p=0.0030) compared with motor disorders. While this review may show

promise, there is not a clear indication on which MS patients would benefit from SCS and on the best time to perform this procedure on these individuals. Prospective RCTs comparing SCS to conventional therapies with longer follow-up are needed to improve patient selection, clarify the best time to perform SCS and better understand the potential loss of effectiveness in individuals with MS. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Fibromyalgia

For individuals with fibromyalgia neuropathic pain who receive SCS, the evidence includes an observational study, no RCTs were found. Relevant outcomes are symptoms, functional outcomes, QOL, medication use, and treatment-related morbidity. In a 11-year retrospective multicenter matched cohort study (D'Souza et. al. 2023) which compared SCS treated individuals with fibromyalgia (n=68) and those without fibromyalgia (n=148). At 6-months post SCS placement there was no statistical difference in the calculated percentage change in pain between the fibromyalgia cohort (46.6 ± 29.0) and the control cohort (50.9 ± 32.8; β, -18.4; 95% CI, -44.3 to 7.6; p = 0.157) and there was no difference between the cohorts in the percentage of individuals taking opioid or neuropathic medications at 6- and 12-months. Similarly, there was no difference between cohorts in the percentage of individuals reporting satisfaction. Prospective RCTs comparing SCS to conventional therapies with large sample sizes and long-term follow-up are needed to determine the safety and efficacy of SCS in the treatment of fibromyalgia neuropathic pain. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Combined Use of Spinal Cord Stimulation and Dorsal Root Ganglion Stimulation

For individuals with complex regional pain syndrome (CRPS) and refractory chronic lower limb neuropathic pain and/or neuropathic back/lower leg pain after spinal surgery who receive combined use SCS and DRGS, the evidence includes one RCT and case series studies. Relevant outcomes are symptoms, functional outcomes, QOL, medication use, and treatment-related morbidity. The RCT Rigoard et al (2025), a prospective, randomized, double-blind, cross-over trial (BOOST-DRG study) compared the efficacy of relieving pain utilizing spinal cord stimulation (SCS), dorsal root ganglion stimulation (DRGS), and DUAL SCS and DRGS stimulation in patients (n=10) with refractory chronic lower limb neuropathic pain and/or neuropathic back/lower leg pain for $\geq$ 6 months after spinal surgery. The ten patients were initially randomized three to SCS-DUAL-DRGS, two to DRGS-SCS-DUAL, two to DUAL-DRGS-SCS, two to DUAL-SCS-DRGS, and one to SCS-DRGS DUAL. While there was 50% VAS decrease for 60% of all treatment modalities, there were no significant difference observed among groups (p = 0.84). At the end of the cross-over period, four patients (40%) preferred SCS, three (30%) DRGS, and three (30%) DUAL, without significant difference among the preference rates of different stimulation targets (p = 0.91). Limitations of this study included early termination which limited the power of clinical outcome interpretations, small sample size and no long term follow up. In the case series studies (Goebel et. al. 2018 and Yang et. al. 2017) which included a total of 3 individuals with recurrent CRPS pain, it was noted there is little evidence available on how CRPS recurrence should be managed. The three individuals were initially treated with conventional SCS, and when the CRPS pain reoccurred with conventional SCS failure, DRGS (n=2) and DRGS-SCS (n=1) systems were implanted. While these case series may have shown promise in the treatment of recurrent CRPS pain after failed conventional SCS with salvage therapy with the placement of DRGS or DRGS-SCS regarding improvement in pain and functional status the sample size is small (n=3) and there is no long-term follow-up. Additional RCTs with larger sample size and long-term follow-up are needed to determine the safety and efficacy regarding the combined use of SCS and DRGS. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Additional Information

Not applicable.

OBJECTIVE

The objectives of this evidence review is to determine 1) whether the use of spinal cord stimulation and dorsal root ganglion neurostimulation for treating patients with treatment-refractory chronic pain of the trunk or limbs improves the net health outcome, and 2) whether the use of spinal cord stimulation for treating patients with critical limb ischemia, refractory angina, heart failure, and cancer-related pain improves the net health outcome.

PRIOR APPROVAL

Not applicable

POLICY

Spinal Cord Stimulation

Implantation of a Temporary (Trial) Spinal Cord Stimulation (SCS) Device

A trial period using a temporary standard or high frequency spinal cord stimulator (SCS) device may be considered **medically necessary** when **ALL** the following criteria are met:

1) An individual has undergone careful screening, including evaluation by a multi-disciplinary team that confirms the existence of one of the following conditions:

    - Failed back syndrome or also known as post-laminectomy syndrome;
    - Complex regional pain syndrome (CRPS), type I or type II (formerly known as reflex sympathetic dystrophy [RSD])
    - Chronic neuropathic pain of certain origins:
        - lumbosacral arachnoiditis (arachnoiditis is usually documented by the presence of high levels of proteins in the cerebrospinal fluid and/or by myelography or MRI);
        - Radiculopathies;
        - Phantom limb syndrome (stump pain);
        - Peripheral neuropathy/diabetic neuropathy**; and**

2) There is documentation in the medical records of the failure of 6 months of conservative treatment modalities (pharmacological, surgical, psychological, or physical therapies), unless judged to be unsuitable or contraindicated;

3) Further surgical intervention is not indicated (the treatment is used only as a last resort);

4) There is documentation in the medical records the individual has been evaluated by a licensed psychologist, psychiatrist, or other licensed mental health professional and has obtained clearance;

5) There is documentation in the medical records there is no evidence of existing untreated substance use disorder;

6) The individual does not have any contraindications to implantation (i.e., sepsis or coagulopathy issues).

Implantation of Permanent Spinal Cord Stimulation (SCS) Device

Placement of a permanent standard or high frequency SCS device may be considered **medically necessary** when the above medical necessity criteria for a trial (temporary) placement of SCS are met, and **ALL** the following is also met:

1) There is $\geq$ 50% reduction in pain with the trial of the temporary spinal cord stimulation (SCS) device of at least 3 to 7 days as documented in the medical record;
2) There is objective evidence per documentation in the medical records of pain relief (e.g., decreased opioid usage, improved range of motion of the affected area, increased activity, increased pain relief according to the Visual Analog Scale [VAS] or the Numeric Pain Intensity Scale)**.**

Dorsal Root Ganglion Stimulation

The implantation of a temporary (trial period) or permanent placement of dorsal root ganglion stimulation (DRGS) is considered **medically necessary** when the individual meets the above medically necessary criteria for SCS above.

Combined use of Spinal Cord Stimulation and Dorsal Root Ganglion

Combined use of SCS and DRGS for any indication is considered **investigational** because the evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Replacement or Revision of Spinal Cord or Dorsal Root Ganglion Stimulator Devices

Replacement or revision of a standard or high frequency SCS or DRGS may be considered **medically necessary** for an individual that meets the above medical necessity criteria and have had positive pain relief/clinical benefit from the existing stimulator and the existing generator/lead/electrodes/programmer or battery are no longer under warranty and cannot be repaired.

Replacement for technological advancements or newly released upgrades to a standard SCS or DRGS device when the original device is still functioning properly and/or there are no changes in the individual's condition are considered **not medically necessary**.

Investigational

Spinal cord stimulation (standard or high frequency) or dorsal root ganglion stimulation is considered **investigational** when the criteria above is not met and for all other indications including but not limited to the following because the evidence is insufficient to determine that the technology results in an improvement in the net health outcome:

- Treatment of cancer related pain
- Treatment of peripheral vascular disease
- Treatment of chronic pain of ischemic origin:
    - Treatment of critical limb ischemia as a technique to forestall amputation
    - Treatment of refractory angina pectoris
- Treatment of Multiple Sclerosis & spasticity disorders
- Treatment of axial and other musculoskeletal pain syndromes
- Treatment of nociceptive pain (resulting from irritation, not damage to nerves)
- Treatment of central deafferentation pain (related to central nervous system damage from a stroke or spinal cord injury)
- Treatment of post-herpetic neuralgia
- Treatment of heart failure
- Treatment of fibromyalgia

POLICY GUIDELINES

Candidate selection focuses on determining whether the individual is refractory to other types of treatment. The FDA made the following recommendations for clinicians to consider:

- Conduct a trial stimulation as described in the device labeling to identify and confirm satisfactory pain relief before permanent implantation.
- Permanent spinal cord stimulation should only be implanted in patients who have undergone and passed a stimulation trial.
- Providers typically perform a stimulation trial on a patient for 3 to 7 days, and success is usually defined by a 50% reduction in pain symptoms. Inform patients about the risks of serious side effects and what to expect during the trial stimulation.
- Before implantation of any spinal cord stimulation, discuss the benefits and risks of the different types of implants and other treatment options, including magnetic resonance imaging compatibility of the devices.
- Before implantation, provide patients with the manufacturer's patient labeling and any other education materials for the device that will be implanted.
- Develop an individualized programming, treatment, and follow-up plan for spinal cord stimulation therapy delivery with each patient.
- Provide each patient with the name of the device manufacturer, model, and the unique device identifier of the implant received.

The following chronic pain considerations may apply in candidate selection:

Pain is neuropathic in nature (i.e., resulting from actual damage to the peripheral nerves). Common indications include, but are not limited to, FBSS, complex regional pain syndrome (i.e., reflex sympathetic dystrophy), arachnoiditis, radiculopathies, phantom limb/stump pain, peripheral neuropathy, and painful diabetic neuropathy. Spinal cord stimulation is generally not effective in treating nociceptive pain (resulting from irritation, not damage to the nerves) and central deafferentation pain (related to central nervous system damage from a stroke or spinal cord injury).

Complex regional pain syndrome (CRPS)

- Type I CRPS is associated with symptomatic tissue injury
- Type II CRPS is associated with nerve injury

Coding

See the Codes table for details.

BACKGROUND

Chronic Pain

Spinal cord stimulation (SCS) has been used in a wide variety of chronic refractory pain conditions, including pain associated with cancer, failed back pain syndromes, arachnoiditis, and complex regional pain syndrome (CRPS; i.e., chronic reflex sympathetic dystrophy). There has also been interest in spinal cord stimulation as a treatment of critical limb ischemia, primarily in patients who are poor candidates for revascularization and in patients with refractory chest pain.

Spinal Cord Stimulation

SCS (also called dorsal column stimulation) involves the use of low-level epidural electrical stimulation of the spinal cord dorsal columns. The neurophysiology of pain relief after SCS is uncertain but may be related to either activation of an inhibitory system or blockage of facilitative circuits.

SCS devices consist of several components: (1) the lead that delivers the electrical stimulation to the spinal cord; (2) an extension wire that conducts the electrical stimulation from the power source to the lead; and (3) a power source that generates the electricity. The lead may incorporate from 4 to 8 electrodes, with 8 electrodes more commonly used for complex pain patterns. There are 2 basic types of power source: 1 type, the power source (battery), can be surgically implanted or worn externally with an antenna over the receiver; the other, a radiofrequency receiver, is implanted. Totally implantable systems are most commonly used.

The individuals pain distribution pattern dictates at what level of the spinal cord the stimulation lead is placed. The pain pattern may influence the type of device used. For example, a lead with 8 electrodes may be selected for those with complex pain patterns or bilateral pain. Implantation of the spinal cord stimulator is typically a 2-step process. Initially, the electrode is temporarily implanted in the epidural space, allowing a trial period of stimulation. Once treatment effectiveness is confirmed (defined as at least 50% reduction in pain), the electrodes and radio-receiver/transducer are permanently implanted. Successful spinal cord stimulation may require extensive programming of the neurostimulators to identify the optimal electrode combinations and stimulation channels.

Dorsal Root Ganglion Stimulation

Dorsal root ganglion neurostimulation (or dorsal root ganglion stimulation, DRGS) uses the same epidural approach technique as spinal cord stimulation but targets a different anatomical target, the dorsal root ganglion. Dorsal root ganglia, situated within the spine as clusters of nerve cell bodies, serve as the "sensory gate" for pain signals entering the spinal cord. DRGS seeks to modulate the activity of these nerve cell bodies, potentially intercepting or diminishing pain signals before they reach the spinal cord. DRGS proves particularly efficacious for localized or chronic nerve pain conditions, such as complex regional pain syndrome, post-amputation pain, and pain following specific surgical procedures. It allows for more precise targeting of specific nerves and pain areas compared to SCS, potentially leading to better pain relief with fewer side effects. Moreover, DRGS may induce less paresthesia (tingling or numbness) than SCS, owing to its focused and precise stimulation. Recovery from DRGS implantation typically spans 6-8 weeks, during which patients are advised to refrain from strenuous activities.

Traditional SCS devices use electrical stimulation with a frequency of 100 to 1000 Hz. High frequency devices use electrical stimulation with a frequency of ⁀10,000 Hz). In 2016, the U.S. Food and Drug Administration (FDA) approved a clinician programmer application that allows a spinal cord stimulation device to provide stimulation in bursts rather than at a constant rate. Burst stimulation is proposed to relieve pain with fewer paresthesia's. The burst stimulation device works in conjunction with standard spinal cord stimulation devices. With the newly approved app, stimulation is provided in five, 500-Hz burst spikes at a rate of 40 Hz, with a pulse width of 1 ms. Other neurostimulators target the dorsal root ganglion.

Regulatory Status

A large number of neurostimulator devices have been approved by the FDA through premarket approval process under FDA product code: LGW (stimulator, spinal-cord, totally implanted for pain relief), PMP (Dorsal Root Ganglion Stimulator for Pain Relief), and GZB (Stimulator, Spinal-Cord, Implanted [Pain Relief]) (Table 1). In October 2016, the FDA approved BurstDR™ stimulation (St. Jude Medical), a clinician programmer application that provides intermittent "burst" stimulation for patients with certain St. Jude spinal cord stimulation devices.

Table 1. Cleared or Approval Devices for Spinal Code and Dorsal Root Ganglion Stimulation

Device	Manufacturer	Original Clearance/ Approval Date	Indication
Algovita SCS System	Nuvectra Corporation	November 2015	Chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with failed back surgery syndrome, intractable low back pain, and leg pain.
Axium (1st generation) and Proclaim DRG (2nd generation) Neurostimulator System, Prodigy,	Abbott Medical	February 2016	Moderate to severe chronic intractable pain of the lower limbs in adult patients with Types I and II CRPS

Device	Manufacturer	Original Clearance/ Approval Date	Indication
Proclaim XR, Proclaim Plus and Externa		May 2023	Approval for expanding the indications to include non-surgical back pain (NSBP) for the tonic and Burst DR stimulation modes, and diabetic peripheral neuropathy (DPN) of the lower extremities for the tonic stimulation mode, for the Prodigy, Proclaim XR, Proclaim Plus; and Externa systems.
Cordis Programmable Neural Stimulator Models 900a	Cordis Corporation	April 1981; Withdrawn in 2016	Stimulator, Spinal-Cord, Totally Implanted for Pain Relief
Freedom SCS	Stimwave Technologies (now Curonix)	August 2016	Chronic, intractable pain of the trunk and/or lower limbs, including unilateral or bilateral pain
Evoke SCS System	Saluda Medical Pty Ltd	February 2022	Chronic intractable pain of the trunk and/or limbs including unilateral or bilateral pain associated with the following: failed back surgery syndrome, intractable low back pain and leg pain.
Genesis And Eon Family Neurostimulation (Ipg) System	St. Jude Medical/ Abbott Medical	November 2001	Chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with failed back surgery syndrome, intractable low back pain and leg pain
Itrel, Restore, Synergy, Intellis/Inceptiv™ and Vanta Spinal Cord Stimulation Systems ***Note***: *Inceptiv™ system is the next generation of*	Medtronic Neuromodulation	November 1984 April 2024	Chronic, intractable pain of the trunk and/or limbs-including unilateral or bilateral pain associated with the following conditions: • Failed Back Syndrome (FBS) or low back

Device	Manufacturer	Original Clearance/ Approval Date	Indication
Medtronic's Intellis™ platform.			syndrome or failed back • Radicular pain syndrome or radiculopathies resulting in pain secondary to FBS or herniated disk • Post-laminectomy pain • Multiple back operations • Unsuccessful disk surgery • Refractory Degenerative Disk Disease (DDD)/herniated disk pain • Peripheral causalgia • Epidural fibrosis • Arachnoiditis or lumbar adhesive arachnoiditis • Complex Regional Pain Syndrome (CRPS), Reflex Sympathetic Dystrophy (RSD), or causalgia • Diabetic peripheral neuropathy of the lower extremities
Precision SCS Systems	Boston Scientific Corporation	April 2004	Chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with failed back surgery syndrome, Types 1 and 2 CRPS, intractable low back pain and leg pain
Senza SCS System	Nevro Corporation	May 2015	Chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome, intractable low back pain, and leg pain When programmed to include a frequency of 10 kHz: Chronic intractable pain of the lower limbs,

Device	Manufacturer	Original Clearance/ Approval Date	Indication
			including unilateral or bilateral pain, associated with diabetic neuropathy; non-surgical refractory back pain (intractable back pain without prior surgery and not a candidate for back surgery)
Nalu Neurostimulation System	Nalu Medical, Inc	March 2019	Chronic, intractable pain of the trunk and/or limbs, including unilateral or bilateral pain
Prospera Spinal Cord Stimulation (SCS) System	Biotronik NRO, Inc	March 2023	Chronic, intractable pain in the trunk and/or limbs, which may include unilateral or bilateral pain, resulting from any of the following: 1) FBS or low back syndrome or failed back; 2) Radicular pain syndrome or radiculopathies resulting in pain secondary to FBS or; 3) Herniated disk; 4) Postlaminectomy pain; 5) Multiple back operations; 6) Unsuccessful disk surgery; 7) DDD/herniated disk pain refractory to conservative and surgical interventions; 8) Peripheral causalgia; 9) Epidural fibrosis;10) Arachnoiditis or lumbar adhesive arachnoiditis; and11) CRPS, RSD, or causalgia.

CRPS:Complex regional pain syndrome; PMA: premarket approval; SCS: spinal cord stimulation.

RATIONALE

This evidence review was created in November 2000 with searches of the PubMed database. The most recent literature update was performed through June 2025.

