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Spinal Cord Stimulation (SCS) and Dorsal Root Ganglion (DRG) Stimulation

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Related Policies (if applicable)
SUR712.033 Occipital Nerve Stimulation

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Coverage

Spinal cord stimulation (SCS) with standard or high-frequency stimulation or dorsal root ganglion neurostimulation **may be considered medically necessary** for the treatment of severe and chronic pain of the trunk or limbs that is refractory to all other pain therapies when the following criteria are met:

- Other treatment modalities (pharmacological, surgical, psychological, or physical, if applicable) have been tried and failed, or there is documented clinical evidence that these modalities are unsuitable or contraindicated; AND
- There is no significant untreated drug habituation or addiction; AND
- There is documentation of at least 50% pain relief achieved from trial electrode implantation prior to permanent SCS implantation.

NOTE 1: The first two bulleted criteria (listed above) should be met to qualify for a trial electrode implantation prior to permanent SCS implantation.

NOTE 2: Common conditions that cause severe, chronic, refractory neuropathic pain include, but are not limited to:

- Failed back surgery syndrome;
- 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 considered experimental, investigational and/or unproven** in all other situations including, but not limited to, treatment of:

- Critical limb ischemia as a technique to forestall amputation;
- Refractory angina pectoris;
- Nociceptive pain (resulting from irritation, not damage to the nerves);
- Central deafferentation pain (related to central nervous system damage from a stroke or spinal cord injury);
- Treatment of cancer-related pain; or
- Heart failure.

The Wavegate StimuLux™ System, Wavegate Corp., **is considered experimental, investigational and/or unproven** for all indications, including but not limited to, treatment of chronic leg or back pain that is refractory to conservative therapy or for individuals who are not candidates for surgery.

Policy Guidelines

None.

Description

Spinal cord stimulation 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.

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 SCS 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 to 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: one 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 patient's 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 SCS may require extensive programming of the neurostimulators to identify the optimal electrode combinations and stimulation channels.

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 paresthesias. 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.

Closed-loop Spinal Cord Stimulator

Closed-loop spinal cord stimulations use the patient's neural response to electrical stimulation (Evoked Compound Action Potential or ECAP) in a feedback mechanism to provide consistent spinal cord activation. The feedback mechanism adjusts stimulation current continuously and automatically to maintain a target ECAP amplitude during physiological changes and movement. By maintaining the neural response within a narrow range, abrupt changes in stimulation (over or under stimulation) resulting from the movement of the electrode with respect to the spinal cord during physiological changes and movement are minimized. (1)

The Evoke Spinal Cord Stimulation System from Saluda Medical is designed to operate in either of two modes: ECAP-controlled closed-loop stimulation mode, or open-loop (fixed-output) stimulation mode. The open-loop stimulation mode is equivalent to other commercially available SCS systems but has an additional feature to measure ECAPs. The Evoke System has the ability to measure ECAPs following every stimulation pulse from two electrodes not involved in stimulation. The recorded ECAP signal is sampled by the stimulator and processed to allow measurement of the ECAP amplitude. ECAP measurement may be performed in either stimulation mode. Additionally, the Evoke System can use ECAPs in a feedback mechanism to deliver closed-loop stimulation. The feedback mechanism minimizes the difference between the measured ECAP amplitude and the ECAP amplitude target (set by the clinician and adjusted by the patient using the pocket console) by automatically adjusting the stimulation current for every stimulus. In doing so, it maintains spinal cord activation near the target level. (2)

The Wavegate StimuLux™ System (Wavegate Corp.) is another closed-loop system; however, it has not yet received clearance for marketing from the U.S. Food and Drug Administration.

Regulatory Status

A large number of neurostimulator devices have been approved by the FDA through the 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 SCS devices.

Table 1. Premarket Approval Information for Spinal Cord and Dorsal Root Ganglion Stimulator Devices

Device	Manufacturer	Product code	Original clearance/ approval date	Original PMA number	Indication
Algovita SCS System	Nuvectra Corporation	LGW	Nov 2015	P130028	Chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with failed back surgery syndrome, intractable LBP, and leg pain.
Axium (1st generation) and Proclaim DRG (2nd generation)	Abbott Medical	PMP	Feb 2016	P150004	Moderate to severe chronic intractable pain of the lower limbs in adult

Neurostimulator System					patients with Types I and II CRPS.
Cordis Programmable Neural Stimulator Models 900a	Cordis Corporation	LGW	Apr 1981[a]	P800040	Stimulator, spinal-cord, totally implanted for pain relief
Freedom SCS	Stimwave Technologies	GZB	Aug 2016	K180981	Chronic, intractable pain of the trunk and/or lower limbs, including unilateral or bilateral pain
Genesis And Eon Family Neurostimulation (Ipg) System; Eterna Spinal Cord Stimulation (SCS) System;Prodigy, Proclaim, and Proclaim XR Spinal Cord Stimulation (SCS) Systems	St. Jude Medical/ Abbott Medical	LGW; QRB	Nov 2001	P010032	Chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome, intractable LBP and leg pain, and diabetic peripheral neuropathy of the lower extremities.
Restore, Itrel, Synergy, Intellis, And Vanta Spinal Cord Stimulation Systems	Medtronic Neuromodulation	LGW	Nov 1984	P840001	Chronic, intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following conditions: • FBS or low back syndrome or failed back • Radicular pain syndrome or radiculopathies resulting in pain secondary to FBS or herniated disk • Postlaminectomy pain

					• Multiple back operations • Unsuccessful disk surgery • Refractory DDD/ herniated disk pain • Peripheral causalgia • Epidural fibrosis • Arachnoiditis or lumbar adhesive arachnoiditis • CRPS, RSD, or causalgia • Diabetic peripheral neuropathy of the lower extremities
Precision SCS Systems	Boston Scientific Corporation	LGW	Apr 2004	P030017	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
Evoke SCS System	Saluda Medical Pty Ltd	LGW	Feb 2022	P190002	Chronic intractable pain of the trunk and/or limbs including unilateral or bilateral pain associated with the following: failed back surgery syndrome, intractable LBP and leg pain.
Senza SCS System	Nevro Corporation	LGW	May 2015	P130022	Chronic intractable pain of the trunk

					and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome, intractable LBP, and leg pain When programmed to include a frequency of 10 kHz: Chronic intractable pain of the lower limbs, 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	GZB	Mar 2019	K183047	Chronic, intractable pain of the trunk and/or limbs, including unilateral or bilateral pain
Prospera Spinal Cord Stimulation (SCS) System	Biotronik NRO, Inc	LGW	Mar 2023	P210037	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; and 11) CRPS, RSD, or causalgia.

CRPS: complex regional pain syndrome; DDD: Degenerative Disk Disease; FBS: failed back syndrome; PMA: premarket approval; RSD: Reflex Sympathetic Dystrophy; SCS spinal cord stimulation; LBP: low back pain.

