7.01.25	Spinal Cord and Dorsal Root Ganglion Stimulation		
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Section:	7.0 Surgery	**Page:**	Page 1 of 46

Policy Statement

I. Spinal cord stimulation with standard or high-frequency stimulation 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 performed according to policy guidelines.

II. Dorsal root ganglion neurostimulation is 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 performed according to policy guidelines.

III. Spinal cord stimulation is considered **investigational** in all other situations including, but not limited to, treatment of critical limb ischemia to forestall amputation and treatment of refractory angina pectoris, heart failure, and cancer-related pain.

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

Candidate selection focuses on determining whether the individual is refractory to other types of treatment. The following considerations may apply.

- The treatment is used only as a last resort; other treatment modalities (pharmacologic, surgical, psychological, physical, if applicable) have failed or are judged to be unsuitable or contraindicated;
- Pain is neuropathic in nature (ie, resulting from actual damage to the peripheral nerves). Common indications include, but are not limited to, failed back surgery syndrome, complex regional pain syndrome (ie, reflex sympathetic dystrophy), arachnoiditis, radiculopathies, phantom limb/stump pain, peripheral neuropathy, and painful diabetic neuropathy. Spinal cord stimulation is generally not effective in treating nociceptive pain (resulting from irritation, not damage to the nerves) and central deafferentation pain (related to central nervous system damage from a stroke or spinal cord injury);
- No serious untreated drug habituation exists;
- Demonstration of at least 50% pain relief with a temporarily implanted electrode precedes permanent implantation;
- All the facilities, equipment, and professional and support personnel required for the proper diagnosis, treatment, and follow-up of the individual are available.

"Burst" neurostimulation is an alternate programming of a standard spinal cord stimulation device. A clinician programmer application is used to configure a standard spinal cord stimulation device to provide stimulation in "bursts" rather than at a constant ("tonic") rate.

Coding

The following HCPCS "C" code was issued for high-frequency neurostimulator generator:

- **C1822**: Generator, neurostimulator (implantable), high frequency, with rechargeable battery and charging system

The Centers for Medicare & Medicaid Services (CMS) has issued instructions that the existing implantable neurostimulator code C1820 should only be used for stimulators that are not high frequency.

Description

Spinal cord stimulation (SCS) delivers low-voltage electrical stimulation to the dorsal columns of the spinal cord to block the sensation of pain; this is achieved through a surgically implanted SCS 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.

Related Policies

- Deep Brain Stimulation

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

A large number of neurostimulator devices, some used for SCS, have been approved by the FDA through the premarket approval process. Examples of fully implantable SCS devices approved through the premarket approval process include the Cordis programmable neurostimulator (Cordis Corp.), approved in 1981; the Itrel® (Medtronic), approved in 1984; the Genesis and Eon devices (St. Jude Medical), approved in 2001; and the Precision Spinal Cord Stimulator (Advanced Bionics), approved in 2004. FDA product code: LGW.

In 2015, the Nevro Senza™ Spinal Cord Stimulator (Nevro Corp.), a totally implantable neurostimulator device, was approved by the FDA for the following indications: "chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome (FBSS), intractable low back pain, and leg pain."[15,] This device uses a higher frequency of electrical stimulation (10 kHz) than standard devices.

In February 2016, the Axium Neurostimulator System (Abbott) was approved by the FDA through the premarket approval process. This implanted device stimulates the DRG. Further, it is indicated as an aid in the management of moderate-to-severe intractable pain of the lower limbs in adults with complex regional pain syndrome types I and II.

In August 2016, the Freedom Spinal Cord Stimulator (Stimwave Technologies), a wireless injectable stimulator, was cleared for marketing by the FDA through the 510(k) process for treating chronic, intractable pain of the trunk and/or lower limbs. The Freedom device has implantable or injectable microstimulators that contain electrode(s). The microstimulators with electrodes are powered by a

wireless battery pack worn externally. The device can be placed to target the spinal cord (i.e., levels T7 to L5) or to target the dorsal root ganglion.

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.

In August 2017, the Precision™ Spinal Cord Stimulator (Boston Scientific) was approved by the FDA through the premarket approval process.

Rationale

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 (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 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 four to eight electrodes, with eight electrodes more commonly used for complex pain patterns. There are two 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 eight 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. In 2015, an SCS device, using a higher frequency (10000 Hz) than predicate devices, was approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process. High-frequency stimulation is proposed to be associated with fewer paresthesias, which are a recognized effect of SCS. In 2016, the FDA approved a clinician programmer application that allows an SCS 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 SCS 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.

The incidence of adverse events related to spinal cord stimulation have been reported to occur in 30% to 40% of cases.[1,] Adverse events can either be hardware-related or biological. Hardware-related complications include lead migration or lead failure or fracture. Biological complications include infection and pain. More severe biological complications are rare, including dural puncture headache (estimated incidence, up to 0.3%) and neurological damage (estimated incidence, 0.25%).