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

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Standard Spinal Cord Stimulation for Refractory Chronic Trunk or Limb Pain

Clinical Context and Therapy Purpose

The purpose of spinal cord stimulation (SCS) in individuals who have treatment-refractory chronic trunk or limb pain is to provide a treatment option that is an alternative to or an improvement on existing therapies.

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

Populations

The relevant population of interest is individuals with treatment-refractory chronic pain of the trunk or limbs. Examples of treatment-refractory chronic pain include failed back surgery syndrome (FBSS), complex regional pain syndrome (CRPS) (i.e., reflex sympathetic dystrophy), arachnoiditis, radiculopathies, phantom limb/stump pain, peripheral neuropathy, and painful diabetic neuropathy.

Interventions

The therapy being considered is standard SCS alone. SCS uses low-level epidural electrical stimulation of the spinal cord dorsal columns. Its mechanism of action is uncertain but may be related to either activation of an inhibitory system or blockage of facilitative circuits. SCS devices consist of several components: (1) the lead delivering electrical stimulation to the spinal cord; (2) an extension wire that conducts the electrical stimulation from the power source to the lead; and (3) a power source. The lead may incorporate 4 to 8 electrodes, depending on the complexity of the pain pattern. The U.S. Food and

Drug Administration (FDA) recommends a trial period in which the electrode is temporarily implanted in the epidural space prior to the permanent implantation. Standard SCS devices operate under a frequency of 100 to 1000 Hz.

In 2016, a supplement to a standard SCS device (in the form of a clinician programmer application), which allows for the provision of burst stimulation, was approved by the FDA.

Comparators

The following practice is currently being used to treat individuals with treatment-refractory chronic pain of the trunk or limbs: medical therapy or surgical therapy.

Outcomes

The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) group has provided recommendations for 4 core chronic pain outcome domains that should be included when selecting outcome measures for clinical trials of treatments for chronic pain: (1) pain intensity; (2) physical functioning; (3) emotional functioning; and (4) participant ratings of overall improvement. The IMMPACT has also suggested specific outcome measures to address these core domains and has proposed provisional benchmarks for identifying clinically important changes in these specific outcome measures (Table 2).

Table 2. Health Outcomes Measures Relevant to Trials of Chronic Pain

Domain	Outcome Measure	Description	Clinically Meaningful Difference
Pain intensity			
	• Numeric rating scale • Verbal rating scale • Visual analog scale	Rating of pain intensity on a scale of 0 (no pain) to 10 (pain as bad as you can imagine) or from 0 to 10 cm	• Minimally important: 10% to 20% decrease • Moderately important: ⩾ 30% decrease • Substantial: ⩾ 50% decrease
Physical functioning			
	Disease-specific	***Measures of the interference of pain with physical functioning***	
	• Multidimensional Pain Inventory Interference Scale	• 60 items, self-report • 12 subscales: interference, support, pain severity, self-control, negative mood, punishing responses, solicitous responses,	• ⩾0.6-point decrease

Domain	Outcome Measure	Description	Clinically Meaningful Difference
		distracting responses, household chores, outdoor work, activities away from home, and social activities • Items rated on 0- to 6-point scale • Interference subscale score calculated by mean of subscale items	
	• Brief Pain Inventory Interference Scale	• 7 items, self-report • Measures intensity, quality, relief, and interference of pain and patients' ideas of the causes of pain • Mean of the 7 interference items can be used as a measure of pain interference	• 1-point decrease
	• Oswestry Disability Index (ODI)	Measures functional impairment due to lower back pain: • 10 sections, self-report • Sections: intensity of pain, lifting, ability to care for oneself, ability to walk, ability to sit, sexual function, ability to stand, social life, sleep quality, and ability to travel • Each section is scored on a 0 to 5 scale with 5 indicating the greatest disability • Total score calculated by taking the mean of the section scores and multiplying by 100	• 10 points
	General	***Generic measure of physical functioning***	
	• 36-Item Short Form Health Survey	Measure overall health status: • 36 items, self-report • 8 domains: physical function, physical role, general health, bodily pain, mental health, social function, vitality/fatigue, and emotional role	• 5 to 10 points

Domain	Outcome Measure	Description	Clinically Meaningful Difference
		• Physical Component Summary and Mental Component Summary scores are aggregate scores that can be calculated • Higher scores indicate better health status	
Emotional functioning			
	• Beck Depression Inventory (BDI)	• 21 items, self-report • Measures severity of current symptoms of depressive disorders • Scores range from 0 to 63	• ⩾5-point decrease
	• Profile of Mood States	• 65 items, self-report • Measures total mood disturbance with 6 subscales: tension, depression, anger, vigor, fatigue, and confusion • Scores range from 0 to 200	• ⩾10- to 15-point decrease
Global rating of improvement			
	• Patient Global Impression of Change (PGI)	• Single-item, self-rating • 7-point scale ranging from 1 (very much worse) to 7 (very much improved)	• Minimally important: minimally improved • Moderately important: much improved • Substantial: very much improved

Adverse events can either be hardware-related to biological. Hardware-related complications include lead migration, failure or fracture. Biological complications include infection and pain. More severe biological complications are rare, including dural puncture headache and neurological damage.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Standard Spinal Cord Stimulation

Review of Evidence

Systematic Reviews

Numerous systematic reviews have been conducted assessing the efficacy of SCS for a variety of chronic pain conditions, including CRPS, spinal pain, FBSS, painful diabetic neuropathy, and mixed chronic pain conditions. However, these reviews only included a subset of the RCTs each of standard SCS; evidence from the relevant individual RCTs is discussed in the next section.

Huygen et al (2024) performed a meta-analysis to assess the efficacy of SCS therapies in comparison with conventional medical management (CMM). RCTs published through 2022 were considered for inclusion that compared SCS therapies with sham (placebo) and/or CMM or standard treatments for adults suffering from chronic back or leg pain who had not previously utilized SCS. The primary outcomes focused on pain-related metrics, including pain intensity (measured by visual analog scale) and the proportion of patients achieving at least 50% pain relief (responder rate) in the back or leg. Additionally, the study considered quality of life (measured by EQ-5D index score) and functional disability (measured by the ODI score).

The network meta-analysis incorporated 13 studies involving 1561 patients, comparing conventional and novel SCS therapies (e.g., high-frequency stimulation, burst stimulation, closed loop, and differential target multiplexed) with CMM across six outcomes at a 6-month follow-up. Both conventional and novel SCS therapies demonstrated superior efficacy compared to CMM in terms of responder rates in the back (conventional SCS: odds ratio [OR], 3.00; 95% Confidence Interval [CI], 1.49 to 6.72; novel SCS: OR, 8.76; 95% CI, 3.84 to 22.31), pain intensity in the back (conventional SCS: mean difference [MD], -1.17; 95% CI, -1.64 to -0.70; novel SCS: MD, -2.34; 95% CI, -2.96 to -1.73), pain intensity in the leg (conventional SCS: MD, -2.89; 95% CI, -4.03 to -1.81; novel SCS: MD, -4.01; 95% CI, -5.31 to -2.75), and EQ-5D index score (conventional SCS: MD, 0.15; 95% CI, 0.09 to 0.21; novel SCS: MD, 0.17; 95% CI, 0.13 to 0.21). Additionally, conventional SCS showed superior results in functional disability compared to CMM (MD, -7.10; 95% CI, -10.91 to -3.36). No statistically significant differences were observed for other comparisons. This meta-analysis suggests that SCS therapies for chronic pain in the back and/or lower extremities offer greater improvements in pain relief compared to CMM, underscoring the potential of SCS therapies as effective and valuable options in chronic pain management.

Randomized Controlled Trials

Seven RCTs (in 12 publications) (range, 36 to 218 patients) have evaluated standard spinal cord stimulation for various chronic pain conditions (Table 3). Patient populations had failed back surgery syndrome, diabetic neuropathy, and CRPS. The comparators were primarily conventional medical management, although 1 RCT compared spinal cord stimulation with reoperation for failed back surgery syndrome another compared spinal cord stimulation with physical therapy and one compared closed-loop SCS with open-loop SCS . All RCTs reported results at 6 months. The most common primary outcome reported was a responder outcome of 50% reduction in pain; Kemler et al (2000) reported the absolute change in visual analog scale (VAS) pain score. Consistent with clinical practice, RCTs included a trial

period of spinal cord stimulation, usually a few days to a week. Patients not reporting improvement in pain during the trial period did not continue receiving spinal cord stimulation during the remainder of follow-up. In most RCTs, these patients were included in the intention-to-treat analyses either as failures to respond or using imputation techniques. All RCTs with the responder primary outcomes reported clinically and statistically significant differences in the primary outcomes at 6 months, favoring spinal cord stimulation (spinal cord stimulation range, 39% to 63% vs. comparator range, 5% to 12%). Outcomes measuring the reduction in analgesic use were consistently numerically larger for spinal cord stimulation, but not statistically significant in all studies. Four of the 5 studies did not report differences in functional, quality of life, or utility outcomes. Device-related complications ranged from 17% to 32%, with the most common being infection and discomfort or pain due to positioning or migration of electrodes or leads. However, 2 studies reported dural puncture headaches and Slangen et al (2014) reported a dural puncture headache ending in death. Two studies reported longer-term results for both treatment groups. In each, results continued to favor spinal cord stimulation at 2 years, but for 1 with 5 years of follow-up, results were not statistically significant at 5 years.

Table 3. Characteristics and Results of RCTs using Standard Spinal Cord Stimulation

Study	**Population**	**Interventions**	**N at Baseline and Follow-Up**	**Results**				**Complications**
				Outcome Measures	***Intervention***	Control	***p***	
North et al (2005)	FBSS	• SCS + CMM • Reoperation + CMM	N=60 n at 6 mo=49	6 mo (SCS vs. reoperation)				17% device-related complications (infections, hardware technical problems)
				Success (50% pain relief and patient satisfaction)	39%	12%	.04	
				Stable or decreased opioids	87%	58%	.025	
				No difference in ADLs impairment due to pain				
Kumar et al (2007, 2008)	FBSS with neuropathic pain	SCS + CMM CMM	N=100 n at 6 mo=93	6 mo (SCS vs. CMM)				32% device-related complications (electrode migration,

Study	Population	Interventions	N at Baseline and Follow-Up	Results				Complications
								infection, loss of paresthesia)
				50% reduction in VAS leg pain	48%	9%	<.001	
				SF-36, favoring SCS all domains except RP			≤.02	
				ODI score	45	56	<.001	
				Opioid use	56%	70%	.21	
				NSAID use	34%	50%	.14	
			n at 24 mo=87	24 mo (SCS vs. CMM)				
				50% reduction in leg pain on VAS	37%	2%	.003	
Kemler et al (2000, 2004, 2008)	CRPS	SCS + PT PT	N=54 n at 6 mo=54	6 mo (SCS vs. PT)				25%device-related complications (dural puncture, infection, unsatisfactory placement of electrode, defective lead) 42% reoperation rate by 5 y
				Reduction in VAS pain score	2.4	0.2	<.001	
				Much improved GPE	39%	6%	.01	
				No difference in functional outcomes or HRQOL				
				2 y (SCS vs. PT)				

Study	Population	Interventions	N at Baseline and Follow-Up	Results				Complications
				Reduction in VAS pain score	2.1	0.0	<.001	
				Much improved GPE	43%	6%	.001	
			n at 5 y=44	5 y (SCS vs. PT)				
				Reduction in VAS pain score	1.7	1.0	.25	
Slangen et al (2014) Zuidema et. al. 2022	Diabetic neuropathy of LEs	• SCS • CMM	N=36 n at 6 mo=36	6 mo (SCS vs. CMM)				2 SAEs (1 infection, 1 post-dural puncture headache ending in death)
				Success (50% reduction in pain for 4 d or at least much improved on patient-reported global impression of change)	59%	7%	<.01	
				Reduction in pain medication	32%	0%		
				No differences in health utility or HRQOL				
			n at 24 mo=17[a]	2 y (SCS only)				
				Success	65%			
				No improvement in health utility vs. baseline				
				~5-point improvement in SF-36 PCS score vs. baseline				

Study	Population	Interventions	N at Baseline and Follow-Up	Results				Complications
			N at 8 to 10 yrs=19[a]	8 to 10 years (SCS only)				
				>50% reduction in VAS pain score, daytime	26%			
				No improvement in health utility or quality of life vs. baseline				
De Vos et al (2014); Duarte et al (2016)	Diabetic neuropathy of LEs	SCS CMM	N=60 n at 6 mo=54	6 mo (SCS vs. CMM)				18% device-related complications (infection, pain due to pulse generator or migration of lead, unsatisfactory placement of electrode)
				50% reduction in pain	62.5%	5%	<.001	
				Reduction in analgesic intake (MQS score)	2.9	-0.09	NR	
				Change in health utility	0.39	0.00	<.05	
Rigoard P (2019)	FBSS	SCS + CMM CMM	N=218 n at 6 mo=116	6 mo (SCS vs. CMM)				18% device-related complications, with 12% requiring surgical re-intervention
				50% reduction in pain	14%	5%	.04	
				Change in SF-36 Short Form	7.5	0	<.001	
Mekhail (2020) ;	Chronic, intractable pain of	Open loop SCS	N=125 n at 12 mo=118	12 mo				

Study	Population	Interventions	N at Baseline and Follow-Up	Results				Complications
Mekahil (2023)	the back and legs	Closed loop SCS						
				50% reduction in pain	83%	61%	<.01	
				36 mo				
				50% reduction in pain	78%	49%	<.01	

ADL: activities of daily living; CMM: conventional medical management; CRPS: complex regional pain syndrome; FBSS: failed back surgery syndrome; GPE: global perceived effect; HRQOL: health-related quality of life; LE: lower extremities; MQS: Medication Quantification Scale III; NR: not reported; NSAID: non-steroidal anti-inflammatory drug; ODI: Oswestry Disability Index; PCS: Physical Component Summary; PT: physical therapy; RCT: randomized controlled trial; RP: role-physical; SAE: serious adverse events; SCS: spinal cord stimulation; SF-36: 36-Item Short-Form Health Survey; VAS: visual analog scale.
[a] SCS only.

Uncontrolled Studies

Because RCT data are available for spinal cord stimulation, uncontrolled studies are discussed if they add information not available from the RCTs (e.g., longer follow-up including adverse events, data on an important subgroup, etc.). Rauck et al (2023) reported an analysis of long-term (>2 years) complications and explantation rates from the RELIEF registry. RELIEF is a global, multicenter, prospective registry including individuals with chronic pain who are eligible to receive neurostimulation therapy to treat pain. Adults who enrolled between January 2013 and November 2021 and were permanently implanted with a commercially available spinal cord stimulation (SCS) system were included in analysis (N=1289). The mean (standard deviation) age at enrollment was 58 (14) years and 57% were women. Participants reported duration of chronic pain of 12 (11) years. Study follow-up visits occurred at 6, 12, 24 and 36 months. Ninety-eight participants (8%) required an explant (annualized explant rate of 3.5%); 32 of the explants were due to inadequate pain relief. High lead impedance (5%) and lead migration/movement (5%) were the most common complications. Thirty-two serious adverse events (SAEs) related to device and 51 SAEs related to procedure were reported; device-related implant site infection (11 events) and procedure-related implant site infection (17 events) were the most common SAEs. There were 5 SAEs related to implant site pain, 3 device- or procedure-related neurological deficits, and 2 life-threatening local infections (implant site infection, meningitis). No deaths were reported.

Mekhail et al (2011) retrospectively reviewed 707 patients treated with SCS between 2000 and 2005. Patients' diagnoses included CRPS (n=345 [49%]), failed back surgery syndrome (n=235 [33%]), peripheral vascular disease (n=20 [3%]), visceral pain in the chest, abdomen, or pelvis (n=37 [5%]), and peripheral neuropathy (n=70 [10%]). Mean follow-up across studies was 3 years (range, 3 months to 7 years). A total of 527 (36%) of the 707 patients eventually underwent permanent implantation of an SCS device. Hardware-related complications included lead migration in 119 (23%) of 527 patients, lead connection failure in 50 (9.5%) patients, and lead break in 33 (6%) patients. Revisions or replacements corrected the hardware problems. The authors noted that rates of hardware failure have decreased due to

advances in SCS technology. Documented infection occurred in 32 (6%) of 527 patients with implants; there were 22 cases of deep infection, and 18 patients had abscesses. There was no significant difference in the infection rate by diagnosis. All cases of infection were managed by device removal.

Standard Spinal Cord Stimulation with Burst

Systematic Reviews

Hou et al (2016) published a systematic review of burst spinal cord stimulation for the treatment of chronic back and limb pain. Reviewers identified 5 studies of burst spinal cord stimulation in patients with intractable chronic pain of more than 3 months in duration who had failed conservative treatment. Three studies, with sample sizes of 12, 15, and 20, respectively, used randomized crossover designs to compare burst stimulation with tonic stimulation; 2 studies also included a placebo stimulation intervention. Also, there were 2 case series with sample sizes of 22 and 48 patients, respectively. Data were collected after 1 to 2 weeks of treatment. Study findings were not pooled. Using the American Academy of Neurology criteria, reviewers originally rated 4 studies as class III and 1 study as class IV. However, given the small sample sizes and short duration of follow-up of the 4 studies, all were downgraded to class IV. Overall, the level of confidence in the evidence on burst spinal cord stimulation for treating chronic pain without paresthesia was rated as "very low."

Randomized Controlled Trials

Deer et al (2024) conducted an US multi-center RCT (DISTINCT, NCT04479787) which enrolled 269 chronic low-back-pain patients who were not candidates for traditional spine surgery, with 162 patients randomized to burst SCS and 107 to CMM. This study allowed a crossover to the alternative treatment arm after six months. Patients underwent a trial and received a permanent implant if they reported ≥50% pain reduction. With nominal changes in baseline pain score, disability, and quality of life, 86% (70/81) of patients crossed over to the SCS arm after the 6 month follow-up, with 94% (66/70) undergoing a trial. Of these patients, 88% reported at least a 50% reduction in pain, leading 55 patients to receive a permanent implant. At the 12-month visit, 71% of these patients sustained a ≥50% pain improvement, with 24.5% experiencing an ≥80% improvement. Additionally, significant reductions in disability and improvements in quality of life measures were observed. The trial further reported that 42% of patients reduced or discontinued opioid usage. Clinical benefits noted at the 12-month mark were maintained through the 18-month follow-up.