[a] Withdrawn in 2016. (3)

In September 2020, the FDA released a letter to healthcare providers reminding them to conduct a trial stimulation period before implanting a spinal cord stimulator as the agency continues to receive reports of serious adverse effects associated with these devices. (4) Between July 27, 2016, and July 27, 2020, the FDA received 107,728 medical device reports related to spinal cord simulators intended for pain including 497 associated with patient death, 77,937 with patient injury, and 29,924 with device malfunction. The most frequently reported patient problem codes were inadequate pain relief (28.1%), pain (15.2%), unexpected therapeutic effects (10.9%), infection (7.5%), and discomfort (5.9%). Additionally, the most frequently reported device problem codes were charging problems (11.2%), impedance (10.6%), migration (7.2%), battery problem (6.4%), and premature discharge of battery (4.2%). 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.

Rationale

This medical policy was created in 1999 and has been updated regularly with searches of the PubMed database. The most recent literature update was performed through February 27, 2024.

Medical policies 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 (QOL), and ability to function–including benefits and harms. Every clinical condition has specific outcomes that are important to patients 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, two domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one 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. Randomized controlled trials 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 policy.

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, 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 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 patients 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 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. (5) The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials 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). (6, 7)

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

Domain	Outcome Measure	Description	Clinically Meaningful Difference
Pain intensity			
	• Numeric rating scale	Rating of pain intensity on a scale of 0 (no pain) to 10 (pain	• Minimally important: 10%-20% decrease

	• Verbal rating scale • Visual analog scale	as bad as you can imagine) or from 0 to 10 cm	• Moderately important: ≥ 30% decrease • Substantial: ≥50% decrease (7)
Physical functioning			
	Disease-specific	***Measures of the interference of pain with physical functioning***	
	• Multidimensional Pain Inventory (8) Interference Scale	• 60 items, self-report • 12 subscales: interference, support, pain severity, self-control, negative mood, punishing responses, solicitous responses, 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	• ≥0.6-point decrease (7)
	• Brief Pain Inventory (9) 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 (7)
		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,	

	• Oswestry Disability Index (10)	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 (11)
	General	***Generic measure of physical functioning***	
	• 36-Item Short Form Health Survey	Measures 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 • Physical Component Summary and Mental Component Summary scores are aggregate scores that can be calculated • Higher scores indicate better health status	• 5-10 points (12-14)
Emotional functioning			
	• Beck Depression Inventory (15)	• 21 items, self-report • Measures severity of current symptoms of depressive disorders • Scores range from 0 to 63	• ≥ 5-point decrease (7)
	• Profile of Mood States (16)	• 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 (7)
Global rating of improvement			

	• Patient Global Impression of Change	• 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 (7)

Adverse events can either be hardware-related or 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

Systematic Reviews

Numerous systematic reviews have been conducted assessing the effectiveness of SCS for a variety of chronic pain conditions, including CRPS (17, 18), spinal pain (19, 20), failed back surgery syndrome (23), painful diabetic neuropathy (22-26), and mixed chronic pain conditions. (27, 28) However, these reviews only included a subset of the RCTs of standard SCS; evidence from the relevant individual RCTs is discussed in the next section.

Randomized Controlled Trials

Seven RCTs (in 12 publications) (29-38) (N=range, 36-218 patients) have evaluated SCS for various chronic pain conditions (Tables 3A and 3B). Patient populations had failed back surgery syndrome, diabetic neuropathy, and CRPS. The comparators were primarily conventional medical management, although 1 RCT compared SCS with reoperation for failed back surgery syndrome, another compared SCS 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. (32) Consistent with clinical practice, RCTs included a trial period of SCS, usually a few days to a week. Patients not reporting improvement in pain during the trial period did not continue receiving SCS 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 SCS (SCS range, 39%-63% vs comparator range, 5%-12%). Outcomes measuring the reduction in analgesic use were consistently numerically larger for SCS, but not statistically significant in all studies. Four of the five studies did not report differences in functional, quality of life (QOL), 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) (35) reported a dural puncture headache ending in death. Two studies reported longer-term results for both treatment groups. In each, results continued to favor SCS at 2 years, but for 1 with 5 years of follow-up, results were not statistically significant at 5 years.

Table 3A. Characteristics and Result of RCTs Using Standard Spinal Cord Stimulation

Study	Population	Interventions	N at Baseline and Follow-Up
North et al. (2005) (29)	FBSS	• SCS + CMM • Reoperation + CMM	N=60 n at 6 mo=49
Kumar et al. (2007, 2008) (30, 31)	FBSS with neuropathic pain	• SCS + CMM • CMM	N=100 n at 6 mo=93
			N at 24 mo=87
Kemler et al. (2000, 2004, 2008) (32-34)	CRPS	• SCS + PT • PT	N=54 n at 6 mo=54
			n at 5 y=44
Slangen et al. (2014) (35); Zuidema et al. (2022) (39)	Diabetic neuropathy of LEs	• SCS • CMM	N=36 n at 6 mo=36
			n at 24 mo=17[a] n at 8 to 10 y=19[a]
De Vos et al. (2014) (36); Duarte et al. (2016) (37)	Diabetic neuropathy of LEs	• SCS • CMM	N=60 n at 6 mo=54
Rigoard et al. (2019) (38)	FBSS	• SCS + CMM • CMM	N=218 n at 6 mo=116
Mekhail et al. (2020) (40); Mekahil et al. (2023) (41)	Chronic, intractable pain of the back and legs	• Open loop SCS • Closed loop SCS	N=125 n at 12 mo=118

CMM: conventional medical management; CRPS: complex regional pain syndrome; FBSS: failed back surgery syndrome; LE: lower extremities; mo: month(s); N: total number; n: number; PT: physical therapy; RCT: randomized controlled trial; SCS: spinal cord stimulation; VAS: visual analog scale.
[a] SCS only.

Table 3B. Characteristics and Result of RCTs Using Standard Spinal Cord Stimulation

Study	Results				Complications
	Outcomes Measures	*Intervention*	*Ctrl*	*p*	
North et al. (2005) (29)	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) (30, 31)	6 mo (SCS vs. CMM)				32% device-related complications (electrode migration, 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	
	24 mo (SCS vs. CMM)				
	• 50% reduction in leg pain on VAS	37%	2%	.003	
Kemler et al. (2000, 2004, 2008) (32-34)	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)				
	• Reduction in VAS pain score	2.1	0.0	<.001	
	• Much improved GPE	43%	6%	.001	
	5 y (SCS vs. PT)				
	• Reduction in VAS pain score	1.7	1.0	.25	
Slangen et al. (2014) (35); Zuidema et al. (2022) (39)	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				
	2 y (SCS only)				

	• Success	65%			
	• No improvement in health utility vs. baseline				
	• ~5-point improvement in SF-36 PCS score vs. baseline				
	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) (36); Duarte et al. (2016) (37)	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 et al. (2019) (38)	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 et al. (2020) (40); Mekahil et al. (2023) (41)	12 mo				
	• 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; ctrl: control; GPE: global perceived effect; HRQOL: health-related quality of life; Int: intervention; LE: lower extremities; mo: month(s); 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; vs: versus.