Eight crossover RCTs with sample sizes ranging from 12 to 269 patients were identified, 5 of which were conducted in Europe and the other in the US (Table 4). The trials by De Ridder et al (2010, 2013) enrolled patients with neuropathic pain, the trial by Schu et al (2014) enrolled patients with failed back surgery syndrome, Kriek et al (2017) enrolled patients with CRPS, Deer et al (2018) enrolled patients with chronic intractable pain of the trunk and/or limbs, and Eldabe et al (2020) enrolled patients with chronic back and leg pain. All trials compared burst stimulation with spinal cord stimulation. Schu et al (2014), De Ridder et al (2013), Kriek et al (2017), and Eldabe et al (2020) also compared burst with a sham stimulation group. Schu et al (2014) and Eldabe et al (2020) included patients receiving standard spinal cord stimulation while De Ridder et al (2010, 2013) and Deer et al (2018) included patients not previously treated with spinal cord stimulation. It was not clear in Kriek et al (2017) whether patients had previously received spinal cord stimulation. Results were reported for 1 week of stimulation in Schu et al (2014) and De Ridder et al (2013), after 2, 1-hour sessions of spinal cord stimulation or burst in De Ridder et al (2010), after 2 weeks of stimulation in Kriek et al (2017) and Eldabe et al (2020), and after 12 weeks of stimulation in Deer et al (2018). All trials reported reductions in absolute pain scores (numeric rating scale or VAS). Schu et al (2014) and De Ridder et al (2013) did not account for their crossover designs in data

analyses, so analyses and p values are incorrect and not reported in Table 4. De Ridder et al (2010) did not provide between-group comparisons. Kriek et al (2017) reported only per-protocol analyses. Four trials reported numerically larger reductions in pain scores with burst than with spinal cord stimulation; Kriek et al (2017) did not report less pain for spinal cord stimulation at any frequency compared with burst. In Kriek et al (2017), 48% of patients preferred the 40-Hz spinal cord stimulation compared with 21%, 14%, 14%, and 3% that preferred 500-Hz spinal cord stimulation, 1200-Hz spinal cord stimulation, and burst and sham, respectively. In Eldabe et al (2020), the mean reduction in pain with 500-Hz spinal cord stimulation was significantly greater than that seen with sham (25%; 95% confidence interval [CI], 8% to 38%; p=.008) or burst (28%; 95% CI, 13% to 41%; p=.002), with no significant differences in pain visual analog score for burst versus sham (p=.59). The interpretation of 5 of the trials was limited by small sample sizes, short follow-up, and incorrect, inadequate, or missing statistical analyses.

The Success Using Neuromodulation with BURST (SUNBURST) trial was reported by Deer et al (2018). SUNBURST was a 12-week, multicenter, randomized, unblinded, crossover, noninferiority trial evaluating traditional spinal cord stimulation or burst stimulation in 100 patients with chronic pain of the trunk and/or limbs enrolled between January 2014 and May 2015. Patients were spinal cord stimulation naive and completed a trial stimulation period. Forty-five patients were randomized to spinal cord stimulation then burst, and the remaining 55 were randomized to burst then spinal cord stimulation. At the end of the second crossover period, patients were allowed to choose the stimulation mode they preferred and were followed for 1 year. Patients' mean age was 59 years, 60% of patients were women, and 42% of patients had failed back surgery syndrome while 37% had radiculopathies. The primary outcome was the difference in mean VAS score, with a noninferiority margin of 7.5 mm. Analyses were intention-to-treat with missing values imputed using the hot deck method. Also, outcomes were imputed for patients who underwent invasive procedures for pain or had medication increases. The estimated difference in the overall VAS score between burst and spinal cord stimulation was -5.1 mm (95% upper CI, -1.14 mm), demonstrating noninferiority (p<.001) and superiority (p<.017). The proportion of patients with a decrease in VAS score of 30% or more was 60% (60/100) during burst stimulation and 51% (51/100) during spinal cord stimulation. The proportion of patients whose global impression was minimally improved, moderately improved, or very much improved was approximately 74% in both groups. There were no significant differences in Beck Depression Inventory scores (p=.230). Patients were asked to rate their satisfaction levels for both periods: 78% were satisfied with both spinal cord stimulation and burst, 4% were dissatisfied with both spinal cord stimulation and burst, 7% were satisfied with spinal cord stimulation but not burst, and 10% were satisfied with burst but not spinal cord stimulation. However, more patients (70.8%) reported preferring burst stimulation over spinal cord stimulation after the 24-week crossover period. After 1 year of follow-up, 60 (68%) of the 88 patients completing follow-up reported preferring burst stimulation. The authors reported that the programming parameters were not standardized at the beginning of the study but a more standardized approach with lower amplitudes was implemented as the trial was ongoing. Trial limitations included the crossover design, which limits comparison of pain over longer periods of time, lack of blinding, and variable burst programming parameters.

Table 4. Characteristics and Result of RCTs using Burst Spinal Cord Stimulation

Study	Population	Interventions	N at Baseline and FU	Results				Complications
2×3 crossover design				Outcome Measure	Pain	Disability	Other	

Study	Population	Interventions	N at Baseline and FU	Results				Complications
Deer et al (2024)	Chronic low-back-pain	CMM Burst SCS	N=70 CMM patients crossed over to burst SCS arm; n=66 completed trial	Pain NRS and Back pain-related physical disability (ODI) for CMM patients crossed over to the SCS arm	88% of patients with 50% reduction in pain; 55 patients received a permanent implant. At 12-month visit, 71% of patients sustained a ⩾50% pain improvement; 24.5% experienced an ⩾80% pain improvement.	79% reduction in disability	42% reduced or discontinued opioid usage. Clinical benefits at 12 months maintained through 18 months.	Post SCS implant, 10 patients reported a device-related event (infection, lead migration, persistent pain at IPG, damage to the IPG).
3×3 crossover design without washout					Burst	SCS	Sham	
Schu et al (2014)	FBSS	Burst stimulation SCS No stimulation (sham-control)	N=20 n=20	1 wk (burst vs. SCS vs. sham)[a]				No SAEs reported
				Mean NRS pain intensity scores, favoring burst	4.7	7.1	8.3	
				Mean SF-MPQ pain quality scores, favoring burst	19.5	28.6	33.5	
				Mean ODI scores, favoring burst	19.8	24.6	29.5	

Study	Population	Interventions	N at Baseline and FU	Results				Complications
De Ridder et al (2013)	Neuropathic limb pain	Burst stimulation SCS No stimulation (sham-control)	N=15 n=15	1 wk (burst vs. SCS vs. sham)[a]				Not reported
				Mean improvement in VAS scores Back pain	3.8	2.2	1.4	
				Limb pain	3.9	3.9	0.9	
2×2 crossover								
De Ridder et al (2010)	Neuropathic pain	Burst stimulation SCS	N=12 n=unclear	Two 1-h sessions (burst vs. SCS)[b]				Not reported
				Mean improvement in VAS scores Axial pain	5.3	1.8		
				Limb pain	7.3	4.4		
				Improvement in SF-MPQ sensory scores	16.7	8.6		
				Improvement in SF-MPQ affective scores	6.7	4.3		
Deer et al (2018)	Chronic intractable pain of the trunk and/or limbs	Burst stimulation SCS	N=100	12 wk (burst vs. SCS)				2 study-related SAEs (persistent pain and/or numbness and 1 unsuccessful lead placement);

Study	Population	Interventions	N at Baseline and FU	Results				Complications
								21 SAEs in total; 158 total adverse events in 67 patients
				Mean VAS scores at end of period, favoring burst	Diff = -5.1 mm (noninferiority) p<.001			
				Responder (≥30% improvement in VAS score)	60%	51%		
Hara et al (2022)	Chronic radicular pain after lumbar spine surgery	Burst stimulation Sham stimulation	N=50; n=47 included in analysis	3 mo				9 patients experienced adverse events
				Mean change in ODI	-11		-9	
5×5 crossover					Diff=-1.3; p=.32			
Kriek et al (2017)	CRPS	Burst stimulation SCS 40 Hz SCS 500 Hz SCS 1200 Hz No stimulation (sham-control)	N=33 n=29	2 wk (burst vs. SCS at 40, 500, and 1200 Hz vs. sham)				No SAEs reported; 3 electrodes became dislodged; 2 patients reported itching
				Mean VAS scores at end of period	48	40[c]	64	
				Mean global perceived effect (7-point scale where 7 [very	4.7	5.3[c]	3.5	

Study	Population	Interventions	N at Baseline and FU	Results				Complications
				satisfied] to 1 [not at all satisfied])				
3×3 crossover design with washout								
Eldabe et al (2020)	Chronic back and leg pain	Burst stimulation SCS 500 Hz Sham	N=19 n=16	2 wk treatment phase (burst vs. SCS at 500 Hz vs. sham); each treatment phase included a washout of 9 days				Increased pain was the most commonly reported adverse event at each treatment phase
				Pain intensity: geometric mean pain VAS	5.4	3.8	5.1	
Parallel design								
Deer et al (2023)	Chronic low back pain in patients who had not undergone and were not candidates for lumbar spine surgery	Burst stimulation CMM	N=269 n=183 at 6 mo		Burst	CMM		
				Responder: 50% reduction in NRS	73%	7%		3 serious and 14 non–serious device- or procedure-related events

CMM: conventional medical management; CRPS: complex regional pain syndrome; Diff: difference; FBSS: failed back surgery syndrome; FU: follow-up; IPG: implantable pulse generator; NRS: numeric rating scale; ODI: Oswestry Disability Index; SAE: serious adverse events; SCS: spinal cord stimulation; SF-MPQ: Short-Form McGill Pain Questionnaire; VAS: visual analog scale;

RCT: randomized controlled trial.
[a] Analyses do not appear to take into account properly the crossover design; therefore, p values are not reported here.
[b] Statistical treatment comparisons not provided.
[c] Results from SCS 40 Hz reported here. Three different levels of SCS were given. Similar results were reported for the other 2 SCS levels and are not shown in this table.

Section Summary: Standard Spinal Cord Stimulation for Refractory Chronic Trunk or Limb Pain

The evidence on the efficacy of standard SCS for the treatment of chronic limb or trunk pain consists of a number of systematic reviews and RCTs evaluating individuals with refractory pain due to FBSS, CRPS, or diabetic neuropathy. RCTs were heterogeneous regarding patient populations and participants were unblinded (no trials used sham surgeries or devices) but they consistently reported reductions in pain, with clinically and statistically significant effect sizes and reductions in medication use for at least 6-months. Even with a sham-controlled surgery or device, blinded outcomes assessment may not be feasible for SCS because active SCS is associated with paresthesia's. Given the extensive treatment effects with consistent findings across studies, this evidence suggests that SCS is a reasonable treatment option.

The evidence for standard SCS with burst stimulation has been evaluated in 6 crossover RCTs. Five of the RCTs had fewer than 35 individuals. Inferences drawn from these trials are limited by small sample sizes, short follow-up, and flawed statistical analyses. The largest RCT (SUNBURST) was a 12-week, multicenter, randomized, unblinded, crossover, noninferiority trial assessing traditional SCS or burst stimulation in 100 patients with chronic pain of the trunk and/or limbs. The burst was noninferior to SCS for overall score (at 12-weeks). The proportion of individuals whose global impression was improved (minimally, moderately, or very much improved) was approximately 74% in both groups. Seventy-eight percent of individuals reported being satisfied with both SCS and burst at the end of the 24-week crossover portion of the trial, while 7% were satisfied with SCS but not burst and 10% were satisfied with burst but not SCS. However, more individuals (70.8%) reported preferring burst stimulation over SCS after the 24-week crossover.

High-Frequency Spinal Cord Stimulation for Refractory Chronic Trunk or Limb Pain

Clinical Context and Therapy Purpose

The purpose of high-frequency SCS in individuals who have treatment-refractory chronic trunk or limb pain is to provide a treatment option that is an alternative to or an improvement on existing therapies.

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

Populations

The relevant population of interest is individuals with treatment-refractory chronic pain of the trunk or limbs. Examples of treatment-refractory chronic pain include FFBS, CRPS (i.e., reflex sympathetic dystrophy), arachnoiditis, radiculopathies, phantom limb/stump pain, peripheral neuropathy, and painful diabetic neuropathy.

Interventions

The therapy being considered is high-frequency SCS. High-frequency SCS devices use a higher frequency (10000 Hz) compared with the standard SCS devices. High-frequency SCS potentially lowers the incidence of paresthesia's compared with standard spinal cord stimulation.

Comparators

The following practice is currently being used to treat individuals with treatment-refractory chronic pain of the trunk or limbs: standard SCS, medical therapy, or surgical therapy.

Outcomes

The IMMPACT group has provided recommendations for 4 core chronic pain outcome domains that should be included when selecting outcome measures for clinical trials of treatments for chronic pain: (1) pain intensity; (2) physical functioning; (3) emotional functioning; and (4) participant ratings of overall improvement. The IMMPACT group has also suggested specific outcome measures to address these core domains and has proposed provisional benchmarks for identifying clinically important changes in these specific outcome measures (Table 2)

Adverse events can either be hardware-related to biological. Hardware-related complications include lead migration, failure or fracture. Biological complications include infection and pain. More severe biological complications are rare, including dural puncture headache and neurological damage.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

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

Review of Evidence

Systematic Reviews

Sun et al (2024) conducted a meta-analysis of 7 RCTs (published through 2023) aimed to systematically evaluate the efficacy and safety of high-frequency SCS in managing chronic pain. The results demonstrated that high-frequency SCS had superior long-term efficacy in chronic pain treatment compared to the control group (relative risk [RR] = 2.44, 95% CI: 1.20 to 4.96, p=0.01), showing a significant improvement in the ODI score (MD=3.77, 95% CI: 1.17 to 6.38, p=0.005). However, high-frequency SCS did not exhibit statistically significant effects in pain assessment (standardized mean difference [SMD] = -0.59, 95% CI: -1.28 to 0.10, p=0.09), PGI score, Clinical Global Impression of Improvement (CGI-I) score, and occurrence of adverse effects.

Bicket et al (2016) published a systematic review of controlled trials on high-frequency spinal cord stimulation. Reviewers searched for RCTs and controlled nonrandomized studies of adults with pain for at least 3 months who were treated with high-frequency spinal cord stimulation (i.e., ≥1000 Hz) and prospectively assessed pain outcomes. Eight studies met these inclusion criteria: 2 RCTs (detailed below)

and 6 controlled nonrandomized studies. Both RCTs and 5 of 6 controlled studies addressed low back pain; the remaining controlled study addressed migraine. Reviewers used the Cochrane criteria to rate bias in the RCTs. One trial (Perruchoud et al [2013]) was not rated as having a high-risk of bias in any domain, and the other (Kapural et al [2015]) was rated as having a high-risk of bias in the domain of performance and detection bias because it was unblinded. Studies were reviewed qualitatively (i.e., study findings were not pooled).

Randomized Controlled Trials

Six RCTs identified addressed high-frequency spinal cord stimulation (Table 5): Perruchoud et al (2013) compared high-frequency spinal cord stimulation (5000 Hz) with sham-control in a crossover design (N=40), Petersen et al (2021) compared high-frequency spinal cord stimulation plus medical management with medical management alone, while Kapural et al (2015) (N=198), Bolash et al (2019) (N=99), and De Andres et al (2017) (N=60) compared high-frequency spinal cord stimulation (10000 Hz) with standard spinal cord stimulation. All 6 trials are summarized in Table 5. The trials with N>100 are described individually.

Petersen et al (2021) randomized 216 participants with painful diabetic neuropathy (baseline lower limb VAS ≥5 cm on a 10 cm scale) refractory to prior pharmacological treatment to high-frequency spinal cord stimulation plus conventional medical management (n=113) versus conventional medical management alone (n=103). All participants were randomized to high-frequency spinal cord stimulation and underwent a trial stimulation period. Participants were eligible for permanent implantation of the stimulation device if at least 50% pain relief was achieved during the trial period. Participants remained in their randomized groups for 6 months, after which time they were eligible to crossover to the other group in the event of inadequate pain relief. The addition of high-frequency spinal cord stimulation to conventional medical management was associated with significantly improved pain scores at 6-month follow-up (Table 5). Results from 12-month follow-up were consistent in finding a significant pain benefit for high-frequency spinal cord stimulation plus medical management versus medical management alone. Limitations of the study include a lack of blinding for participants and investigators.

Kapural et al (2015, 2016) included 198 patients with chronic leg and back pain who had received conventional medical management but not spinal cord stimulation. Kapural et al (2015) included an active, but unblinded, comparator (standard spinal cord stimulation) and included a trial spinal cord stimulation period up to 2 weeks post-randomization after which only responders continued with stimulation. Outcomes were reported after 3, 12, and 24 months of treatment. The response in the standard spinal cord stimulation group was similar to previous trials of spinal cord stimulation, between 45% and 50% for back pain and 50% to 55% for leg pain at 3, 12, and 24 months. The response was clinically and statistically significantly higher with high-frequency spinal cord stimulation than with spinal cord stimulation for both back (range, »75% to 85%) and leg pain (range, »70% to 85%) at all time points. A limitation of the Kapural et al (2015, 2016) trial was that nonresponders during the stimulation trial period were excluded from statistical analysis. Instead, assuming patients who were not implanted were nonresponders corresponds to response rates at 3 months of about 75% in high-frequency spinal cord stimulation and 37% in spinal cord stimulation for back pain and 74% and 46% for leg pain (calculated, data not shown).