Uncontrolled studies

Because RCT data are available for SCS, 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. (42) 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 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. (43) 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 SCS for the treatment of chronic back and limb pain. (44) Reviewers identified 5 studies of burst SCS 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 American Academy of Neurology criteria, reviewers originally rated four studies as class III and one study as class IV. However, given the small sample sizes and short durations of follow-up of the four studies, all were downgraded to class IV. Overall, the level of confidence in the evidence on burst SCS for treating chronic pain without paresthesia was rated as "very low."

Randomized Controlled Trials

Eight RCTs with sample sizes ranging from 12 to 269 patients were identified, 5 of which were conducted in Europe and the other in the United States (Table 4). The trials by De Ridder et al. (2010, 2013) (45, 46) enrolled patients with neuropathic pain, the trial by Schu et al. (2014) (47) enrolled patients with failed back surgery syndrome, Kriek et al. (2017) (48) enrolled patients with CRPS, Deer et al. (2018) (49) 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. (50). All trials compared burst stimulation with SCS. 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 SCS while De Ridder et al. (2010, 2013) and Deer et al. (2018) included patients not previously treated with SCS. It was not clear in Kriek et al. (2017) whether patients had previously received SCS. Results were reported for 1 week of stimulation in Schu et al. (2014) and De Ridder et al. (2013), after two, 1-hour sessions of SCS 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 SCS; Kriek et al. (2017) did not report less pain for SCS at any frequency compared with burst. In Kriek et al. (2017), 48% of patients preferred the 40-Hz SCS compared with 21%, 14%, 14%, and

3% that preferred 500-Hz SCS, 1200-Hz SCS, and burst and sham, respectively. In Eldabe et al. (2020), the mean reduction in pain with 500-Hz SCS was significantly greater than that seen with sham (25%; 95% confidence interval [CI], 8%-38%; p=0.008) or burst (28%; 95% CI, 13%-41%; p=0.002), with no significant differences in pain VAS for burst versus sham (p=0.59). The interpretation of five 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). (49) SUNBURST was a 12-week, multicenter, randomized, unblinded, crossover, non-inferiority trial evaluating traditional SCS or burst stimulation in 100 patients with chronic pain of the trunk and/or limbs enrolled between January 2014 and May 2015. Patients were SCS-naive and completed a trial stimulation period. Forty-five patients were randomized to SCS then burst, and the remaining 55 were randomized to burst then SCS. At the end of the second crossover period, patients were allowed to choose the stimulation mode they preferred and were followed for one 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 non-inferiority 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 SCS was -5.1 mm (95% upper CI, -1.14 mm), demonstrating non-inferiority (p<0.001) and superiority (p<0.017). 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 SCS. 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=0.230). Patients were asked to rate their satisfaction levels for both periods: 78% were satisfied with both SCS and burst, 4% were dissatisfied with both SCS and burst, 7% were satisfied with SCS but not burst, and 10% were satisfied with burst but not SCS. However, more patients (70.8%) reported preferring burst stimulation over SCS 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 Results of RCTs Using Burst Spinal Cord Stimulation

Study	**Population**	**Interventions**	**N at Baseline and FU**	**Results**				**Complications**
3×3 crossover design without washout				*Outcome Measures*	*Burst*	*SCS*	*Sham*	

Schu et al. (2014) (47)	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	
De Ridder et al. (2013) (45)	Neuro-pathic limb pain	• Burst stimulation • SCS • No stimulation (sham-control)	N=15 n=15	1 wk (burst vs SCS vs sham)[a]				Not reported
				• Mean improve-ment 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) (46)	Neuro-pathic pain	• Burst stimulation • SCS	N=12 n= unclear	Two 1-h sessions (burst vs SCS)[b]				Not reported
				• Mean improve-ment in VAS scores: ○ Axial pain	5.3	1.8		
				○ Limb pain	7.3	4.4		
				• Improve-ment in SF-MPQ sensory scores	16.7	8.6		
				• Improve-ment in SF-MPQ affective scores	6.7	4.3		
Deer et al. (2018) (49)	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); 21 SAEs in total; 158 total adverse events in 67 patients
				• Mean VAS scores at end of period, favoring burst	Diff = -5.1 mm (non-inferiority) p<0.001			

				Responder (≥30% improve-ment in VAS score)	60%	51%		
Hara et al. (2022) (51)	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) (48)	CRPS	• Burst stimulation • SCS 40 Hz • SCS 500 Hz • SCS 1200 Hz • No simulation (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 satisfied] to 1 [not at all satisfied])	4.7	5.3[c]	3.5	
3×3 crossover design with washout								
				2 wk treatment phase				Increased pain was the most commonly

Eldabe et al. (2020) (50)	Chronic back and leg pain	• Burst stimulation • SCS 500 Hz • Sham	N=19 n=16	(burst vs. SCS at 500 Hz vs. sham); each treatment phase included a washout of 9 days				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) (52)	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; 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, wk: week; vs: versus.

[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 patients with refractory pain due to failed back surgery syndrome, CRPS, or diabetic neuropathy. RCTs were heterogenous 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 six 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. 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 patients. 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 VAS score (at 12 weeks). The proportion of patients whose global impression was improved (minimally, moderately, or very much improved) was approximately 74% in both groups. Seventy-eight percent of patients 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 patients (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 policy.

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, 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 compared with standard SCS.

Comparators

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

Outcomes
The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials 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. (5) The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials 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). (6, 7)

Adverse events can either be hardware-related or 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.

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.

Systematic Reviews
Bicket et al. (2016) published a systematic review of controlled trials on high-frequency SCS. (53) Reviewers searched for RCTs and controlled nonrandomized studies of adults with pain for at least 3 months who were treated with high-frequency SCS (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] [54]) was not rated as having a high-risk of bias in any domain, and the other (Kapural et al. [2015] [55]) 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 addressed high-frequency SCS (Tables 5A and 5B): Perruchoud et al. (2013) (54) compared high-frequency SCS (5000 Hz) with sham-control in a crossover design (N=40), Petersen et al. (2021) (56) compared high-frequency SCS plus medical management with medical management alone, while Kapural et al. (2015) (N=198) (55), Bolash et al. (2019)

(N=99) (57), and De Andres et al. (2017) (N=60) (58) compared high-frequency SCS (10,000 Hz) with standard SCS. All 6 trials are summarized in Table 5. The trials with N>100 are described individually.

Petersen et al. (2021) (56) 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 SCS plus conventional medical management (n=113) versus conventional medical management alone (n=103). All participants were randomized to high-frequency SCS 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 SCS 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 SCS plus medical management versus medical management alone. (59) Limitations of the study include a lack of blinding for participants and investigators.

Kapural et al. (2015, 2016) (55, 60) included 198 patients with chronic leg and back pain who had received conventional medical management but not SCS. Kapural et al. (2015) included an active, but unblinded, comparator (standard SCS) and included a trial SCS 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 SCS group was similar to previous trials of SCS, 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 SCS than with SCS 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 non-responders during the stimulation trial period were excluded from statistical analysis. Instead, assuming patients who were not implanted were non-responders corresponds to response rates at 3 months of about 75% in high-frequency SCS and 37% in SCS for back pain and 74% and 46% for leg pain (calculated, data not shown).

Kapural et al. (2022) (61) 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 5A. Characteristics and Results of RCTs Using High-Frequency Spinal Cord Stimulation

Study	Population	Interventions	N at Baseline and Follow-Up	Results			
				Outcomes Measure	*Int*	*Ctrl*	*p*
Perruchoud et al. (2013) (54)	Chronic LBP radiating in 1 or both legs; previously treated with SCS	• HFSCS • Sham • 2x2 crossover design with conventional SCS before both arms	• N=40 • n=33	2 wk (HFSCS vs. sham)			
				• 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, 2022, 2023) (56, 62, 63)	Painful diabetic neuropathy	• HFSCS + medical management • Medical management	N=216 n at 6 mo= 187	6 mo (HFSCS + medical management vs. medical management)			
				• Responder (proportion with ≥50% change in VAS without a meaningful worsening of baseline neurological deficits)	86%	5%	<.0001
				• Remitter (proportion with pain VAS ≤3 cm for 6 consecutive months)	60%	1%	<.001

				• Quality of life (EQ-5D-5L Index, mean change from baseline)	0.130 (SD .159)	-.031 (SD .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)		
			n=142 HFSCS and crossovers	• Responder (proportion with ≥50% change in VAS)	90%		
Kapural et al. (2015, 2016) (55, 60)	Chronic back and leg pain	• HFSCS • SCS	N=198 n at 3 mo =171 n at 24 mo=156	3 mo (HFSCS vs. SCS)			
				• 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 ○ Back pain	77%	49%	<.001
				○ Leg pain	73%	49%	<.001
De Andes et al. (2017) (58)	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	
				Improvement in NRS score	6.1	5.9	.56
				Improvement in ODI score	23.0	22.1	.96
Bolash et al. (2019) (57)	FBSS	HFSCS SCS	N=99 n=72 analyzed	6 mo (HFSCS vs SCS)			
				Responder (≥50% reduction VAS for back pain)	92%	82%	Non-inferio-rity <.001
				Remission (VAS for back pain of ≤25 mm)	84%	47%	
Kapural et al. (2022) (61); Patel et al. (2023) (64)	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 (.14)	0.004 (.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 (.13)	-0.04 (.14)	<.001
			N=98	24 mo (HFSCS only)			
				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; mo: month(s); N: total number; n: number; NR: not reported; NRS: numeric rating scale; ODI: Oswestry Disability Index; SCS: spinal cord stimulation; VAS: visual analog scale; RCT: randomized controlled trial; yr: year(s); LBP: low back pain.
[a] Despite the responder criteria being stated to be the primary outcome, the results for this outcome were not reported.

Table 5B. Characteristics and Results of RCTs Using High-Frequency Spinal Cord Stimulation

Study	Complications
Perruchoud et al. (2013) (54)	One patient had malaise attributed to a vasovagal attack
Petersen et al. (2021, 2022, 2023) (56, 62, 63)	• SAEs, 12% vs. 0% • Wound complications (dehiscence, impaired healing, or infection): 6% vs. 0%
Kapural et al. (2015, 2016) (55, 60)	• Stimulation discomfort, 0% vs. 47% • No stimulated-rated SAEs or neurologic deficits
De Andes et al. (2017) (58)	-
Bolash et al. (2019) (57)	-
Kapural et al. (2022) (61); Patel et al. (2023) (64)	-

SAE: serious adverse events; RCT: randomized controlled trial.

Case Series

Because RCT data are available for HFSCS, case series are discussed if they add information not available from the RCTs (e.g., longer follow-up, data on an important subgroup). Al-Kaisy et al. (2017) reported 36-month results for 20 patients with chronic low back pain without previous spinal surgery who were treated with 10-kHz HFSCS. (65) Seventeen patients completed the 36-month follow-up; 1 patient died (unrelated to study treatment), 1 patient was explanted due to lack of efficacy, and 1 patient had new leg pain. Among patients analyzed, the mean VAS score for pain intensity decreased from 79 to 10 mm ($p<0.001$) and the mean ODI score decreased from 53 to 20 ($p<0.001$). At baseline, 90% of the patients were using opioids compared with 12% at 36 months.

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, RCTs, and a case series. Two RCTs that enrolled participants not previously treated with SCS reported clinically and statistically significant benefits associated with HFSCS. A crossover RCT enrolling patients 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.

Closed-loop Spinal Cord Stimulation (Evoke® Spinal Cord Stimulation System)
In 2018 Russo et al. published the preliminary results of the Avalon study on the Evoke® Spinal Cord Stimulation System (Evoke System). (66) Safety and effectiveness of the closed-loop system was evaluated through six-months post-implantation. Ratings of pain (100-mm visual analogue scale [VAS] and Brief Pain Instrument [BPI]), quality of life (EuroQol instrument [EQ-5D-5L]), function (Oswestry Disability Index [ODI]), and sleep (Pittsburgh Sleep Quality Index [PSQI]) were collected at baseline and repeated three and six months after implantation. A total of 51 individuals underwent a trial procedure and permanent implants were placed in 36 individuals. The proportion of subjects with ≥50% relief was 92.6% (back) and 91.3% (leg) at three months, and 85.7% (back) and 82.6% (leg) at six months. The proportion with ≥80% pain relief was 70.4% (back) and 56.5% (leg) at three months, and 64.3% (back) and 60.9% (leg) at six months. Statistically significant improvements in mean BPI, EQ-5D-5L, ODI, and PSQI were also observed at both time points. The majority of subjects experienced profound pain relief at three and six months, providing preliminary evidence for the effectiveness of the closed-loop SCS system. The exact mechanism of action for these outcomes is still being explored, although one likely hypothesis holds that evoked compound action potential (ECAP) feedback control may minimize recruitment of Aβ nociceptors and Aδ fibers during daily use of SCS.