Kapural et al (2022) enrolled 159 individuals with nonsurgical refractory back pain, defined as patients with chronic back pain refractory to conventional medical management (CMM) who have no history of spine surgery and are not acceptable candidates for spine surgery, who were randomized in a 1:1 ratio to CMM with and without high-frequency (10-kHz) SCS (HFSCS) from September 2018 to January 2020. Conventional medical management was generally consistent with clinical guidelines. Participants

randomized to HFSCS received trial stimulation of up to 14 days. Follow-up visits were completed at 1, 3, 6, 9, and 12 months. The median age was between 53 and 58 years and median time from diagnosis was 8 years. Eighty-one percent of CMM + HFSCS participants versus 1% of CMM participants were responders (primary outcome, ≥ 50% pain relief) at 3 months (p<.001) and 80% versus 3% were responders at 6 months (p<.001). The study was not blinded and nonresponders during the stimulation period were excluded from further analysis.

Table 5. Characteristics and Result of RCTs of using High-Frequency Spinal Cord Stimulation

Study	**Population**	**Interventions**	**N at Baseline and Follow-Up**	**Results**				**Complications**
				Outcome Measure	*Int*	*Ctrl*	*p*	
Perruchoud et al (2013)	Chronic low back pain radiating in 1 or both legs; previously treated with SCS	• HFSCS • Sham • 2×2 crossover design with conventional SCS before both arms	N=40 n=33	2 wk (HFSCS vs. sham)				One patient had malaise attributed to a vasovagal attack
				Responder (at least minimal improvement on patient-reported global impression of change)	42%	30%	.30	
				VAS score	4.35	4.26	.82	
				Health utility	0.48	0.46	.78	
Petersen et al (2021); Petersen et al (2022) Peterson et al (2023)	Painful diabetic neuropathy	• HFSCS + medical management • Medical management	N=216 n at 6 mo=187	6 mo (HFSCS + medical management vs. medical management)				SAEs, 12% vs. 0% Wound complications (dehiscence, impaired healing, or infection): 6% vs. 0%
				Responder (proportion with ≥50% change in VAS without	86%	5%	<.0001	

Study	Population	Interventions	N at Baseline and Follow-Up	Results				Complications
				a meaningful worsening of baseline neurological deficits)				
				Remitter (proportion with pain VAS ≤3 cm for 6 consecutive months)	60%	1%	<.001	
				Quality of life (EQ-5D-5Index, mean change from baseline)	0.130 (SD 0.159)	-0.031 (SD 0.127)	<.001	
		Originally assigned to HFSCS and crossovers to HFSCS combined	n=104 HFSCS and n=77 crossovers to HFSCS	12 mo (HFSCS + crossovers to HFSCS)				
				Responder (proportion with ≥50% change in VAS)	85%			
				Quality of life (EQ-5D-5L Index, mean change from baseline)	0.14 (95% CI, 0.10 to 0.17)			
			142 HFSCS and cross-overs	Responder (proportion with ≥50% change in VAS)	90%			
Kapural et al (2015, 2016)	Chronic back and leg pain	• HFSCS • SCS	N=198 n at 3 mo=171 n at 24 mo=156	3 mo (HFSCS vs. SCS)				Stimulation discomfort, 0% vs. 47% No stimulated-rated SAEs

Study	Population	Interventions	N at Baseline and Follow-Up	Results				Complications
								or neurologic deficits
				Responder (≥50% back pain reduction with no stimulation-related neurologic deficit): Back pain	85%	44%	<.001	
				  Leg pain	83%	55%	<.001	
			n at 12 mo=171	12 mo (HFSCS vs. SCS)				
				Responders Back pain	80%	50%	NR	
				  Leg pain	80%	56%	NR	
				Decreased opioid use	36%	26%	.41	
				Improvement in ODI score	16.5	13.0	NR	
				24 mo (HFSCS vs. SCS)				
				Responders o Back pain	77%	49%	<.001	
				o Leg pain	73%	49%	<.001	
De Andes et al (2017)	FBSS	• HFSCS • SCS	N=60 n=55 analyzed	12 mo (HFSCS vs. SCS)				
				Responder (≥50% in pain intensity in NRS score at 12 mo)[a]	NR	NR		

Study	Population	Interventions	N at Baseline and Follow-Up	Results				Complications
				Improvement in NRS score	6.1	5.9	.56	
				Improvement in ODI score	23.0	22.1	.96	
Bolash et al (2019)	FBSS	• HFSCS SCS	N=99 n=72 analyzed	6 mo (HFSCS vs SCS)				
				Responder (≥50% reduction VAS for back pain)	92%	82%	Noninferiority <.001	
				Remission (VAS for back pain of ≤25 mm)	84%	47%		
Kapural et al (2022); Patel et al (2023)	Nonsurgical refractory back pain	• HFSCS + medical management • Medical management	N=159 n=143 analyzed	3 mo (HFSCS+medical management vs medical management)				
				Responder (≥ 50% pain relief)	81%	1%	<.001	
				Mean change in EQ-5D-5L score (SD)	0.21 (0.14)	0.004 (0.02)	<.001	
			n=140	6 mo (HFSCS+medical management vs medical management)				
				Responder (≥ 50% pain relief)	80%	3%	<.001	
				Mean change in EQ-5D-5L score (SD)	0.21 (0.13)	-0.04 (0.14)	<.001	
			n=98	24 mo (HFSCS only)				

Study	Population	Interventions	N at Baseline and Follow-Up	Results				Complications
				Responder (≥50% pain relief)	82%			
				Mean change in EQ-5D-5L score	0.19 (NR)			

Ctrl: control; EQ-5D-5L: EuroQol 5-Dimension Questionnaire; FBSS: failed back surgery syndrome; HFSCS: high-frequency spinal cord stimulation; Int: intervention; NR: not reported; NRS: numeric rating scale; ODI: Oswestry Disability Index; SAE: serious adverse events; SCS: spinal cord stimulation; VAS: visual analog scale; RCT: randomized controlled trial.
[a] Despite the responder criteria being stated to be the primary outcome, the results for this outcome were not reported.

Section-Summary: High Frequency Spinal Cord Stimulation for Refractory Chronic Trunk or Limb Pain

The evidence for HFSCS compared with standard SCS consists of a systematic review and RCTs. Two RCTs that enrolled participants not previously treated with SCS reported clinically and statistically significant benefits associated with HFSCS. A crossover RCT enrolling individuals with pain despite previous treatment with SCS reported no difference between HFSCS and sham stimulation. However, interpretation of this trial is limited due to the significant period effect.

Dorsal Root Ganglion Neurostimulation for Refractory Chronic Trunk or Limb Pain

Clinical Context and Therapy Purpose

The purpose of dorsal root ganglion neurostimulation (DRGS) in individuals who have treatment-refractory chronic trunk or limb pain is to provide a treatment option that is an alternative to or an improvement on existing therapies.

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

Populations

The relevant population of interest is individuals with treatment-refractory chronic pain of the trunk or limbs. Examples of treatment-refractory chronic pain include FBSS, CRPS (i.e., reflex sympathetic dystrophy), arachnoiditis, radiculopathies, phantom limb/stump pain, peripheral neuropathy, and painful diabetic neuropathy.

Interventions

The therapy being considered is DRGS. Dorsal root ganglion uses the same epidural approach technique as SCS but targets a different anatomical target, the dorsal root ganglion. Dorsal root ganglia consist of sensory cell bodies that transmit input from the peripheral nervous system to the central nervous system and play a role in neuropathic pain perception. Dorsal root ganglia are located in the epidural space

between spinal nerves and the spinal cord on the posterior root in a minimal amount of cerebrospinal fluid, amenable to epidural access.

Comparators

The following practice is currently being used to treat individuals with treatment-refractory chronic pain of the trunk or limbs: standard SCS, medical therapy, or surgical therapy.

Outcomes

The IMMPACT group has provided recommendations for 4 core chronic pain outcome domains that should be included when selecting outcome measures for clinical trials of treatments for chronic pain: (1) pain intensity; (2) physical functioning; (3) emotional functioning; and (4) participant ratings of overall improvement. The IMMPACT group has also suggested specific outcome measures to address these core domains and has proposed provisional benchmarks for identifying clinically important changes in these specific outcome measures (Table 2).

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

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

Review of Evidence

Dorsal Root Ganglion Implanted Device

Systematic Reviews

Campos-Fajardo et al (2024) conducted a qualitative systematic review to evaluate the efficacy of DRGS in the management of chronic pain. The review included 29 articles published between 2018 and 2024, covering a range of patient diagnoses extending beyond CRPS. The majority of these studies were observational (21), supplemented by 5 clinical trials, 1 secondary analysis, and 2 pilot studies. This systematic review confirmed the effectiveness of DRGS therapy in managing various chronic pain conditions. It highlighted significant improvements in patients' quality of life, functionality, and mood states, positioning DRGS as a viable alternative for those who have not responded to traditional treatments.

Mattie et al (2024) conducted a qualitative systematic review of 6 RCTs that showed significant pain reduction in CRPS patients treated with SCS and DRGS. Preference for specific SCS settings varied among patients, with no clear superiority of one setting over another. Innovations in SCS technology, including novel waveforms and frequencies, demonstrated potential for enhanced efficacy and patient comfort.

Several systematic reviews of dorsal root ganglion devices have been published: Vuka et al (2019), Deer et al (2020), Monan et al (2021) and D'Souza et al (2022). The reviews all include one RCT (ACCURATE) and several observational studies. The RCT is described in the following section.

Randomized Controlled Trial

The ACCURATE study (NCT01923285) compared dorsal root ganglion neurostimulation with standard spinal cord stimulation. As reported by Deer et al (2017), eligibility criteria for this multicenter, unblinded, noninferiority trial included chronic (≥6 months) intractable (failed ≥2 drugs from different classes) neuropathic pain of the lower limbs associated with a diagnosis of CRPS or causalgia and no previous neurostimulation. Patients were randomized to dorsal root ganglion stimulation with the Axium device or standard spinal cord stimulation. Patients first underwent a temporary trial of stimulation lasting 3 to 30 days, depending on the protocol at each site. Patients who had a 50% or greater reduction in lower limb pain after the temporary trial were eligible for permanent stimulation. Those who failed temporary stimulation exited the trial but were included in the analysis as treatment failures. Trial characteristics are shown in Table 6.

A total of 152 patients were randomized, and 115 (n=61 dorsal root ganglion, n=54 spinal cord stimulation) had a successful temporary trial and continued to permanent implantation. The primary outcome was a composite measure of treatment success. Success was defined as (1) a 50% or greater reduction in VAS score and (2) no stimulation-related neurologic deficits. The noninferiority margin was set at 10%. Results are shown in Table 7. No patients experienced neurologic deficits in either group. Regarding paresthesia's, at 3 months and 12 months, spinal cord stimulation patients were significantly more likely to report paresthesia's in nonpainful areas than dorsal root ganglion patients. At 3 months, 84.7% of dorsal root ganglion patients and 65% of spinal cord stimulation patients reported paresthesia's only in their painful areas; at 12 months, these percentages were 94.5% and 61.2%, respectively. Limitations in study relevance, design, and conduct are shown in Tables 8 and 9.

Mekhail et al (2019) conducted a sub-analysis on the patients receiving dorsal root ganglion neurostimulation in the ACCURATE study, to evaluate the occurrence and risk factors for paresthesia. Among the 61 patients with dorsal root ganglion implants, the rates of paresthesia at 1 month, 3 months, 6 months, 9 months, and 12 months were 84%, 84%, 66%, 62%, and 62%, respectively. The patients who were paresthesia-free reported similar or better outcomes for pain and quality of life. Risk factors for paresthesia occurrence included higher stimulation amplitudes and frequencies, number of implanted leads, and younger age.

Table 6. RCT Characteristics of DRG Implanted Devices

				Interventions		
Study	**Countries**	**Sites**	**Dates**	**Participants**	**DRG**	**SCS**
Deer et al (2017) ACCURATE (NCT01923285)	U.S.	22	2013-2016	• CRPS or causal lower extremities • Chronic pain (6 mo) • Stimulation-naïve	AXIUM Neurostimulator System (n=76)	RestoreUltra and RestoreSensor (n=76)

				• Failed ≥2 pharmacologic treatments		

ACCURATE: A Prospective, Randomized, Multi-Center, Controlled Clinical Trial to Assess the Safety and Efficacy of the Spinal Modulation™ AXIUM™ Neurostimulator System in the Treatment of Chronic Pain; CRPS: complex regional pain syndrome; DRG: dorsal root ganglion; RCT: randomized controlled trial; SCS: spinal cord stimulation.

Table 7. RCT Results of DRG Implanted Devices

Study	≥50% Reduction in VAS Scores for Pain	Physical Functioning	Emotional Functioning	Quality of Life		Safety
		Mean BPI Interference	*POMS Total Score*	*SF-36 PCS*	*SF-36 MCS*	*SAEs*
Deer et al (2017)						
At 3 months						
n	139	113	NR	113	113	NR
DRG	81%	4.2	NR	11.8	8.3	
SCS	56%	3.0	NR	9.4	4.8	
TE (95% CI) (p)	NR (noninferiority p<.001; superiority p<.001)	1.1 (0.2 to 2.1) (<.05 favoring DRG)	NR (.04 favoring DRG)	2.5 (-0.7 to 5.7)	3.5 (-0.5 to 7.5)	
At 12 months						
n	132	105	NR	105	105	152
DRG	74%	3.9	»18	11.5	6.2	11%
SCS	53%	2.6	»8	8.0	3.6	15%
TE (95% CI) (p)	NR (noninferiority p<.001; superiority p<.001)	1.3 (0.2 to 2.3)(<.05 favoring DRG)	NR (<.001)	3.5 (-0.1 to 7.1)(.04 favoring DRG)	2.6 (-1.9 to 7.1)	NR (.62)

BPI: Brief Pain Inventory; CI: confidence interval; DRG: dorsal root ganglion; MCS: Mental Component Summary; NR: not reported; POMS: Profile of Mood States; PCS: Physical Component Summary; RCT: randomized controlled trial; SAE: serious adverse event; SCS: spinal cord stimulation; SF-36: 36-Item Short-Form Health Survey; TE: treatment effect; VAS: visual analog scale.

Table 8. Study Relevance Limitations for RCTs of DRG Implanted Devices

Study	Population	Intervention	Comparator	Outcomes	Follow-Up

Deer et al (2017)					

DRG: dorsal root ganglion; RCT: randomized controlled trial.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use; 5. Enrolled study populations do not reflect relevant diversity
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 9. Study Design and Conduct Limitations for RCTs of DRG Implanted Devices

Study	Allocation	Blinding	Selective Reporting	Follow-Up	Power	Statistical
Deer et al (2017)		1, 2. Patients and study staff not blinded. Outcomes mostly patient reported which could lead to bias. However, an active control (SCS) was used.				4. Treatment effects not reported for some outcomes, but p values reported

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

Observational Studies

Because RCT data are available for dorsal root ganglion neurostimulation, observational studies are discussed if they add information not available from the RCTs (e.g., longer follow-up including adverse events, data on an important subgroup, etc.). Deer et al (2019) compared the safety and complaint records from the manufacturers of dorsal root ganglion neurostimulation (n=500+) and spinal cord stimulation (n=2000+) devices, from April 2016 through March 2018. The overall safety event rate for the study timeframe was 3.2% for dorsal root ganglion systems and 3.1% for spinal cord stimulation systems. Persistent pain was reported at a rate of 0.2% by patients with dorsal root ganglion implants and 0.6% by patients with spinal cord stimulation implants. Infection rates were 1.1% in both groups of patients. Cerebrospinal leaks were reported in 0.5% of patients with dorsal root ganglion implants and in 0.3% of patients with spinal cord stimulation implants.

A retrospective analysis of the FDA's Manufacturer and User Facility Device Experience (MAUDE) database provided information on complications related to the use of dorsal root ganglion stimulation. The MAUDE database was queried for dorsal root ganglion stimulation reports through 2017, identifying 979 episodes. Complications were predominantly device-related (47%; lead migration and lead damage), with the remaining comprised of procedural complications (28%; infection, new neurologic symptoms, and dural puncture), patient complaints (12%; site pain and unwanted stimulation), serious adverse events (2.4%), and "other" complications (4.6%). The prevalence of complications cannot be estimated using the MAUDE database; while facilities are mandated to report events, patients and health care providers may report events, but are not mandated to do so.

Dorsal Root Ganglion Wireless Injectable Device

Case Series

A case series, which included 11 patients, was published by Weiner et al (2016). This study included patients with failed back surgery syndrome who had chronic intractable neuropathic pain of the trunk and/or lower limbs. Five patients participated in phase 1 of the study (device not anchored), and 6 additional patients participated in phase 2 (device anchored). During phase 1, the device migrated more than was recommended and thus it was anchored in the remaining patients. Baseline VAS scores were 5 or higher in all patients. Seven (63%) of the 11 patients reported good to excellent overall pain relief (VAS score reduction, ≥50%), 2 patients reported fair overall intensity pain relief (25% to 50% reduction), and 2 patients reported poor or no overall pain relief (0% to 25%). No adverse events were reported.

Section Summary: Dorsal Root Ganglion Neurostimulators for Refractory Chronic Trunk or Limb Pain

Systematic reviews, 1 unblinded RCT, and case series have evaluated DRGS in individuals with chronic trunk and/or limb pain. The RCT (N=152) found that individuals receiving DRGS had significantly higher rates of treatment success (physical functioning score and QOL measures) at 3 and 12 months compared with those receiving standard SCS devices. In addition, DRGS was found to be noninferior to SCS in the percentage achieving ≥50% pain reduction, emotional functioning score, and 36-Item Short-Form Health Survey scores. Both groups experienced paresthesia's but individuals in the dorsal root ganglion group reported less postural variation in paresthesia and reduced extraneous stimulation in nonppainful areas. Individuals in the dorsal root ganglion group also reported more improvement in interference with physical functioning and mood states. Rates of serious adverse events were similar.

Spinal Cord Stimulation for Critical Limb Ischemia

Clinical Context and Therapy Purpose

The purpose of SCS in individuals who have critical limb ischemia is to provide a treatment option that is an alternative to or an improvement on existing therapies.