Russo et al. (2020) published the 12-month results of the prospective, multicenter, open-label Avalon study. (67) Fifty patients with lower back and/or leg pain who were successfully trialed received a permanent system (Evoke; Saluda Medical, Sydney, Australia). Ratings of pain (visual analog scale), quality of life, function, sleep, and medication use were collected at baseline and at each visit. Spinal cord (SC) activation levels were reported in summary statistics. The therapeutic window for each individual patient was defined as the range of ECAP amplitudes between sensation threshold and uncomfortably strong stimulation. At 12 mo., the proportion of patients with ≥50% relief was 76.9% (back), 79.3% (leg), and 81.4% (overall), and the proportion with ≥80% pain relief was 56.4% (back), 58.6% (leg), and 53.5% (overall). Patients spent a median of 84.9% of their time with stimulation in their therapeutic window, and 68.8% (22/32) eliminated or reduced their opioid intake. Statistically significant improvements in secondary outcomes were observed. The majority of patients experienced more than 80% pain relief with stable SC activation, as measured by ECAP amplitude at 12 mo., providing evidence for the long-term effectiveness of the Evoke closed-loop SCS system. The 12-mo results from the Avalon study show the highest degree of pain relief recorded for an SCS system to date. The authors postulate that the stable level of SC activation is the main factor contributing to achieving this profound level of pain relief. To further test this hypothesis, the Avalon study was extended to a follow-up of 24 mo. for consenting patients. Additionally, the Evoke SCS system is currently being evaluated in a randomized, controlled, double-blind study in the United States,

comparing the safety and efficacy of open-loop SCS to closed-loop SCS utilizing ECAP measurements.

Brooker et al. published the final results of the Avalon study in 2021. Fifty patients implanted with the Evoke system were followed for 24-months. (68) Pain, QOL, function, sleep, and medication use were collected at baseline and each scheduled visit. ECAP amplitudes and programming adjustments were also monitored. At 24 months, responder rates (≥ 50% pain reduction) and high responder rates (≥ 80% pain reduction) for overall pain were 89.5% and 68.4%, respectively, the latter up from 42.2% at 3 months. Significant improvements from baseline were observed in QOL, function, and sleep over the 24 months, including ≥ 80% experiencing a minimally important difference in QOL and > 50% experiencing a clinically significant improvement in sleep. At 24 months, 82.8% of patients with baseline opioid use eliminated or reduced their opioid intake. Over the course of the study, reprogramming need fell to an average of less than once a year. Over a 24-month period, the Evoke closed-loop SCS maintained its therapeutic efficacy despite a marked reduction in opioid use and steady decrease in the need for reprogramming. Despite promising results, the authors felt ongoing research using a larger patient pool will investigate whether the degree of pain relief correlates with the degree of improvements in wellbeing when using the Evoke closed-loop SCS system.

Mekhail et al. (2020) randomly assigned (1:1) 134 individuals in a multicenter, double-blind, parallel-arm randomized controlled trial (Evoke) to receive either ECAP-controlled closed-loop SCS (investigational group) or fixed-output, open-loop SCS (control group). (69) Randomization was computer generated, and patients, investigators, and site staff were masked to the treatment assignment. Patients with chronic, intractable pain of the back and legs (Visual Analog Scale [VAS] pain score ≥60 mm; Oswestry Disability Index [ODI] score 41-80) who were refractory to conservative therapy, on stable pain medications, had no previous experience with spinal cord stimulation, and were appropriate candidates for a spinal cord stimulation trial were screened. The primary outcome was the proportion of patients with a reduction of 50% or more in overall back and leg pain with no increase in pain medications. The intention-to-treat analysis comprised 125 patients at 3 months (62 in the closed-loop group and 63 in the open-loop group) and 118 patients at 12 months (59 in the closed-loop group and 59 in the open-loop group). The primary outcome was achieved in a greater proportion of patients in the closed-loop group than in the open-loop group at 3 months (51 [82·3%] of 62 patients vs 38 [60·3%] of 63 patients; difference 21·9%, 95% CI 6·6-37·3; p=0·0052) and at 12 months (49 [83·1%] of 59 patients vs 36 [61·0%] of 59 patients; difference 22·0%, 6·3-37·7; p=0·0060). There were no observed differences in safety profiles between the two groups. The most frequently reported study-related adverse events in both groups were lead migration (nine [7%] patients), implantable pulse generator pocket pain (five [4%]), and muscle spasm or cramp (three [2%]). ECAP-controlled closed-loop stimulation provided significantly greater and more clinically meaningful pain relief up to 12 months than open-loop spinal cord stimulation. Greater spinal cord activation seen in the closed-loop group suggests a mechanistic explanation for the superior results, which aligns with the putative mechanism of action for spinal cord stimulation and warrants further investigation.

Thirty-six-month follow-up data of the Evoke trial was published by Mekhail et al. in 2022. (70) At 24 months, significantly more closed-loop than open-loop patients were responders (≥50% reduction) in overall pain (53 of 67 [79.1%] in the closed-loop group; 36 of 67 [53.7%] in the open-loop group; difference, 25.4% [95% CI, 10.0%-40.8%]; P = .001). There was no difference in safety profiles between groups (difference in rate of study-related adverse events: 6.0 [95% CI, −7.8 to 19.7]). Improvements were also observed in health-related quality of life, physical and emotional functioning, and sleep, in parallel with opioid reduction or elimination. Objective neurophysiological measurements substantiated the clinical outcomes and provided evidence of activation of inhibitory pain mechanisms. ECAP-controlled, closed-loop SCS, which elicited a more consistent neural response, was associated with sustained superior pain relief at 24 months, consistent with the 3- and 12-month outcomes.

Dorsal Root Ganglion Neurostimulation for Refractory Chronic Trunk or Limb Pain

Clinical Context and Therapy Purpose

The purpose of dorsal root ganglion (DRG) neurostimulation 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 policy.

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, CRPS (i.e., reflex sympathetic dystrophy), arachnoiditis, radiculopathies, phantom limb/stump pain, peripheral neuropathy, and painful diabetic neuropathy.

Interventions

The therapy being considered is DRG neurostimulation. DRG uses the same epidural approach technique as SCS but targets a different anatomical target, the DRG. 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. DRG 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 patients with treatment-refractory chronic pain of the trunk or limbs: standard SCS, medical therapy, or surgical therapy.

Outcomes

The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials 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. (5) The Initiative on Methods, Measurement, and Pain Assessment in Clinical

Trials 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). (6, 7)

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.

Dorsal Root Ganglion Implanted Device

Systematic Reviews

Several systematic reviews of dorsal root ganglion devices have been published: Vuka et al. (2019) (71), Deer et al. (2020) (72), Moman et al. (2022) (73), and D'Souza et al. (2022) (74). 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 DRG neurostimulation with standard SCS. (75, 76) 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 DRG stimulation with the Axium device or standard SCS. Patients first underwent a temporary trial of stimulation lasting 3 to 30 days, depending on the protocol at each site. Patients who had 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 DRG, n=54 SCS) 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) 50% or greater reduction in VAS score and: 2) no stimulation-related neurologic deficits. The non-inferiority margin was set at 10%. Results are shown in Table 7. No patients experienced neurologic deficits in either group. Regarding paresthesia, at 3 months and 12 months, SCS patients were significantly more likely to report paresthesia in nonpainful areas than DRG patients. At 3 months, 84.7% of DRG patients and 65% of SCS patients reported paresthesia 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 DRG neurostimulation in the ACCURATE study, to evaluate the occurrence and risk factors for paresthesia. (77) Among the 61 patients with DRG 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 Dorsal Root Ganglion Implanted Devices

Study	Countries	Sites	Dates	Participants	Interventions	
					DRG	SCS
Deer et al. (2017) (75); ACCURATE (NCT01923285)	U.S.	22	2013-2016	• CRPS or causal lower extremities • Chronic pain (6 mo) • Stimulation-naïve • Failed ≥2 pharmacologic treatments	AXIUM Neurostimulator System (n=76)	RestoreUltra and RestoreSensor (n=76)

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; mo: month; n: number; SCS: spinal cord stimulation; RCT: randomized controlled trial.

Table 7. RCT Results of Dorsal Root Ganglion 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) (75)						
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 (non-inferiority p<0.001; superiority p<0.001)	1.1 (0.2 to 2.1) (<0.05 favoring DRG)	NR (0.04 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 (non-inferiority p<0.001; superiority p<0.001)	1.3 (0.2 to 2.3) (<0.05 favoring DRG)	NR (<0.001)	3.5 (-0.1 to 7.1) (0.04 favoring DRG)	2.6 (-1.9 to 7.1)	NR (0.62)

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) (75)					

DRG: dorsal root ganglion; RCT: randomized controlled trial.

The study limitations stated in this table are those notable in the current literature 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.

[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[a]	Blinding[b]	Selective Reporting[c]	Follow-Up[d]	Power[e]	Statistical[f]
Deer et al. (2017) (75)		1, 2. Patients and study staff not blinded. Outcomes mostly patient reported which could lead to bias. However, an				4. Treatment effects not reported for some outcomes but p values reported

		active control (SCS) was used.				

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 literature 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. (78) 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. (79) 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). (80) 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%-50% reduction), and 2 patients reported poor or no overall pain relief (0%-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 DRG neurostimulators in patients with chronic trunk and/or limb pain. The RCT (N=152) found that patients receiving DRG neurostimulation 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, DRG neurostimulation was found to be non-inferior to SCS in percentage achieving ≥50% pain reduction, emotional functioning score, and SF-36 scores. Both groups experienced paresthesia, but patients in the DRG group reported less postural variation in paresthesia and reduced extraneous stimulation in non-painful areas. Patients in the DRG group 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 policy.

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 patients 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 patients as a technique to relieve pain and decrease the incidence of amputation.

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

Outcomes
The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials 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. (5) The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials 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). (6, 7)

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.

Systematic Reviews
An updated Cochrane review by Ubbink and Vermeulen (2013) assessed the use of SCS in peripheral vascular diseases. (81) Reviews included RCTs and non-RCTs evaluating the efficacy of SCS in adults with non-reconstructable, chronic critical leg ischemia. Six trials were identified; all were conducted in Europe and 5 were single-country studies. SCS was compared with other nonsurgical interventions. One study was not randomized, and none was blinded. In a pooled analysis of data from all 6 studies, there was a significantly higher rate of limb survival in the SCS group than in the control group at 12 months (RR, 0.75; 95% Cl, 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% Cl, 0.58 to 1.04; absolute risk difference, -0.09; 95% CI, -0.19 to 0.01). The SCS 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 SCS to treat patients with critical limb ischemia. (82) 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 the control groups. The RR of amputation was 0.79 (95% Cl, 0.59 to 1.06), with a risk difference of -0.07 (95% Cl, -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. (83) 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 SCS.

A systematic review of non-revascularization-based treatments by Abu Dabrh et al. (2015) for patients with critical limb ischemia included SCS as one of the treatments. The review identified 5 RCTs for inclusion. (84) In pooled analysis, reviewers found that SCS 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 SCS with usual care have assessed patients with critical limb ischemia. In pooled analyses from 3 systematic reviews, SCS 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 SCS 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, or cancer-related 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 policy.

Populations

The relevant populations of interest are individuals with treatment-refractory angina pectoris, heart failure, or cancer-related pain.

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.

Outcomes

The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials 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. (5) The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials 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). (6, 7)

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.

Refractory Angina Pectoris

Systematic Reviews

Pan et al. (2017) identified 12 RCTs that evaluated SCS versus control in patients with refractory angina pectoris. (85) 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). (86) It included 9 RCTs evaluating SCS for refractory angina: 7 compared SCS with low or no stimulation and 2 compared SCS 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: "two 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 2-3)." Most trials comparing SCS with low or no stimulation found improvements in outcomes with SCS; however, given limitations in the evidence base, reviewers concluded that larger multicenter RCTs would be needed to assess the efficacy of SCS for angina.

Randomized Controlled Trials
Two of the largest RCTs included in the systematic reviews were Zipes et al. (2012) (87) and Lanza et al. (2011). (88)

Zipes et al. (2012) published an industry-sponsored, single-blind, multicenter trial with sites in the United States and Canada. (87) 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 SCS 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=0.81). 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: SCS with standard stimulation (n=10), SCS with low-level stimulation (75%-80% of the sensory threshold) (n=7), or very low-intensity SCS (n=8). (88) 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 one 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=0.002). Nonsignificant variables included the use of nitroglycerin, QOL, 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. (89) 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 SCS 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

Randomized Controlled Trials

Findings of a small pilot crossover RCT evaluating SCS for heart failure were published by Torre-Amione et al. (2014). (90) Eligibility included symptomatic heart failure despite optimal medical therapy, left ventricular ejection fraction less than 30%, hospitalization or need for intravenous inotropic support in the past year, and inability to walk more than 450 meters on a 6-minute walk test. All patients had an implanted heart device. Nine patients underwent SCS implantation and received 3 months of active and 3 months of inactive (off position) treatment, in random order. There was a 1-month washout period between treatments. The primary outcome was a composite of death, hospitalization for worsening heart failure, and symptomatic bradyarrhythmia or tachyarrhythmia requiring high-voltage therapy. Four patients experienced at least one of the events in the composite endpoint. The events occurred in 2 patients while the device was turned on and in two while it was turned off. One patient died about 2 months after implantation with the device turned off. The SCS devices did not interfere with the functioning of implantable cardioverter defibrillators.