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

Populations

The relevant population of interest is individuals with critical limb ischemia. Critical limb ischemia is described as pain at rest or the presence of ischemic limb lesions.

Interventions

The therapy being considered is SCS. SCS uses low-level epidural electrical stimulation of the spinal cord dorsal columns. Its mechanism of action is uncertain but may be related to either activation of an inhibitory system or blockage of facilitative circuits. SCS devices consist of several components: (1) the lead delivering electrical stimulation to the spinal cord; (2) an extension wire that conducts the electrical stimulation from the power source to the lead; and (3) a power source. The lead may incorporate 4 to 8 electrodes, depending on the complexity of the pain pattern. A trial period in which the electrode is temporarily implanted in the epidural space is recommended, prior to the permanent implantation. Most SCS devices operate under a frequency of 100 to 1000 Hz.

If individuals are not suitable candidates for limb revascularization (typically due to insufficient distal runoff), amputation may be required. SCS has been investigated in this subset of indviduals as a technique to relieve pain and decrease the incidence of amputation.

Comparators

The following practice is currently being used to treat individuals with critical limb ischemia: medical therapy or surgical therapy (revascularization surgery or amputation).

Outcomes

The IMMPACT group has provided recommendations for 4 core chronic pain outcome domains that should be included when selecting outcome measures for clinical trials of treatments for chronic pain: (1) pain intensity; (2) physical functioning; (3) emotional functioning; and (4) participant ratings of overall improvement. The IMMPACT group has also suggested specific outcome measures to address these core domains and has proposed provisional benchmarks for identifying clinically important changes in these specific outcome measures (Table 2).

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

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

Review of Evidence

Systematic Reviews

An updated Cochrane review by Ubbink and Vermeulen (2013) assessed the use of spinal cord stimulation in peripheral vascular diseases. Reviewers included RCTs and non-RCTs evaluating the efficacy of spinal cord stimulation in adults with non-reconstructable, chronic critical leg ischemia. Six trials were identified; all were conducted in Europe and 5 were single-country studies. Spinal cord

stimulation was compared with other nonsurgical interventions. One study was not randomized, and none were-blinded. In a pooled analysis of data from all 6 studies, there was a significantly higher rate of limb survival in the spinal cord stimulation group than in the control group at 12 months (relative risk [RR], 0.75; 95% CI, 0.57 to 0.95; absolute risk difference, -0.11; 95% CI, -0.20 to -0.02). The 11% difference in the rate of limb salvage means that 9 patients would need to be treated to prevent 1 additional amputation (95% CI, 5 to 50 patients). However, when the nonrandomized study was excluded, the difference in the rate of amputation no longer differed significantly between groups (RR, 0.78; 95% CI, 0.58 to 1.04; absolute risk difference, -0.09; 95% CI, -0.19 to 0.01). The spinal cord stimulation patients required significantly fewer analgesics, and more patients reached Fontaine stage II (intermittent claudication) than in the control group. There was no difference in ulcer healing (but only 2 studies were included in this analysis). In the 6 trials, 31 (15%) of 210 patients had a change in stimulation requiring intervention, 8 (4%) experienced the end of battery life, and 6 (3%) infections required device removal.

Previously, Klomp et al (2009) published a meta-analysis of RCTs that used spinal cord stimulation to treat patients with critical limb ischemia. The same 5 RCTs identified in the Cochrane review were included. Reviewers did not find a statistically significant difference in the rate of amputation in the treatment or control groups. The RR of amputation was 0.79 (95% CI, 0.59 to 1.06), with a risk difference of -0.07 (95% CI, -0.17 to 0.03). Reviewers also conducted additional analyses of data from their 1999 RCT to identify factors associated with better or worse prognoses. They found that patients with ischemic skin lesions had a higher risk of amputation than patients with other risk factors. There were no significant interactions between this and any other prognostic factor. The analyses did not identify subgroups of patients who might benefit from spinal cord stimulation.

A systematic review of non-revascularization-based treatments by Abu Dabrh et al (2015) for patients with critical limb ischemia included spinal cord stimulation as 1 of the treatments. The review identified 5 RCTs for inclusion. In the pooled analysis, reviewers found that spinal cord stimulation was associated with reduced risk of amputation (odds ratio [OR], 0.53; 95% CI, 0.36 to 0.79); risk difference was not reported.

Section Summary: Critical Limb Ischemia

Five relatively small RCTs comparing spinal cord stimulation with usual care have assessed patients with critical limb ischemia. In pooled analyses from 3 systematic reviews, spinal cord stimulation was associated with a lower risk of amputation versus control, but results were not consistently statistically significant due to differences in methodologies. This evidence is not sufficient to determine whether spinal cord stimulation would improve outcomes for patients with critical limb ischemia.

Spinal Cord Stimulation for Selected Other Medical Conditions

Clinical Context and Therapy Purpose

The purpose of SCS in individuals who have other medical conditions (e.g., angina pectoris, heart failure, cancer-related pain, multiple sclerosis and spasticity disorders, post herpetic neuralgia, fibromyalgia, axial and other musculoskeletal pain syndromes and treatment of nociception pain [resulting from irritation and not damage to nerves]) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

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

Populations

The relevant populations of interest are individuals with treatment-refractory angina pectoris, heart failure, cancer-related pain multiple sclerosis and spasticity disorders, post herpetic neuralgia, fibromyalgia, axial and other musculoskeletal pain syndromes and treatment of nociception pain [resulting from irritation and not damage to nerves])

Interventions

The therapy being considered is SCS. SCS uses low-level epidural electrical stimulation of the spinal cord dorsal columns. Its mechanism of action is uncertain but may be related to either activation of an inhibitory system or blockage of facilitative circuits. SCS devices consist of several components: (1) the lead delivering electrical stimulation to the spinal cord; (2) an extension wire that conducts the electrical stimulation from the power source to the lead; and (3) a power source. The lead may incorporate 4 to 8 electrodes, depending on the complexity of the pain pattern. A trial period in which the electrode is temporarily implanted in the epidural space is recommended, prior to the permanent implantation. Most SCS devices operate under a frequency of 100 to 1000 Hz.

Comparators

The following practice is currently being used to treat patients with

- Refractory angina pectoris: medical therapy or coronary revascularization.
- Heart failure: medical therapy or coronary revascularization.
- Cancer-related pain: medical therapy.
- Post-herpetic neuralgia: antidepressants, antiseizure medication, short term narcotic pain medications, and topical creams.
- Multiple Sclerosis: medications to help control symptoms and rehabilitation to improve and maintain function.
- Fibromyalgia: medications to help control symptoms, exercise, relaxation, and stress-reduction measures.
- Nociceptive Pain and central deafferentation pain: NSAIDs and opioid medications.

Outcomes

The IMMPACT group has provided recommendations for 4 core chronic pain outcome domains that should be included when selecting outcome measures for clinical trials of treatments for chronic pain: (1) pain intensity; (2) physical functioning; (3) emotional functioning; and (4) participant ratings of overall improvement. The IMMPACT group has also suggested specific outcome measures to address these core domains and has proposed provisional benchmarks for identifying clinically important changes in these specific outcome measures (Table 2).

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Methodologically credible studies were selected using the following principles:

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

Review of Evidence

Refractory Angina Pectoris

Systematic Reviews

Pan et al (2017) identified 12 RCTs that evaluated spinal cord stimulation versus control in patients with refractory angina pectoris. Most studies had small sample sizes (i.e., <50 patients; N=476). Follow-up ranged widely from 2 weeks to 12 months, and control interventions were not well described in the systematic review. The included studies were generally assessed to have low risk of bias. Pooled analyses favored the spinal cord stimulation group for most outcomes (e.g., for exercise time after the intervention, pain level [VAS score], angina frequency) but there were no significant differences between intervention and control groups for physical limitation or angina stability.

Another systematic review was published by Tsigaridas et al (2015). It included 9 RCTs evaluating spinal cord stimulation for refractory angina: 7 compared spinal cord stimulation with low or no stimulation and 2 compared spinal cord stimulation with alternative medical or surgical therapy for angina. Reviewers found that most RCTs were small and variable in quality based on modified Jadad criteria. Reviewers reported: "2 of the RCTs were of high quality (Jadad score 4); 2 were of low quality (Jadad score 1), and the remaining ones were of intermediate quality (Jadad score 2 to 3)." Most trials comparing spinal cord stimulation with low, or no stimulation found improvements in outcomes with spinal cord stimulation; however, given limitations in the evidence base, reviewers concluded that larger multicenter RCTs would be needed to assess the efficacy of spinal cord stimulation for angina.

Randomized Controlled Trials

Two of the largest RCTs included in the systematic reviews were Zipes et al (2012) and Lanza et al (2011).

Zipes et al (2012) published an industry-sponsored, single-blind, multicenter trial with sites in the United States and Canada. This trial was terminated early because interim analysis by the data and safety monitoring board found the treatment futile. A total of 118 patients with severe angina, despite maximal medical treatment, were enrolled. Of the 118 patients, 71 (60%) underwent spinal cord stimulation implantation with the Intrel III neurostimulator (Medtronic). The remaining 47 patients did not meet eligibility criteria post-enrollment or had other issues (e.g., withdrew consent). The investigators had originally been planning to randomize up to 310 patients, but enrollment was slow. Implantation was successful in 68 patients; this group was randomized to high-stimulation (n=32) or a low-stimulation control (n=36). The low-stimulation control was designed so that patients would feel paresthesia, but the effect of stimulation would be subtherapeutic. The primary outcome was a composite of major adverse cardiac events, which included death from any cause, acute myocardial infarction, or revascularization through 6 months. Fifty-eight (85%) of 68 patients contributed data to the 6-month analysis; analysis was by intention-to-treat. The proportion of patients experiencing major adverse cardiac events at 6 months did not differ significantly between groups (12.6% in the high-stimulation group vs. 14.6% in the low-stimulation group; p=.81). The trial sample size was small, and it might have been underpowered for clinically meaningful differences.

A controlled trial from Italy by Lanza et al (2011) randomized 25 patients to 1 of 3 treatment groups: spinal cord stimulation with standard stimulation (n=10), spinal cord stimulation with low-level stimulation (75% to 80% of the sensory threshold) (n=7), or very low-intensity spinal cord stimulation (n=8).[73,] Thus,

patients in groups 2 and 3 were unable to feel sensation during stimulation. After a protocol adjustment at 1 month, patients in the very low-intensity group were re-randomized to 1 of the other groups of which there were 13 patients in the standard stimulation group and 12 patients in the low-level stimulation group. At the 3-month follow-up (2 months after re-randomization), there were statistically significant between-group differences in 1 of 12 outcome variables. There was a median of 22 angina episodes in the standard stimulation group and 10 in the low-level stimulation group (p=.002). Nonsignificant variables included the use of nitroglycerin, quality of life, VAS score, Canadian Cardiovascular Society angina class, exercise-induced angina, and scores on 5 subscales of the Seattle Angina Questionnaire.

Uncontrolled Studies

Because RCT data are available for spinal cord stimulation, uncontrolled studies are discussed if they add information not available from the RCTs (e.g., longer follow-up including adverse events, data on an important subgroup, etc.). Lanza et al (2012) reviewed observational studies on spinal cord stimulation in patients with refractory angina pectoris. They identified 16 studies (N=1204 patients) but noted that patients might have been included in more than 1 report. The most frequently reported complications were lead issues (i.e., electrode dislodgement or fracture requiring repositioning) or internal programmable generator failure during substitution. Lead issues were reported by 10 studies (N=450 patients). In these studies, 55 cases of lead or internal programmable generator failure were reported. No fatalities related to spinal cord stimulation treatment were reported.

Section Summary: Refractory Angina Pectoris

Numerous small RCTs have evaluated spinal cord stimulation as a treatment for refractory angina. While some studies have reported benefits, most have not. In 2 more recent RCTs, there were no significant benefits for the primary outcomes. Overall, this evidence is mixed and insufficient to permit conclusions on whether health outcomes are improved.

Heart Failure

Systematic Reviews

Ashrafpour (2024) conducted a systematic review to investigate the efficacy of SCS as an adjunctive therapy in heart failure. 4 studies (2 RCTs and 2 pilot studies) with a total of 125 patients were selected. Participants had heart failure with NYHA classification ranging from 2 to 3. Primary endpoints included heart failure-related symptoms, left ventricular ejection function, VO2 max, and NT-proBNP (N-terminal Pro-Brain Natriuretic Peptide). The studies demonstrated the safety and feasibility of SCS therapy, although outcomes varied. Two studies reported improvements in New York Heart Association classification, Minnesota Living with Heart Failure Questionnaire (MLHFQ), and quality of life parameters, while only one study showed positive changes in Left Ventricular Ejection Fraction and VO2 max. No studies found significant changes in NT-proBNP following SCS therapy. Discrepancies in results could be due to methodological variations and induction technique diversity. Further studies are needed to develop a solid approach for employing SCS in heart failure patients.

Section Summary: Heart Failure

A 2024 systematic review was conducted to investigate the efficacy of SCS as an adjunctive therapy in heart failure. Four studies (including 2 RCTs) with a total of 125 patients were selected. Two studies reported improvements in New York Heart Association classification, and QOL parameters, while only one study showed positive changes in left ventricular ejection function and VO2 max. No studies found

significant changes in NT-proBNP (N-terminal Pro-Brain Natriuretic Peptide) following SCS therapy. Discrepancies in results could be due to methodological variations and induction technique diversity. Further studies are needed to develop a solid approach for employing SCS in heart failure patients.

Cancer- Related Pain

Systematic Reviews

A Cochrane review by Lihua et al (2013) assessed spinal cord stimulation for the treatment of cancer-related pain in adults. Reviewers did not identify any RCTs evaluating the efficacy of spinal cord stimulation in this population. Four case series using a before-after design (N=92 patients) were identified. Peng et al (2015) updated this review, finding no new studies meeting inclusion criteria identified. They concluded: "Current evidence is insufficient to establish the role of spinal cord stimulation in treating refractory cancer-related pain."

Section Summary: Cancer-Related Pain

A Cochrane review did not identify any RCTs evaluating spinal cord stimulation for the treatment of cancer-related pain.

Postherpetic Neuralgia

Systematic Review

In 2023, Isagulyan et al performed a systematic review regarding the effectiveness of various types of electrical stimulation (dorsal root ganglion stimulation [DRGS], burst spinal cord stimulation [SCS] and high frequency SCS) of the spinal cord in patients which chronic postherpetic neuralgia pain. Twelve articles were included with 134 patients with postherpetic neuralgia (PHN) that were analyzed in which disproportionally large amount of traditional SCS were utilized compared to alternative SCS: DRGS (13 patients), burst SCS (2 patients) and high-frequency SCS (2 patients). Pain relief was achieved in 91 patients (68.9%). The mean VAS score improvement was 61.4% with a mean follow-up time of 12.85 months. Even though there were a limited number of patients that utilized alternative SCS almost all patients showed a good response to therapy with more than 50% VAS improvement and reduction of analgesic dosage. The authors concluded that alternative stimulation strategies such as burst, high-frequency stimulation and DSRG may be a possible solution in the treatment of PHN due to their ability to provide pain relief without unpleasant parethesias, however, despite some promising results demonstrating a decrease in pain intensity there was conflicting evidence regarding efficacy in the alternative SCSs. “Large randomized controlled trials comparing alternative and traditional modes of SCS are required, with a substantial amount of PHN patients enrolled.”

Observational Study

In 2017, Dao-Song et al retrospectively evaluated the efficacy of short- term spinal cord stimulation (stSCS) ranging from 7 to 14 days in patients with refractory acute/subacute zoster related pain. A total of 62 patients with zoster related pain who underwent stSCS were examined and a total of 46 patients (22 men and 24 women) satisfied the inclusion and exclusion criteria and were enrolled. The inclusion criteria were patients with herpes zoster (HZ) within 120 days from rash onset and had received at least one interventional procedure before stSCS and were still experiencing severe pain based on the visual analog

scale (VAS) ≥ 6. The severity of HZ associated pain was measured using the VAS system over a period of 24 hours, and following stSCS treatment a decrease of at least 3 points was considered an important improvement in accordance with the guidelines of minimal clinically important difference (MCID) associated with adequate pain management. Quality of life (QOL) was assessed using the 12-items Short Form Health Survey (SF-12) with a score range of 0 to 100 points and a score < 50 indicates below-average status. The VAS, SF-12, and analgesic consumption (including antiepileptic agents) were recorded before stSCS, post-stSCS, 2 weeks, and 1, 3, 6, 9, and 12 months after treatment. Among the 45 patients enrolled in this study, all patients were followed up to 6- months, 34 patients were followed up to 9-months, and 20 patients continued follow-up for more than 12-months. Post-stSCS 32 patients (69.9%, 32.46) achieved the minimal clinically important difference (MCID), including 18 patients (39.1%, 18/46) achieved complete pain relief (VAS ≤ 2). During the follow-up period the efficacy of stSCS did not decrease, but VAS scores declined. QOL scores (SF-12) and analgesic consumption improved after stSCS treatment. No serious adverse effects were observed. The limitations of this study included that it was not a randomized prospective controlled study, outcomes of patients with mild to moderate pain were not compared and did not compare the efficacy of stSCS treatment with conventional therapies. The authors concluded “stSCS can provide pain relief and improvement in QOL in patients with refractory and severe acute/subacute zoster related pain.”

Case Series

In 2018, Kurklinsky, et. al. performed a retrospective chart review for all patients (n=2) that underwent subcutaneous peripheral nerve stimulation (sPNS) for postherpetic neuralgia (PHN) at Mayo Clinic Florida and reviewed the literature regarding the use of spinal cord stimulation (SCS) and sPNS for the treatment of PHN. There were 16 reports for permanent implantation of SCS with a total of 255 patients with PHN that found 120 patients received long-term pain relief (47.1%). In these 16 reports, detailed pain scores were available in 11 of the reports with a total of 66 patients with an average pain relief of 79.0%. Follow-up data was available in 12 reports with an average follow-up of 50.8 months. The discussion on use of medication after SCS in addition to the precise location of the SCS implantation was quite limited. The largest study of sPNS had 12 patients with PHN, however, the patients were not separated by the type of neuropathic pain and conclusion on the success rate could not be made. The main limitation of this study was the small sample size. The authors concluded “It would be beneficial to the neurostimulation field and patients if a multisite clinical trial and registry of current sPNS cases were established in order to standardize techniques and collect outcome data.”