Zipes et al. (2016) reported on the results of the Determining the Feasibility of Spinal Cord Neuromodulation for the Treatment of Chronic Heart Failure (DEFEAT-HF) study, a prospective, multicenter, single-blind RCT comparing SCS using active stimulation with sham-control in patients who had New York Heart Association functional class III heart failure and a left ventricular ejection fraction of 35% or less. (91) Sixty-six patients were implanted with a SCS and randomized 3:2 to SCS on (n=42) or SCS off (sham; n=24). For the trial's primary endpoint

(change in left ventricular end-systolic volume index from baseline to 6 months), there was no significant difference between groups (p=0.30). Other endpoints related to heart failure hospitalization and heart failure-related QOL scores and symptoms did not differ significantly between groups. After completion of the 6-month randomization period, all subjects received active SCS. From baseline to 12-month follow-up, there were no significant treatment effects in the overall patient population for echocardiographic parameters (p=0.36). The trial was originally powered based on a planned enrollment of 195 implanted patients, but enrollment was stopped early due to futility. The nonsignificant difference between groups might have been the result of underpowering. However, the absence of any treatment effects or between-group differences is further suggestive of a lack of efficacy of SCS for heart failure.

Section Summary: Heart Failure

Two RCTs have evaluated SCS as a treatment for heart failure. One was a small pilot crossover trial (N=9) that reported at least 1 adverse event in 2 patients with the device turned on and in 2 patients with the device turned off. The other RCT (N=66) was sham-controlled; it did not find significant differences between groups but might have been underpowered.

Cancer-Related Pain

Systematic Reviews

A Cochrane review by Lihua et al. (2013) assessed SCS for the treatment of cancer-related pain in adults. (92) Reviewers did not identify any RCTs evaluating the efficacy of SCS 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. (93) They concluded: "Current evidence is insufficient to establish the role of SCS in treating refractory cancer-related pain."

Section Summary: Cancer-Related Pain

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

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 patients 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, quality of life, medication use, and treatment-related morbidity. Two RCTs that enrolled participants not previously treated with SCS reported clinically and statistically significant benefit associated with high-frequency SCS. Another RCT in patients 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 (DRG) neurostimulation, 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 patients receiving DRG neurostimulation 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. DRG neurostimulation 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, but patients in the DRG group reported less postural variation in paresthesia and reduced extraneous stimulation in non-painful areas. Rates of serious adverse events were similar between the two 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, quality of life, morbid events, hospitalizations, and treatment-related morbidity. In pooled analyses, SCS was associated with a lower rate 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, quality of life, 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 RCTs.

Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, morbid events, hospitalizations, and treatment-related morbidity. An RCT (N=66) comparing spinal cord stimulation using active stimulation with sham-control in patients who had New York Heart Association functional class III heart failure and a left ventricular ejection fraction of 35% or less did not find significant differences between groups but might have been underpowered to do so. The evidence is insufficient to determine that the technology results in an improvement in the net health outcomes.

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 SCS in this population were identified. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

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. (94) 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 Interventional Pain Physicians

In 2013, the American Society of Interventional Pain Physicians updated its evidence-based guidelines on interventional techniques in the management of chronic spinal pain. (95) The guidelines included a statement that there is fair evidence for the following recommendation for SCS: “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. (96) The guideline found that SCS may be considered for 1) treatment of refractory cancer pain (level 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. (97) 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. (98) The guidelines recommendations for spinal cord stimulation are summarized in Table 10.

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	1-A	Strong
Treatment of non-surgical low back pain	B	1-C	Moderate
Treatment of lumbar spinal stenosis	C	1-C	Moderate

International Association for the Study of Pain

In 2013, the International Association for the Study of Pain published recommendations on the management of neuropathic pain. (99) The Association issued recommendations on spinal cord stimulation (SCS), considered weak due to the amount and consistency of the evidence. The recommendations supported the use of SCS for failed back surgery syndrome (FBSS) and for complex regional pain syndrome (CRPS) (Table 11). In regards to high-frequency stimulation and dorsal root ganglion (DRG) stimulation, the publication states that long-term effectiveness of these techniques needs to be determined with further studies.

Table 11. International Association for the Study of Pain Recommendations for Spinal Cord Stimulation

Indication	Comments	Quality of Evidence	Strength of Recommendation
CRPS 1	Long-term benefits demonstrated, though benefits may diminish over time (in RCT, reoperation rate was 42%). May be considered for patients not responding to non-invasive treatments and sympathetic nerve blocks or for whom nerve blocks would be inappropriate.	Moderate	Weak
CRPS 2	Limited evidence	Low	Inconclusive
FBSS with radiculopathy	Based on 2 RCTs, appears to be better than reoperation and conventional medical management. However, response rates were relatively low and complication rates were relatively high.	Moderate	Weak

CRPS: complex regional pain syndrome; FBSS: failed back surgery syndrome; RCT: randomized controlled trial.

International Neuromodulation Society

The International Neuromodulation Society (2019) convened a Neuromodulation Appropriateness Consensus Committee (NACC) to develop best practices for the use of DRG stimulation for the treatment of chronic pain syndromes. (100) The NACC was comprised of experts in anesthesiology, neurosurgery, and pain medicine. The NACC performed a systematic literature search through June 2017 and identified 29 publications providing evidence for the consensus recommendations. The evidence was graded using the modified Pain Physician criteria and the U.S. Preventive Services Task Force criteria. Table 12 summarizes the consensus recommendations on the use of DRG stimulation. Additional recommendations on the DRG stimulation procedure are provided in the publication.

Table 12. NACC Consensus Recommendations for the Use of Dorsal Root Ganglion Stimulation

Recommendation	Level	Grade	Consensus
DRG stimulation should be considered primarily for patients with focal neuropathic pain syndromes with identified pathology.	I	A	Strong
DRG stimulation is recommended for CRPS type I or type II of the lower extremity.	I	A	Strong
DRG stimulation for CRPS type I or type II of the upper extremity requires more study.	II-2	A	Strong
DRG stimulation for DPN may be effective based on limited data. Since there is good evidence for SCS, the use of DRG must be justified.	III	C	Strong
Evidence for DRG stimulation for non-diabetic peripheral neuropathy is limited; use should be determined on a case-by case basis.	III	B	Moderate

Evidence for DRG stimulation for chronic postoperative surgical pain is limited; use should be determined on a case-by-case basis.	III	C	Moderate
DRG stimulation for pelvic pain should be used under strict criteria depending on mechanism of injury and visceral/somatic designation. Psychologic comorbidity is a contraindication.	III	I	Moderate
DRG stimulation for groin pain is recommended.	II-2	B	Strong
DRG stimulation is superior to standard SCS for unilateral focal pain from CRPS type I or type II of the lower extremity.	I	A	Strong
No evidence for DRG stimulation over SCS for other indications.			

CRPS: complex regional pain syndrome; DPN: diabetic peripheral neuropathy; DRG: dorsal root ganglion; GRADE: Grading of Recommendations Assessment, Development and Evaluation; NACC: Neuromodulation Appropriateness Consensus Committee; SCS: spinal cord stimulation.