Section Summary: Postherpetic Neuralgia

In a systematic review (Isagulyan et. al. 2023) which evaluated the effectiveness of various types of electrical stimulation (traditional, burst, high-frequency and DRGS) in 134 patients with PHN. Pain relief was achieved in 91 patients (68.9%). The mean VAS score improvement was 61.4% with a mean follow-up time of 12.85 months. Even though there were a limited number of individuals that utilized alternative SCS almost all individuals showed a good response to therapy with more than 50% VAS improvement and reduction of analgesic dosage. Despite some promising results demonstrating a decrease in pain intensity there was conflicting evidence regarding efficacy in the alternative electrical stimulation types. RCTs are needed with larger sample sizes, comparing alternative and traditional modes of SCS to conventional therapies to establish the safety and effectiveness of SCS in the treatment of PHN.

Multiple Sclerosis

Systematic Review

In 2021, Rapisarda et. al. performed a systemic review regarding the use of spinal cord stimulation (SCS) in the management of patients with multiple sclerosis (MS). Seven studies were included with 373 MS patients who were submitted for SCS trial in which 285/372 (76.4%) were enrolled for permanent stimulation with a mean follow-up 44.40 ± 25.00 months. Overall improvement was observed in 193 out 346 (55.8%) of patients with motor disorders, 90 out of 134 (67.13%) patients with urinary dysfunction and in 28 out of 34 (82.35%) patients with neuropathic pain. The efficacy of SCS was higher for urinary dysfunction (p=0.0144) and neuropathic pain (p=0.0030) compared with motor disorders. The authors noted that the effectiveness of SCS in the treatment of MS has been debated in the literature without a definitive conclusion, there currently is not clear indication on which MS patients would benefit from SCS and on the best time to perform this procedure in these patients. Adverse events occurred in 65% of the patients treated which included system malfunctioning or breakage, wound or system infections, and epidural hematoma. The limitations of these studies included retrospective nature of the data and the different evaluation scales utilized among the different studies, which did not allow further subgroup analyses (different MS types, different motor and urinary symptoms and different pain locations). The authors concluded “The results of this systematic review suggests that SCS is effective in MS patients. Further studies with longer follow-up are needed to improve the patient selection, clarify the best timing to perform SCS in these patients, and better understand the potential loss of effectiveness of SCS over time.”

Section Summary: Multiple Sclerosis

In a systematic review (Rapisard et. al. 2021) evaluated the use of SCS in the management of patients with MS. Seven studies were included with 373 MS patients who were submitted for SCS trial in which 285/372 (76.4%) were enrolled for permanent stimulation with a mean follow-up 44.40 ± 25.00 months. Overall improvement was observed in 193 out 346 (55.8%) of patients with motor disorders, 90 out of 134 (67.13%) patients with urinary dysfunction and in 28 out of 34 (82.35%) patients with neuropathic pain. The efficacy of SCS was higher for urinary dysfunction (p=0.0144) and neuropathic pain (p=0.0030) compared with motor disorders. While this review may show promise, there is not a clear indication on which MS patients would benefit from SCS and on the best time to perform this procedure on these patients. Prospective RCTs comparing SCS to conventional therapies with longer follow-up are needed to improve patient selection, clarify the best time to perform SCS and better understand the potential loss of effectiveness in patients with MS.

Fibromyalgia

No RCTs were found regarding the use of SCS in the treatment of fibromyalgia.

Observational Study

In 2023, D’Souza et al performed an 11-year retrospective multicenter matched cohort study comparing spinal cord stimulation (SCS) treated patients with fibromyalgia and those without fibromyalgia. The primary outcome measure was the comparison in mean calculated percentage pain relief between cohorts at 6-months after SCS and secondary outcome measures included the comparison of patient satisfaction and the percentage of patients reporting opioid and neuropathic medication intake between 6- and 12-months after SCS implantation. Ninety patients with fibromyalgia who underwent SCS trial, 18 patients (20%) failed their SCS trial and did not proceed to permanent implantation. Sixty-eight patients

with fibromyalgia were matched to 141 patients in the control cohort based on age, sex, Charlson comorbidity index, and the American Society of Anesthesiologists physical status score. At six months after SCS implantation, there was no statistical difference in calculated percentage change in pain intensity between the fibromyalgia cohort (46.6 ± 29.0) and the control cohort (50.9 ± 32.8; β, -18.4; 95% CI, -44.3 to 7.6; p = 0.157). At baseline, a greater percentage of patients in the fibromyalgia cohort reported preoperative opioid intake (51.5% vs 22.7%, p < 0.001) and preoperative neuropathic medication intake (67.6% vs 15.6%, p < 0.001). However, there was no difference between cohorts in the percentage of patients taking opioid or neuropathic medications at 6- and 12- months after SCS implantation. Similarly, there was no difference between cohorts in the percentage of patients that reported satisfaction between 6- and 12-months.

Section Summary: Fibromyalgia

No RCTs were found regarding the use of SCS in the treatment of fibromyalgia. In a 11-year retrospective multicenter matched cohort study (D'Souza et. al. 2023) which compared SCS treated patients with fibromyalgia (n=68) and those without fibromyalgia (n=148). At 6 months post SCS placement there was no statistical difference in the calculated percentage change in pain between the fibromyalgia cohort (46.6 ± 29.0) and the control cohort (50.9 ± 32.8; β, -18.4; 95% CI, -44.3 to 7.6; p = 0.157) and there was no difference between the cohorts in the percentage of patients taking opioid or neuropathic medications at 6- and 12-months. Similarly, there was no difference between cohorts in the percentage of patients reporting satisfaction. Prospective RCTs comparing SCS to conventional therapies with large sample sizes and long-term follow-up are needed to determine the safety and efficacy of SCS in the treatment of fibromyalgia neuropathic pain.

Combined Use of Spinal Cord Stimulation and Dorsal Root Ganglion Stimulation

Randomized Controlled Trials

Rigoard et al (2025) in a prospective, randomized, double-blind, cross-over trial (BOOST-DRG study) compared the efficacy of relieving pain utilizing spinal cord stimulation (SCS), dorsal root ganglion stimulation (DRGS), and DUAL SCS and DRGS stimulation in patients with persistent spinal pain syndrome after spinal surgery (PSPS-T2). After the 3-month cross-over period, stimulation programming was switched to Burst. Primary outcome evaluated proportion of patients achieving $\geq$ 50% global pain VAS decrease at one month treatment follow-up (cross-over period) compared with baseline (M0). Secondary outcomes assessed pain intensity, area of pain, area of paresthesia coverage, quality of life (QOL), functional disability, psychological distress, medical intake, and Multidimensional Clinical Response Index (MCRI) at each follow-up visit up to 12-months. The study was designed to be delivered in two phases with 12 patients in the first phase and 54 in the second phase (n=66 in total), however, after the first phase the funder terminated the study. Therefore, only 12 patients (n=12; 7 patients female [70%]) were included, mean age 49.6 $\pm$ 13.0 years with refractory chronic lower limb neuropathic pain and/or neuropathic back pain for $\geq$ 6 months. One patient was exclude due to noncompliance. Eleven patients underwent a successful trial period with permanent implantation. Due to study related infection after implantation and randomization a patient was excluded from analysis which left 10 to be analyzed. Three patients were randomized to SCS-DUAL-DRGS, two to DRGS-SCS-DUAL, two to DUAL-DRGS-SCS, two to DUAL-SCS-DRGS, and one to SCS-DRGS DUAL. For the per protocol (PP) based on the treatment by the patient and not randomized, one patient underwent SCS instead of the randomized DRGS treatment owing to pain recurrence (DUAL-SCS-SCS); one patient underwent DRGS instead of SCS (DRGS-DRGS-DUAL) for the same reason; and one patient had DRGS-DUAL-SCS instead of the randomized SCS-DUAL-DRGS due to a technical issue of lead misidentification during the programming session. The rate of patients with 50% VAS decrease was 60% for all treatment modalities, and no

significant difference was observed among groups (p = 0.84). Regarding MCRI responders the change in MCRI was ≥1.05-point. For all treatment modalities the reviewers found the rate of responders 90% for SCS, 90% for DRGS, and 100% for DUAL without a significant difference among groups (p = 0.95). At the end of the cross-over period, four patients (40%) preferred SCS, three (30%) DRGS, and three (30%) DUAL, without significant difference among the preference rates of different stimulation targets (p = 0.91). At 12-month follow-up, one patient switched from DRGS to SCS, and another from SCS to DUAL (40% SCS, 30% DRGS, and 30% DUAL) (p = 0.91). At the four-month follow-up visit, eight patients (80%) reported a preference for tonic stimulation, and two (20%) preferred Burst, without significant difference between the preference rates of the different stimulation waveforms (p = 0.057). At 12-month follow-up, another patient switched from tonic to Burst (60% tonic and 40% Burst) (p = 0.53). Secondary outcomes 3-4-6-12-months compared to baseline found global response VAS (p < 0.0001), pain surface (p = 0.018), ODI score (p = 0.00048), EQ-5D (p = 0.0039), HADS depression (p = 0.0012) and anxiety (p = 0.044) scores, MQS score (p =0.00069), and MCRI score (p < 0.0001). Thirteen adverse events were reported in nine (n=12 [75%]) of the patients, however, only two were serious which included infection at lead level and post-implantation back pain. Limitations of this study included early termination which limited the power of clinical outcome interpretations. Also, the limitations for Burst programming to a single area which prevented combination Burst stimulation at both the spinal and ganglion levels failing to realize the full potential of the therapy.

Case Series

In 2018, Goebel et. al. in a case series reported on the details in the management of a patient with complex regional pain syndrome (CRPS) that reoccurred 2 years after mid-tibial amputation. It was noted there is little evidence available on how CRPS recurrence should be managed. Conventional spinal cord stimulation (SCS) did not achieve para esthetic coverage, or pain relief in the stump, whereas the L4 dorsal root ganglion stimulation (DRGS) initially achieved modest pain relief and over time substantial pain relief. The authors concluded when conventional SCS treatment has failed in the treatment CRPS, DRGS should be considered as a potential treatment.

In 2017, Yang and Hunter in a case series evaluated 2 patients with complex regional pain syndrome (CRPS) that was treated with traditional spinal cord stimulation (t-SCS) placement, however, their pain relapsed despite reprogramming and both patients were offered dorsal root ganglion (DRG) stimulation after failed t-SCS as salvage therapy. While DRG and t-SCS target different spinal pathways and has been shown that both forms of stimulation are effective in the treatment of CRPS, the efficacy in patients who have previously failed t-SCS and using DRG as salvage treatment is unknown. Patient 1 reported 90% reduction in pain with gait improvement during the DRG trial period and proceeded to permanent placement with t-SCS removed. Patient 2 was unable to undergo a trial with DRG-SCS, and elected to undergo a surgical revision of the existing t-SCS system in which a DRG-SCS system was added to create a hybrid system with 2 implantable pulse generators. Post implantation of the DRG-SCS system the patient reported immediate improvement of pain. The patient was instructed to document pain scores with each system individually as well as with both on. The lowest pain scores were reported with the DRG-SCS on by itself. At the eight-month follow-up both patients reported sustained pain improvement and retained functional gains. The authors concluded “Our case series demonstrates that a failure of t-SCS is not necessarily a failure of neurostimulation as a whole. The efficacy of DRG-SCS is independent of prior t-SCS therapy outcomes in these two patients and a history of t-SCS failure serves no predictive value in these two patients for future DRG stimulation success. Therefore, DRG-SCS can be considered as a reasonable next-step to salvage patients with CRPS who had failed other SCS treatments.”

Section Summary: Combined Use of Spinal Cord Stimulation and Dorsal Root Ganglion Stimulation

One RCT has been published Rigoard et al (2025), however, the majority of the current evidence regarding the combined use of SCS and DRGS is case series (Goebel 2018 and Yang 2017). The RCT by Rigouard (2025) a prospective, randomized, double-blind, cross-over trial (BOOST-DRG study) compared the efficacy of relieving pain utilizing spinal cord stimulation (SCS), dorsal root ganglion stimulation (DRGS), and DUAL SCS and DRGS stimulation in patients (n=10) with refractory chronic lower limb neuropathic pain and/or neuropathic back pain for ≥ 6 months after spinal surgery. The ten patients were initially randomized three to SCS-DUAL-DRGS, two to DRGS-SCS-DUAL, two to DUAL-DRGS-SCS, two to DUAL-SCS-DRGS, and one to SCS-DRGS DUAL. While there was 50% VAS decrease for 60% of all treatment modalities, there were no significant difference observed among groups ($p = 0.84$). At the end of the cross-over period, four patients (40%) preferred SCS, three (30%) DRGS, and three (30%) DUAL, without significant difference among the preference rates of different stimulation targets ($p = 0.91$). Limitations of this study included early termination which limited the power of clinical outcome interpretations. The case series which included a total of 3 individuals with recurrent CRPS pain, it was noted there is little evidence available on how CRPS recurrence should be managed. The three individuals were initially treated with conventional SCS, and when the CRPS pain reoccurred with conventional SCS failure, DRGS (n=2) and DRGS-SCS (n=1) systems were implanted. While these case series may have shown promise in the treatment of recurrent CRPS pain after failed conventional SCS with salvage therapy with the placement of DRGS or DRGS-SCS regarding improvement in pain and functional status the sample size is small (n=3) and there is no long-term follow-up. Additional RCTs with larger sample size and long-term follow-up are needed to determine the safety and efficacy regarding the combined use of SCS and DRGS. The current evidence is insufficient to support the combined use of SCS and DRGS in the treatment of CRPS or any other indication.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in ‘Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Association of Clinical Endocrinology

In 2022, the American Association of Clinical Endocrinology published evidence-based recommendations for the care of individuals with diabetes mellitus. The guidelines state that 'Neuromodulatory techniques such as high-frequency spinal cord stimulation and combining pharmacological with nonpharmacological approaches should be considered in those with refractory painful DPN [diabetic peripheral neuropathy]'. The evidence for the statement was rated as Grade B [Strong]; BEL [best evidence level] 1 [Randomized controlled trial; Meta-analysis of only randomized controlled trials].

American Society of Regional Anesthesia and Pain Medicine

In 2023, American Society of Regional Anesthesia and Pain Medicine published evidence-based consensus guidelines on patient selection and trial stimulation for spinal cord stimulation (SCS) therapy for chronic non-cancer pain. Recommendations included that SCS trial should be performed before a definitive SCS implant except in anginal pain (grade B). All patients must be screened with an objective validated instrument for psychosocial factors, and this must include depression (grade B). Despite some limitations, a trial helps patient selection and provides patients with an opportunity to experience the therapy. These recommendations are expected to guide practicing physicians and other stakeholders and should not be mistaken as practice standards. Physicians should continue to make their best judgment based on individual patient considerations and preferences.

American Society of Interventional Pain Physicians

In 2013, the American Society of Interventional Pain Physicians updated its evidence-based guidelines on interventional techniques for the management of chronic spinal pain. The guidelines included a statement that there is fair evidence for the following recommendation for spinal cord stimulation: "spinal cord stimulation is indicated in chronic low back pain with lower extremity pain secondary to failed back surgery syndrome, after exhausting multiple conservative and interventional modalities".

American Society of Pain and Neuroscience

The American Society of Pain and Neuroscience issued a comprehensive guideline in 2021 on the management of cancer-related pain. The guideline found that spinal cord stimulation may be considered for 1) treatment of refractory cancer pain (II-3-C evidence: multiple series compared over time, with or without intervention, and surprising results in noncontrolled experience; treatment is neither recommendable nor inadvisable), and 2) on a case-by-case basis for "pain that is related to cancer treatment such as chemotherapy-induced peripheral neuropathy" (level III-C evidence: clinical experiences-based opinions, descriptive studies, clinical observations, or reports of expert committee; treatment is neither recommendable nor inadvisable).

The American Society of Pain and Neuroscience published consensus guidelines on interventional therapies for knee pain in 2022. The guidelines state that "Chronic pain that is refractory to acute treatment is managed by progressing to spinal cord stimulator, dorsal root ganglion stimulator, or botulinum toxin (Botox) injection." They also include the statement that "DRG [Dorsal Root Ganglion Stimulation] is a safe and effective treatment option for chronic post-surgical and focal neuropathic pain of the knee (i.e., complex regional pain syndrome [CRPS]); Level I, Grade A, Consensus Strong."

The American Society of Pain and Neuroscience published consensus guidelines on interventional therapies for back pain in 2022. The guidelines make the following recommendations for spinal cord stimulation:

Table 10. American Society of Pain and Neuroscience Recommendations for Spinal Cord Stimulation for Back Pain

Recommendation	Grade	Level of Evidence	Level of Certainty of Net Benefit

Following lumbar surgery	A	I-A	Strong
Treatment of non-surgical low back pain	B	I-C	Moderate
Treatment of lumbar spinal stenosis	C	I-C	Moderate

National Institute for Health and Care Excellence

In 2008, NICE issued guidance on spinal cord stimulation for chronic pain of neuropathic or ischemic origin, which was reaffirmed in 2014. The NICE recommended spinal cord stimulation as a treatment option for adults with chronic pain of neuropathic origin (measuring at least 50 mm on a 0 to 100 mm visual analog scale) that continues for at least 6 months despite appropriate conventional medical management, and who have had a successful trial of stimulation as part of an assessment by a specialist team.

In the same guidance, the NICE stated that spinal cord stimulation was not recommended for chronic pain of ischemic origin except in the context of research.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review can be located at clinicaltrials.gov.

REFERENCES

1. Food and Drug Administration. Cordis Programmable Neural Stimulator: Premarket Approval. Accessed Feb 27, 2024.
2. U.S. Food and Drug Administration. Conduct a trial stimulation period before implanting a spinal cord stimulator (SCS) - letter to health care providers. September 3, 2020. https://www.fda.gov/medical-devices/letters-health-care-providers/conduct-trial-stimulation-period-implanting-spinal-cord-stimulator-scs-letter-health-care-providers. Accessed Feb 27, 2024.
3. Turk DC, Dworkin RH, Allen RR, et al. Core outcome domains for chronic pain clinical trials: IMMPACT recommendations. Pain. Dec 2003; 106(3): 337-345. PMID 14659516
4. Dworkin RH, Turk DC, Farrar JT, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain. Jan 2005; 113(1-2): 9-19. PMID 15621359
5. Dworkin RH, Turk DC, Wyrwich KW, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. J Pain. Feb 2008; 9(2): 105-21. PMID 18055266
6. Kerns RD, Turk DC, Rudy TE. The West Haven-Yale Multidimensional Pain Inventory (WHYMPI). Pain. Dec 1985; 23(4): 345-356. PMID 4088697
7. Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. Ann Acad Med Singap. Mar 1994; 23(2): 129-38. PMID 8080219

8. Fairbank JC, Pynsent PB. The Oswestry Disability Index. Spine (Phila Pa 1976). Nov 15 2000; 25(22): 2940-52; discussion 2952. PMID 11074683

9. Ostelo RW, Deyo RA, Stratford P, et al. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. Spine (Phila Pa 1976). Jan 01 2008; 33(1): 90-4. PMID 18165753

10. Wells GA, Tugwell P, Kraag GR, et al. Minimum important difference between patients with rheumatoid arthritis: the patient's perspective. J Rheumatol. Mar 1993; 20(3): 557-60. PMID 8478873

11. Kosinski M, Zhao SZ, Dedhiya S, et al. Determining minimally important changes in generic and disease-specific health-related quality of life questionnaires in clinical trials of rheumatoid arthritis. Arthritis Rheum. Jul 2000; 43(7): 1478-87. PMID 10902749

12. Angst F, Aeschlimann A, Stucki G. Smallest detectable and minimal clinically important differences of rehabilitation intervention with their implications for required sample sizes using WOMAC and SF-36 quality of life measurement instruments in patients with osteoarthritis of the lower extremities. Arthritis Rheum. Aug 2001; 45(4): 384-91. PMID 11501727

13. Beck ATS, R.A. Beck Depression Inventory. San Antonio, TX: Psychological Corporation; 1993.

14. Curran SL, Andrykowski MA, Studts JL. Short Form of the Profile of Mood States (POMS-SF): Psychometric information. Psychol Assess 1995;7:80-83.

15. Visnjevac O, Costandi S, Patel BA, et al. A Comprehensive Outcome-Specific Review of the Use of Spinal Cord Stimulation for Complex Regional Pain Syndrome. Pain Pract. Apr 2017; 17(4): 533-545. PMID 27739179

16. O'Connell NE, Wand BM, McAuley J, et al. Interventions for treating pain and disability in adults with complex regional pain syndrome. Cochrane Database Syst Rev. Apr 30 2013; 2013(4): CD009416. PMID 23633371

17. Grider JS, Manchikanti L, Carayannopoulos A, et al. Effectiveness of Spinal Cord Stimulation in Chronic Spinal Pain: A Systematic Review. Pain Physician. Jan 2016; 19(1): E33-54. PMID 26752493

18. Traeger AC, Gilbert SE, Harris IA, et al. Spinal cord stimulation for low back pain. Cochrane Database Syst Rev. Mar 07 2023; 3(3): CD014789. PMID 36878313

19. Head J, Mazza J, Sabourin V, et al. Waves of Pain Relief: A Systematic Review of Clinical Trials in Spinal Cord Stimulation Waveforms for the Treatment of Chronic Neuropathic Low Back and Leg Pain. World Neurosurg. Nov 2019; 131: 264-274.e3. PMID 31369885

20. Duarte RV, Nevitt S, Maden M, et al. Spinal cord stimulation for the management of painful diabetic neuropathy: a systematic review and meta-analysis of individual patient and aggregate data. Pain. Nov 01 2021; 162(11): 2635-2643. PMID 33872236

21. Henson JV, Varhabhatla NC, Bebic Z, et al. Spinal Cord Stimulation for Painful Diabetic Peripheral Neuropathy: A Systematic Review. Pain Ther. Dec 2021; 10(2): 895-908. PMID 34244979

22. Raghu ALB, Parker T, Aziz TZ, et al. Invasive Electrical Neuromodulation for the Treatment of Painful Diabetic Neuropathy: Systematic Review and Meta-Analysis. Neuromodulation. Jan 2021; 24(1): 13-21. PMID 32588933

23. Strand NH, Burkey AR. Neuromodulation in the Treatment of Painful Diabetic Neuropathy: A Review of Evidence for Spinal Cord Stimulation. J Diabetes Sci Technol. Mar 2022; 16(2): 332-340. PMID 34842478

24. Hoelzer BC, Edgar D, Lu SP, et al. Indirect Comparison of 10 kHz Spinal Cord Stimulation (SCS) versus Traditional Low-Frequency SCS for the Treatment of Painful Diabetic Neuropathy: A Systematic Review of Randomized Controlled Trials. Biomedicines. Oct 19 2022; 10(10). PMID 36289892

25. O'Connell NE, Ferraro MC, Gibson W, et al. Implanted spinal neuromodulation interventions for chronic pain in adults. Cochrane Database Syst Rev. Dec 02 2021; 12(12): CD013756. PMID 34854473

26. Zhou M, Zhong H, Xing C, et al. Comparison of clinical outcomes associated with spinal cord stimulation (SCS) or conventional medical management (CMM) for chronic pain: a systematic review and meta-analysis. Eur Spine J. Jun 2023; 32(6): 2029-2041. PMID 37067600

27. North RB, Kidd DH, Farrokhi F, et al. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial. Neurosurgery. 2005; 56(1): 98-106; discussion 106-7. PMID 15617591

28. Kumar K, Taylor RS, Jacques L, et al. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomised controlled trial in patients with failed back surgery syndrome. Pain. Nov 2007; 132(1-2): 179-88. PMID 17845835

29. Kumar K, Taylor RS, Jacques L, et al. The effects of spinal cord stimulation in neuropathic pain are sustained: a 24-month follow-up of the prospective randomized controlled multicenter trial of the effectiveness of spinal cord stimulation. Neurosurgery. Oct 2008; 63(4): 762-70; discussion 770. PMID 18981888

30. Kemler MA, Barendse GA, van Kleef M, et al. Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. N Engl J Med. Aug 31 2000; 343(9): 618-24. PMID 10965008

31. Kemler MA, De Vet HC, Barendse GA, et al. The effect of spinal cord stimulation in patients with chronic reflex sympathetic dystrophy: two years' follow-up of the randomized controlled trial. Ann Neurol. Jan 2004; 55(1): 13-8. PMID 14705107

32. Kemler MA, de Vet HC, Barendse GA, et al. Effect of spinal cord stimulation for chronic complex regional pain syndrome Type I: five-year final follow-up of patients in a randomized controlled trial. J Neurosurg. Feb 2008; 108(2): 292-8. PMID 18240925

33. Slangen R, Schaper NC, Faber CG, et al. Spinal cord stimulation and pain relief in painful diabetic peripheral neuropathy: a prospective two-center randomized controlled trial. Diabetes Care. Nov 2014; 37(11): 3016-24. PMID 25216508

34. de Vos CC, Meier K, Zaalberg PB, et al. Spinal cord stimulation in patients with painful diabetic neuropathy: a multicentre randomized clinical trial. Pain. Nov 2014; 155(11): 2426-31. PMID 25180016

35. Duarte RV, Andronis L, Lenders MW, et al. Quality of life increases in patients with painful diabetic neuropathy following treatment with spinal cord stimulation. Qual Life Res. Jul 2016; 25(7): 1771-7. PMID 26694963

36. Rigoard P, Basu S, Desai M, et al. Multicolumn spinal cord stimulation for predominant back pain in failed back surgery syndrome patients: a multicenter randomized controlled trial. Pain. Jun 2019; 160(6): 1410-1420. PMID 30720582

37. Zuidema X, van Daal E, van Geel I, et al. Long-Term Evaluation of Spinal Cord Stimulation in Patients With Painful Diabetic Polyneuropathy: An Eight-to-Ten-Year Prospective Cohort Study. Neuromodulation. Jul 2023; 26(5): 1074-1080. PMID 36587999

38. Mekhail N, Levy RM, Deer TR, et al. Long-term safety and efficacy of closed-loop spinal cord stimulation to treat chronic back and leg pain (Evoke): a double-blind, randomised, controlled trial. Lancet Neurol. Feb 2020; 19(2): 123-134. PMID 31870766

39. Mekhail NA, Levy RM, Deer TR, et al. ECAP-controlled closed-loop versus open-loop SCS for the treatment of chronic pain: 36-month results of the EVOKE blinded randomized clinical trial. Reg Anesth Pain Med. Aug 27 2023. PMID 37640452

40. Rauck RL, Loudermilk E, Thomson SJ, et al. Long-term safety of spinal cord stimulation systems in a prospective, global registry of patients with chronic pain. Pain Manag. Feb 2023; 13(2): 115-127. PMID 36691862

41. Mekhail NA, Mathews M, Nageeb F, et al. Retrospective review of 707 cases of spinal cord stimulation: indications and complications. Pain Pract. 2011; 11(2): 148-53. PMID 21371254

42. Hou S, Kemp K, Grabois M. A Systematic Evaluation of Burst Spinal Cord Stimulation for Chronic Back and Limb Pain. Neuromodulation. Jun 2016; 19(4): 398-405. PMID 27139915

43. De Ridder D, Plazier M, Kamerling N, et al. Burst spinal cord stimulation for limb and back pain. World Neurosurg. Nov 2013; 80(5): 642-649.e1. PMID 23321375

44. De Ridder D, Vanneste S, Plazier M, et al. Burst spinal cord stimulation: toward paresthesia-free pain suppression. Neurosurgery. May 2010; 66(5): 986-90. PMID 20404705

45. Schu S, Slotty PJ, Bara G, et al. A prospective, randomised, double-blind, placebo-controlled study to examine the effectiveness of burst spinal cord stimulation patterns for the treatment of failed back surgery syndrome. Neuromodulation. Jul 2014; 17(5): 443-50. PMID 24945621

46. Kriek N, Groeneweg JG, Stronks DL, et al. Preferred frequencies and waveforms for spinal cord stimulation in patients with complex regional pain syndrome: A multicentre, double-blind, randomized and placebo-controlled crossover trial. Eur J Pain. Mar 2017; 21(3): 507-519. PMID 27714945

47. Deer T, Slavin KV, Amirdelfan K, et al. Success Using Neuromodulation With BURST (SUNBURST) Study: Results From a Prospective, Randomized Controlled Trial Using a Novel Burst Waveform. Neuromodulation. Jan 2018; 21(1): 56-66. PMID 28961366

48. Eldabe S, Duarte R, Gulve A, et al. Analgesic Efficacy of "Burst" and Tonic (500 Hz) Spinal Cord Stimulation Patterns: A Randomized Placebo-Controlled Crossover Study. Neuromodulation. Apr 2021; 24(3): 471-478. PMID 33251662

49. Hara S, Andresen H, Solheim O, et al. Effect of Spinal Cord Burst Stimulation vs Placebo Stimulation on Disability in Patients With Chronic Radicular Pain After Lumbar Spine Surgery: A Randomized Clinical Trial. JAMA. Oct 18 2022; 328(15): 1506-1514. PMID 36255427

50. Deer T, Gilligan C, Falowski S, et al. Treatment of Refractory Low Back Pain Using Passive Recharge Burst in Patients Without Options for Corrective Surgery: Findings and Results From the DISTINCT Study, a Prospective Randomized Multicenter Controlled Trial. Neuromodulation. Oct 2023; 26(7): 1387-1399. PMID 37642628

51. Bicket MC, Dunn RY, Ahmed SU. High-Frequency Spinal Cord Stimulation for Chronic Pain: Pre-Clinical Overview and Systematic Review of Controlled Trials. Pain Med. Dec 2016; 17(12): 2326-2336. PMID 28025366

52. Perruchoud C, Eldabe S, Batterham AM, et al. Analgesic efficacy of high-frequency spinal cord stimulation: a randomized double-blind placebo-controlled study. Neuromodulation. 2013; 16(4): 363-9; discussion 369. PMID 23425338

53. Kapural L, Yu C, Doust MW, et al. Novel 10-kHz High-frequency Therapy (HF10 Therapy) Is Superior to Traditional Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: The SENZA-RCT Randomized Controlled Trial. Anesthesiology. Oct 2015; 123(4): 851-60. PMID 26218762

54. Petersen EA, Stauss TG, Scowcroft JA, et al. Effect of High-frequency (10-kHz) Spinal Cord Stimulation in Patients With Painful Diabetic Neuropathy: A Randomized Clinical Trial. JAMA Neurol. Jun 01 2021; 78(6): 687-698. PMID 33818600

55. Bolash R, Creamer M, Rauck R, et al. Wireless High-Frequency Spinal Cord Stimulation (10 kHz) Compared with Multiwaveform Low-Frequency Spinal Cord Stimulation in the Management of Chronic Pain in Failed Back Surgery Syndrome Subjects: Preliminary Results of a Multicenter, Prospective Randomized Controlled Study. Pain Med. Oct 01 2019; 20(10): 1971-1979. PMID 30908577

56. De Andres J, Monsalve-Dolz V, Fabregat-Cid G, et al. Prospective, Randomized Blind Effect-on-Outcome Study of Conventional vs High-Frequency Spinal Cord Stimulation in Patients with Pain and Disability Due to Failed Back Surgery Syndrome. Pain Med. Dec 01 2017; 18(12): 2401-2421. PMID 29126228

57. Petersen EA, Stauss TG, Scowcroft JA, et al. Durability of High-Frequency 10-kHz Spinal Cord Stimulation for Patients With Painful Diabetic Neuropathy Refractory to Conventional Treatments: 12-Month Results From a Randomized Controlled Trial. Diabetes Care. Jan 01 2022; 45(1): e3-e6. PMID 34844993

58. Kapural L, Yu C, Doust MW, et al. Comparison of 10-kHz High-Frequency and Traditional Low-Frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: 24-Month Results From a Multicenter, Randomized, Controlled Pivotal Trial. Neurosurgery. Nov 2016; 79(5): 667-677. PMID 27584814

59. Kapural L, Jameson J, Johnson C, et al. Treatment of nonsurgical refractory back pain with high-frequency spinal cord stimulation at 10 kHz: 12-month results of a pragmatic, multicenter, randomized controlled trial. J Neurosurg Spine. Feb 11 2022: 1-12. PMID 35148512

60. Petersen EA, Stauss TG, Scowcroft JA, et al. High-Frequency 10-kHz Spinal Cord Stimulation Improves Health-Related Quality of Life in Patients With Refractory Painful Diabetic Neuropathy: 12-Month Results From a Randomized Controlled Trial. Mayo Clin Proc Innov Qual Outcomes. Aug 2022; 6(4): 347-360. PMID 35814185

61. Petersen EA, Stauss TG, Scowcroft JA, et al. Long-term efficacy of high-frequency (10 kHz) spinal cord stimulation for the treatment of painful diabetic neuropathy: 24-Month results of a randomized controlled trial. Diabetes Res Clin Pract. Sep 2023; 203: 110865. PMID 37536514

62. Patel NP, Jameson J, Johnson C, et al. Durable responses at 24 months with high-frequency spinal cord stimulation for nonsurgical refractory back pain. J Neurosurg Spine. Feb 01 2024; 40(2): 229-239. PMID 37976509

63. Al-Kaisy A, Palmisani S, Smith TE, et al. Long-Term Improvements in Chronic Axial Low Back Pain Patients Without Previous Spinal Surgery: A Cohort Analysis of 10-kHz High-Frequency Spinal Cord Stimulation over 36 Months. Pain Med. Jun 01 2018; 19(6): 1219-1226. PMID 29077889

64. Vuka I, Marciuš T, Došenović S, et al. Neuromodulation with electrical field stimulation of dorsal root ganglion in various pain syndromes: a systematic review with focus on participant selection. J Pain Res. 2019; 12: 803-830. PMID 30881093

65. Deer TR, Hunter CW, Mehta P, et al. A Systematic Literature Review of Dorsal Root Ganglion Neurostimulation for the Treatment of Pain. Pain Med. Aug 01 2020; 21(8): 1581-1589. PMID 32803221

66. Moman RN, Peterson AA, Maher DP, et al. Infectious Complications of Dorsal Root Ganglion Stimulation: A Systematic Review and Pooled Analysis of Incidence. Neuromodulation. Oct 2022; 25(7): 956-964. PMID 34096135

67. D'Souza RS, Kubrova E, Her YF, et al. Dorsal Root Ganglion Stimulation for Lower Extremity Neuropathic Pain Syndromes: An Evidence-Based Literature Review. Adv Ther. Oct 2022; 39(10): 4440-4473. PMID 35994195

68. Deer TR, Levy RM, Kramer J, et al. Dorsal root ganglion stimulation yielded higher treatment success rate for complex regional pain syndrome and causalgia at 3 and 12 months: a randomized comparative trial. Pain. Apr 2017; 158(4): 669-681. PMID 28030470

69. Food and Drug Administration. Summary of Safety and Effectiveness Data (SSED): Axium Neurostimulator System. 2016; https://www.accessdata.fda.gov/cdrh_docs/pdf15/P150004b.pdf. Accessed Feb 27, 2024.