National Institute for Health and Care Excellence (NICE)

In 2008, the NICE issued guidance on SCS for chronic pain of neuropathic or ischemic origin, which was reaffirmed in 2014. (101) The NICE recommended SCS as a treatment option for adults with chronic pain of neuropathic origin (measuring at least 50 mm on a 0-100 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 SCS was not recommended for chronic pain of ischemic origin except in the context of research.

Medicare National Coverage

According to Medicare policy, the implantation of central nervous system stimulators may be covered as therapies for the relief of chronic intractable pain, subject to the following conditions:

- "The implantation of the stimulator is used only as a late resort (if not a last resort) for patients with chronic intractable pain;
- With respect to item a, other treatment modalities (pharmacological, surgical, physical, or psychological therapies) have been tried and did not prove satisfactory, or are judged to be unsuitable or contraindicated for the given patient;
- Patients have undergone careful screening, evaluation, and diagnosis by a multidisciplinary team prior to implantation. (Such screening must include psychological, as well as physical evaluation);
- All the facilities, equipment, and professional and support personnel required for the proper diagnosis, treatment training, and follow-up of the patient (including that required to satisfy item c) must be available; and

- Demonstration of pain relief with a temporarily implanted electrode precedes permanent implantation." (102)

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this policy are listed in Table 13.

Table 13. Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04479787[a]	Dorsal Spinal Cord Stimulation vs Medical Management for the Treatment of Low Back Pain (DISTINCT)	270	Jan 2024
NCT05466110	sPinal coRd stimulatiOn coMpared With Lumbar InStrumEntation for Low Back Pain After Previous Lumbar Decompression (PROMISE): a Prospective Randomized Controlled Study	84	May 2025
NCT04915157	Efficacy of Spinal Cord Stimulation in Patients With Refractory Angina Pectoris; a Randomized Controlled Trial	72	Jun 2025
NCT05372822	Spinal Cord Burst Stimulation for Chronic Radicular Pain Following Lumbar Spine Surgery: A Randomized Double-blind Sham-controlled Crossover Trial	50	Aug 2025
NCT06158529	A Multicentre Clinical Study of High-frequency Electrical Spinal Cord Stimulation Versus Electrical Spinal Cord Stimulation in the Treatment of Diabetic Peripheral Neuropathic Pain	1	Dec 2025
NCT03681262	Comparing Long-Term Effectiveness of High Frequency and Burst Spinal Cord Stimulation	160	Dec 2026
Unpublished			
NCT02514590[a]	Multi-center, Prospective, Clinical Trial of Wireless Spinal Cord Stimulation in the Treatment of Chronic Pain	49	Jul 2019
NCT02093793[a]	A Randomized Controlled Study to Evaluate the Safety and Effectiveness of the Precision Spinal Cord Stimulator System Adapted for High-Rate Spinal Cord Stimulation.	383	Aug 2019
NCT02902796	Comparison of 1000 Hertz (Hz), Burst, and Standard Spinal Cord Stimulation in Chronic Pain Relief.	20	Dec 2019

NCT03014583	Prospective, Randomized Study Comparing Conventional, Burst and High Frequency (HF) Spinal Cord Stimulation (SCS) in Refractory Failed Back Surgery Syndrome (FBSS) Patients After a 32-contact Surgical Lead Implantation	28	Sep 2021
NCT03312010	A European, Prospective, Multi-Center, Double-Blind, Randomized, Controlled, Clinical Trial Investigating the Effects of High-Frequency Wireless Spinal Cord Stimulation (SCS) Over Exiting Nerve Roots in the Treatment of Chronic Back Pain	38	Dec 2022
NCT03957395	Comparison of Effectiveness of Tonic, High Frequency and Burst Spinal Cord Stimulation in Chronic Pain Syndromes: a Double-blind, Randomised, Cross-over, Placebo-Controlled Trial	50	Dec 2022

NCT: national clinical trial.

[a] Denotes industry-sponsored or cosponsored trial.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	63650, 63655, 63661, 63662, 63663, 63664, 63685, 63688, 95970, 95971, 95972, 0784T, 0785T, 0788T, 0789T
HCPCS Codes	C1767, C1778, C1787, C1816, C1820, C1822, C1826, C1883, C1897, L8679, L8680, L8685, L8686, L8687, L8688

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been changed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
11/15/2024	Document updated with literature review. Coverage unchanged. References 1, 2, 20, 26, 28, 41, 51-52, 63-64, and 102; others removed/revised.
02/01/2024	Document updated with literature review. Coverage unchanged. References 36, 37, 50, 54, 55, 65, 70, 85, 88 and 89 added; others removed.
07/01/2023	Document updated with literature review. The following change was made to Coverage: The Wavegate StimuLux™ System, Wavegate Corp. is considered experimental, investigational and/or unproven for all indications, including but not limited to, treatment of chronic leg or back pain that is refractory to conservative therapy or for individuals who are not candidates for surgery. Added references 78-82.
8/1/2022	Document updated with literature review. The following change was made to Coverage: Added "painful diabetic neuropathy" to example list of common conditions that cause severe, chronic, refractory neuropathic pain. Added references 4, 21-25, 46, 48, 53, 54 and 75; others removed.
11/1/2021	Document updated with literature review. Coverage unchanged. The following references were added: 3, 21, 41, 47, and 48; others deleted or updated.
1/15/2021	Reviewed. No changes
2/15/2020	Document updated with literature review. Coverage for dorsal root ganglion (DRG) neurostimulation was changed from experimental, investigational and/or unknown (EIU) to conditionally medically necessary. The following references were added: 1-14, 19-20, 22, 35, 37-38, 40, 44-46, 48-49, 52-58, and 77-78.
4/15/2018	Document updated with literature review. The following was added to the coverage: "Dorsal root ganglion (DRG) stimulation is considered experimental, investigational and/or unproven for the treatment of severe and chronic pain of the trunk or limbs." Title changed from Spinal Cord Stimulation (SCS).
9/15/2016	Document updated with literature review. The wording "standard or high-frequency" was added to the coverage statements as spinal cord stimulation

	device methods. In addition, heart failure was added to the listing of experimental, investigational and/or unproven indications.
5/15/2015	Reviewed. No changes.
8/15/2014	Document updated with literature review. Cancer related pain was added as an indication to the listing of experimental, investigational and/or unproven indications for spinal cord stimulation.
11/1/2012	Document updated with literature review. The following was added to coverage: “NOTE: The first three bulleted criteria (listed above) should be met to qualify for a trial electrode implantation prior to permanent SCS implantation”.
9/15/2010	Document updated with literature review. The following change was made to coverage: List of experimental, investigational and unproven indications was revised. CPT/HCPCS codes updated.
1/15/2008	Coverage Revised.
8/15/2007	Revised/Updated Entire Document.
7/15/2005	Revised/Updated Entire Document.
8/15/2003	Revised/Updated Entire Document.
5/1/2000	Revised/Updated Entire Document.
8/1/1999	New Medical Document.