70. Mekhail N, Deer TR, Kramer J, et al. Paresthesia-Free Dorsal Root Ganglion Stimulation: An ACCURATE Study Sub-Analysis. Neuromodulation. Feb 2020; 23(2): 185-195. PMID 30861286

71. Deer T, Pope J, Hunter C, et al. Safety Analysis of Dorsal Root Ganglion Stimulation in the Treatment of Chronic Pain. Neuromodulation. Feb 2020; 23(2): 239-244. PMID 30861617

72. Sivanesan E, Bicket MC, Cohen SP. Retrospective analysis of complications associated with dorsal root ganglion stimulation for pain relief in the FDA MAUDE database. Reg Anesth Pain Med. Jan 2019; 44(1): 100-106. PMID 30640660

73. Weiner RL, Yeung A, Montes Garcia C, et al. Treatment of FBSS Low Back Pain with a Novel Percutaneous DRG Wireless Stimulator: Pilot and Feasibility Study. Pain Med. Oct 2016; 17(10): 1911-1916. PMID 27125284

74. Ubbink DT, Vermeulen H. Spinal cord stimulation for non-reconstructable chronic critical leg ischaemia. Cochrane Database Syst Rev. Feb 28 2013; 2013(2): CD004001. PMID 23450547

75. Klomp HM, Steyerberg EW, Habbema JD, et al. What is the evidence on efficacy of spinal cord stimulation in (subgroups of) patients with critical limb ischemia?. Ann Vasc Surg. 2009; 23(3): 355-63. PMID 19128928

76. Klomp HM, Spincemaille GH, Steyerberg EW, et al. Spinal-cord stimulation in critical limb ischaemia: a randomised trial. ESES Study Group. Lancet. Mar 27 1999; 353(9158): 1040-4. PMID 10199350

77. Abu Dabrh AM, Steffen MW, Asi N, et al. Nonrevascularization-based treatments in patients with severe or critical limb ischemia. J Vasc Surg. Nov 2015; 62(5): 1330-9.e13. PMID 26409842

78. Pan X, Bao H, Si Y, et al. Spinal Cord Stimulation for Refractory Angina Pectoris: A Systematic Review and Meta-analysis. Clin J Pain. Jun 2017; 33(6): 543-551. PMID 27875377

79. Tsigaridas N, Naka K, Tsapogas P, et al. Spinal cord stimulation in refractory angina. A systematic review of randomized controlled trials. Acta Cardiol. Apr 2015; 70(2): 233-43. PMID 26148385

80. Zipes DP, Svorkdal N, Berman D, et al. Spinal cord stimulation therapy for patients with refractory angina who are not candidates for revascularization. Neuromodulation. 2012; 15(6): 550-8; discussion 558-9. PMID 22494013

81. Lanza GA, Grimaldi R, Greco S, et al. Spinal cord stimulation for the treatment of refractory angina pectoris: a multicenter randomized single-blind study (the SCS-ITA trial). Pain. Jan 2011; 152(1): 45-52. PMID 21084162

82. Lanza GA, Barone L, Di Monaco A. Effect of spinal cord stimulation in patients with refractory angina: evidence from observational studies. Neuromodulation. 2012; 15(6): 542-9; disdcussion 549. PMID 22364309

83. Torre-Amione G, Alo K, Estep JD, et al. Spinal cord stimulation is safe and feasible in patients with advanced heart failure: early clinical experience. Eur J Heart Fail. Jul 2014; 16(7): 788-95. PMID 24961194

84. Zipes DP, Neuzil P, Theres H, et al. Determining the Feasibility of Spinal Cord Neuromodulation for the Treatment of Chronic Systolic Heart Failure: The DEFEAT-HF Study. JACC Heart Fail. Feb 2016; 4(2): 129-136. PMID 26682789

85. Lihua P, Su M, Zejun Z, et al. Spinal cord stimulation for cancer-related pain in adults. Cochrane Database Syst Rev. Feb 28 2013; (2): CD009389. PMID 23450600

86. Peng L, Min S, Zejun Z, et al. Spinal cord stimulation for cancer-related pain in adults. Cochrane Database Syst Rev. Jun 29 2015; 2015(6): CD009389. PMID 26121600

87. Blonde L, Umpierrez GE, Reddy SS, et al. American Association of Clinical Endocrinology Clinical Practice Guideline: Developing a Diabetes Mellitus Comprehensive Care Plan-2022 Update. Endocr Pract. Oct 2022; 28(10): 923-1049. PMID 35963508

88. Manchikanti L, Abdi S, Atluri S, et al. An update of comprehensive evidence-based guidelines for interventional techniques in chronic spinal pain. Part II: guidance and recommendations. Pain Physician. Apr 2013; 16(2 Suppl): S49-283. PMID 23615883

89. Aman MM, Mahmoud A, Deer T, et al. The American Society of Pain and Neuroscience (ASPN) Best Practices and Guidelines for the Interventional Management of Cancer-Associated Pain. J Pain Res. 2021; 14: 2139-2164. PMID 34295184

90. Hunter CW, Deer TR, Jones MR, et al. Consensus Guidelines on Interventional Therapies for Knee Pain (STEP Guidelines) from the American Society of Pain and Neuroscience. J Pain Res. 2022; 15: 2683-2745. PMID 36132996

91. Sayed D, Grider J, Strand N, et al. The American Society of Pain and Neuroscience (ASPN) Evidence-Based Clinical Guideline of Interventional Treatments for Low Back Pain. J Pain Res. 2022; 15: 3729-3832. PMID 36510616

92. Dworkin RH, O'Connor AB, Kent J, et al. Interventional management of neuropathic pain: NeuPSIG recommendations. Pain. Nov 2013; 154(11): 2249-2261. PMID 23748119

93. Deer TR, Pope JE, Lamer TJ, et al. The Neuromodulation Appropriateness Consensus Committee on Best Practices for Dorsal Root Ganglion Stimulation. Neuromodulation. Jan 2019; 22(1): 1-35. PMID 30246899

94. National Institute for Health and Care Excellence (NICE). Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin [TA159]. 2008; https://www.nice.org.uk/guidance/ta159

95. Kurlinsky S, Palmer S, Arroglia M et. al. Neuromodulation in postherpetic neuralgia: Case reports and review of the literature. Pain Medicine 2018; 19: 1237-1244

96. Dao-Song D, Yu X, Wan CF, et. al. Efficacy of short-term spinal cord stimulation in acute/subacute zoster-related pain: A retrospective study. Pain Physician 2017 Jul; 20(5): E633-E645. PMID 28727708

97. Isagulyan E, Tkachenko V, Semenov D et. al. The effectiveness of various types of electrical stimulation of the spinal cord for chronic pain in patients with postherpetic neuralgia: A literature review. Pain Research and Management. Volumem 2023 Article ID 6015680. PMID 37007861

98. Rapisarda A, Ioannoni E, Izzo A, et. al. Is there a place for spinal cord stimulation in the management of patients with multiple sclerosis? A systematic review of the literature. Minim Invasive Surg. 2021 Apr 19:2021:9969010. PMID 33986958

99. McHugh C, Taylor C, Mockler D, et. al. Epidural spinal cord stimulation for motor recovery in spinal cord injury: A systematic review. NeuroRehabilitation 2021;49(1):1-22 PMID 33967072

100. D'Souza R, Barman R, Schappell J, et.al. Does fibromyalgia affect the outcomes of spinal cord stimulation: An 11-year, multicenter, retrospective matched cohort study. Neuromodulation 2023 Jan;26(1):206-214. PMID 35840522

101. Vannemreddy P and Slavin K. Spinal cord stimulation: Current applications for treatment of chronic pain. Anesth Essays Res 2011 Jan-Jun; 5(1): 20-27. PMID 25885295

102. Yang A and Hunter CW. Dorsal root ganglion stimulation as a salvage treatment for complex regional pain syndrome refractory to dorsal column spinal cord stimulation. A case series. Neuromodulation. 2017;20(7):703-707

103. Yang A and Hunter CW. Dorsal root ganglion stimulation as a salvage treatment for complex regional pain syndrome refractory to dorsal column spinal stimulation: A case series. Neuromodulation 2017 Oct;20(7):703-707. PMID 28621025

104. Goebel A, Lewis S, Phillip R, et. al. Dorsal root ganglion stimulation for complex regional pain syndrome (CRPS) recurrence after amputation for CRPS, and failure for conventional spinal cord stimulation. Pain Pract 2018 Ja;18(1):104-108. PMID 28422399

105. Centers for Medicare and Medicaid Services. National Coverage Determination (NCD) for Electrical Nerve Stimulators (160.7). 1995; https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=240&ncdver=1&bc=AAAAgAAAAAAA&

106. Ashrafpour S, Ashrafpour M. Efficacy of spinal cord stimulation as an adjunctive therapy in heart failure: A systematic review. Neurophysiol Clin. May 2024; 54(3): 102945. PMID 38422720

107. Campos-Fajardo S, Sierra-Peña JA, Suárez-Monsalve S, et al. Effectiveness of Dorsal Root Ganglion Stimulation in Chronic Pain Management: A Systematic Review. World Neurosurg. Oct 2024; 190: 157-171. PMID 38945208

108. Deer T, Heros R, Tavel E, et al. Comparing Conventional Medical Management to Spinal Cord Stimulation for the Treatment of Low Back Pain in a Cohort of DISTINCT RCT Patients. J Pain Res. 2024; 17: 2741-2752. PMID 39193462

109. Shanthanna H, Eldabe S, Provenzano DA, et al. Evidence-based consensus guidelines on patient selection and trial stimulation for spinal cord stimulation therapy for chronic non-cancer pain. Reg Anesth Pain Med. Jun 2023; 48(6): 273-287. PMID 37001888

110. Sun S, Yin J, Wei H, et al. Long-Term Efficacy and Safety of High-Frequency Spinal Stimulation for Chronic Pain: A Meta-Analysis of Randomized Controlled Trials. Clin J Pain. Jul 01 2024; 40(7): 415-427. PMID 38595082

111. Huygen FJPM, Soulanis K, Rtveladze K, et al. Spinal Cord Stimulation vs Medical Management for Chronic Back and Leg Pain: A Systematic Review and Network Meta-Analysis. JAMA Netw Open. Nov 04 2024; 7(11): e2444608. PMID 39541119

112. Mattie R, Lin AB, Bhandal H, et al. Spinal cord stimulation for the treatment of complex regional pain syndrome: A systematic review of randomized controlled trials. Interv Pain Med. Dec 2024; 3(4): 100527. PMID 39717450

113. Hayes, a SymplrCompany Health Technology Assessment Dorsal Root Ganglion Stimulation for the Treatment of Complex Regional Pain Syndrome December 2024

114. Hayes, a SymplrCompany Evolving Evidence Review Evoke Spinal Cord Stimulation (Saluda Medical Pty Ltd) for Chronic Intractable Pain December 2024

115. Hayes, a SymplrCompany Evidence Analysis Research Brief Proclaim XR Spinal Cord Stimulation System (Abbott) for Management of Diabetic Peripheral Neuropathy September 2023

116. Hayes, a SymplrCompany Health Technology Assessment Electrical Spinal Cord Stimulation of Intractable Angina Pectoris October 2018

117. Hayes, a SymplrCompany Health Technology Assessment Spinal Cord Stimulation for Relief for Neuropathic Pain March 2023

118. Hayes, a SymplrCompany Evidence Analysis Brief Freedom Spinal Cord Stimulator System (Curonix LLC) for Treatment of Chronic Low Back Pain May 28, 2025

119. Biotronik: New Data Show Significant Pain Relief, Reduced Opioid Use, Decreased Patient Time and Cost Burdens with the Prospera™ SCS System. Press Release January 29, 2025. Also available at https://www/biotronik.com

120. UpToDate. Spinal cord stimulation: Placement and management. Topic last updated January 22, 2025. Also available at https://www.uptodate.com

121. UpToDate. Interventional therapies for chronic pain. Topic last updated January 2025. Also available at https://www.uptodate.com

122. UpToDate. New therapies for angina pectoris. Topic last updated. November 2024. . Also available at https://www.uptodate.com

123. UpToDate. Complex regional pain syndrome (CRPS) in adults: Treatment, prognosis and prevention. Topic last updated March 2025. Also available at https://www.uptodate.com

124. UpToDate. Subacute and chronic low back pain: Surgical treatment. Topic last updated September 2023. Also available at https://www.uptodate.com

125. UpToDate. Microvascular angina: Angina pectoris with normal coronary arteries. Topic last updated March 2025. Also available at https://www.uptodate.com

126. UpToDate. Management of diabetic neuropathy. Topic last updated December 2024. Also available at https://www.uptodate.com

127. UpToDate. Postherpetic neuralgia. Topic last updated March 2025. Also available at https://www.uptodate.com

128. Goodwin B, Mahmud R, TomThundyil S, et. al. The efficacy of spinal code stimulators in the reduction of multiple sclerosis spasticity: A narrative systematic review. Brain Neurorehabil. 2023 Jul 19;16(2):e19.doi:10.12786/bn2023.16.e19. PMID 37554254

129. Mullins C, Palumbo GJ, Harris S, et. al. Effectiveness of combined dorsal root ganglion and spinal cord stimulation: a retrospective, single-centre case series for chronic focal neuropathic pain. Pain Med. 2024 Fe 1;25(2):116-124.doi:10 10.1093/pm/pnad128. PMID 37738574

130. Rigoard P, Ounajim A, Bouche B, et. al. Comparison of spinal cord stimulation, dorsal root ganglion stimulation and association of both patients with refractory chronic back and/or lower limb neuropathic pain: A prospective, randomized, double-blind, cross-over trial (BOOST-DRG Study). Neuromodulation. 2025 Feb;28(2):283-296. PMID 39580743

131. Naidu R, Kapural L, Li S, et. al A review of the Prospera Spinal Cord Stimulation System with multiphase stimulation and proactive care. Current Pain and Headache Reports January 2025. https://www.doi.org/10.1007//s11916-024-0318-3

CODES

To report provider services, use appropriate CPT codes, HCPCS codes, Revenue codes, and/or ICD diagnosis codes.

Codes	Number	Description
CPT		
	63650	Percutaneous implantation of neurostimulator electrode array, epidural
	63655	Laminectomy for implantation of neurostimulator electrodes, plate/paddle, epidural
	63661	Removal of spinal neurostimulator electrode percutaneous array(s), including fluoroscopy, when performed
	63662	Removal of spinal neurostimulator electrode plate/paddle(s) placed via laminotomy or laminectomy, including fluoroscopy, when performed

	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
	63688	Revision or removal of implanted spinal neurostimulator pulse generator or receiver, with detachable connection to electrode array
	95970	Electronic analysis of implanted neurostimulator pulse generator/transmitter (e.g., contact group(s), interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with brain, cranial nerve, spinal cord, peripheral nerve, or sacral nerve, neurostimulator pulse generator/transmitter, without programming
	95971	Electronic analysis of implanted neurostimulator pulse generator/transmitter (e.g., contact group(s), interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with simple spinal cord or peripheral nerve (e.g., sacral nerve) neurostimulator pulse generator/transmitter programming by physician or other qualified health care professional
	95972	Electronic analysis of implanted neurostimulator pulse generator/transmitter (e.g., contact group(s), interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with complex spinal cord or peripheral nerve (e.g., sacral nerve) neurostimulator pulse generator/transmitter programming by physician or other qualified health care professional
	0784T	Insertion or replacement of percutaneous electrode array, spinal, with integrated neurostimulator, including imaging guidance, when performed
	0785T	Revision or removal of neurostimulator electrode array, spinal, with integrated neurostimulator

	0788T	Electronic analysis with simple programming of implanted integrated neurostimulation system (eg, electrode array and receiver), including contact group(s), amplitude, pulse width, frequency (Hz), on/off cycling, burst, dose lockout, patient-selectable parameters, responsive neurostimulation, detection algorithms, closed-loop parameters, and passive parameters, when performed by physician or other qualified health care professional, spinal cord or sacral nerve, 1-3 parameters
	0789T	Electronic analysis with complex programming of implanted integrated neurostimulation system (eg, electorde array and receiver), including contact group(s), amplitude, pulse width, frequency (Hz), on/off cycling, burst, dose lockout, patient-selectable parameters, responsive neurostimulation, detection algorithms, closed-loop parameters, and passive parameters, when performed by physician or other qualified health care professional, spinal cord or sacral nerve, 4 or more parameters
HCPCS		
	C1767	Generator neurostimulator (implantable) non-rechargeable
	C1778	Lead, neurostimulator
	C1787	Patient programmer, neurostimulator
	C1816	Receiver and/or transmitter neurostimulator (implantable)
	C1820	Generator neurostimulator (implantable), non- high frequency with rechargeable battery and charging system
	C1822	Generator neurostimulator (implantable), high frequency with rechargeable battery and charging system
	C1826	Generator, neurostimulator (implantable), includes closed feedback loop leads and all implantable components, with rechargeable battery and charging system
	C1827	Generator, neurostimulator (implantable), non-rechargeable, with implantable stimulation lead and external paired stimulation controller
	C1883	Adaptor/extension, pacing lead or neurostimulator lead (implantable)
	C1897	Lead neurostimulator test kit (implantable)
	L8679	Implantable neurostimulator, pulse generator any type
	L8680	Implantable neurostimulator electrode, each
	L8681	Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only
	L8682	Implantable neurostimulator radiofrequency receiver

	L8683	Radiofrequency transmitter (external) for use with 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
	L8989	External recharging system for battery (internal)for use with implantable neurostimulator, replacement only
Type of Service	Surgical	
Place of Service	Inpatient/Outpatient	

POLICY HISTORY

Date	Action	Action
June 2025	Annual Review	Policy Revised
June 2024	Annual Review	Policy Revised
June 2023	Annual Review	Policy Revised
August 2022	Annual Review	Policy Renewed
August 2021	Annual Review	Policy Renewed
August 2020	Annual Review	Policy Revised
August 2019	Annual Review	Policy Revised
August 2018	Annual Review	Policy Revised
August 2017	Annual Review	Policy Revised
August 2016	Annual Review	Policy Renewed

Date	Action	Action
September 2015	Annual Review	Policy Revised
February 2015	Interim Review	Policy Revised
October 2014	Annual Review	Policy Revised
May 2014	Interim Review	Policy Revised
January 2014	Annual Review	Policy Revision, New Policy Created
January 2013	Annual Review	Policy Renewed
January 2012	Annual Review	Policy Renewed
February 2011	Annual Review	Policy Revised
October 2010	Annual Review	Policy Renewed

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
Medical Policy Analyst
PO Box 9232
Des Moines, IA 50306-9232

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