Other neurostimulators target the dorsal root ganglion (DRG). Dorsal root ganglia consists of sensory cell bodies that transmit input from the peripheral nervous system to the central nervous system, and play a role in neuropathic pain perception. Dorsal root ganglia are located in the epidural space between spinal nerves and the spinal cord on the posterior root in a minimal amount of cerebrospinal fluid, amenable to epidural access . Two systems targeting the DRG have received approval or clearance from the FDA.

A retrospective analysis of the FDA's Manufacturer and User Facility Device Experience (MAUDE) database provided information on complications related to the use of DRGstimulation.[2,] The MAUDE database was queried for DRG 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.

Outcome Measures

The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials group has provided recommendations for four 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.[3,] 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 (see Table 1).[4,5,]

Table 1. Health Outcome Measures Relevant to Trials of Chronic Pain

Domain	Outcome Measure	Description	Clinically Meaningful Difference
Pain intensity			
	• Numeric rating scale • Verbal rating scale • Visual analog scale	Rating of pain intensity on a scale of 0 (no pain) to 10 (pain as bad as you can imagine) or from 0 to 10 cm	• Minimally important: 10%-20% decrease • Moderately important: ≥30% decrease • Substantial: ≥50% decrease[5,]
Physical functioning			
	Disease specific	Measures of the interference of pain with physical functioning	
	• Multidimensional Pain Inventory[6,] 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	• ≥0.6-point decrease[5,]

Domain	Outcome Measure	Description	Clinically Meaningful Difference
		work, activities away from home, and social activities • Items rated on 0- to 6-point scale • Interference subscale score calculated by mean of subscale items	
	• Brief Pain Inventory[7,]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[5,]
	• Oswestry Disability Index[8,]	Measures functional impairment due to lower back pain: • 10 sections, self-report • Sections: intensity of pain, lifting, ability to care for oneself, ability to walk, ability to sit, sexual function, ability to stand, social life, sleep quality, and ability to travel • Each section is scored on a 0 to 5 scale with 5 indicating the greatest disability • Total score calculated by taking the mean of the section scores and multiplying by 100	• 10 points[9,]
General		**Generic measure of physical functioning**	
	• 36-Item Short Form Health Survey	• Measure overall health status: • 36 items, self-report • 8 domains: physical function, physical role, general health, bodily pain, mental health, social function, vitality/fatigue, and emotional role • Physical Component Summary and Mental Component Summary scores are aggregate scores that can be calculated • Higher scores indicate better health status	• 5-10 points[10,11,12,]
Emotional functioning			
	• Beck Depression Inventory[13,]	• 21 items, self-report • Measures severity of current symptoms of depressive disorders • Scores range from 0 to 63	• ≥5-point decrease[5,]

Domain	Outcome Measure	Description	Clinically Meaningful Difference
	• Profile of Mood States[14,]	• 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[5,]
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[5,]

Literature Review

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

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

Standard Spinal Cord Stimulation for Refractory Chronic Trunk or Limb Pain

Clinical Context and Therapy Purpose

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

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

Populations

The relevant population of interest is individuals with treatment-refractory chronic pain of the trunk or limbs. Examples of treatment-refractory chronic pain include failed back surgery syndrome,

complex regional pain syndrome (CRPS) (ie, reflex sympathetic dystrophy), arachnoiditis, radiculopathies, phantom limb/stump pain, peripheral neuropathy, and painful diabetic neuropathy.

Interventions

The therapy being considered is standard spinal cord stimulation alone. Spinal cord stimulation 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. Spinal cord stimulation 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 spinal cord stimulation devices operate under a frequency of 100 to 1000 Hz.

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

Comparators

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

Outcomes

The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials 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.[3,] 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).[4,5,]

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

Domain	Outcome Measure	Description	Clinically Meaningful Difference
Pain intensity			
	• Numeric rating scale • Verbal rating scale • Visual analog scale	Rating of pain intensity on a scale of 0 (no pain) to 10 (pain as bad as you can imagine) or from 0 to 10 cm	• Minimally important: 10% to 20% decrease • Moderately important: ≥ 30% decrease • Substantial: ≥50% decrease[5,]
Physical functioning			
	Disease-specific	*Measures of the interference of pain with physical functioning*	
	• Multidimensional Pain Inventory[6,] Interference Scale	• 60 items, self-report • 12 subscales: interference, support, pain severity, self-control, negative mood, punishing responses, solicitous responses, distracting responses,	• ≥0.6-point decrease[5,]

Domain	Outcome Measure	Description	Clinically Meaningful Difference
		household chores, outdoor work, activities away from home, and social activities • Items rated on 0- to 6-point scale • Interference subscale score calculated by mean of subscale items	
•	• Brief Pain Inventory[7], 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[5],
•	• Oswestry Disability Index[8],	Measures functional impairment due to lower back pain: • 10 sections, self-report • Sections: intensity of pain, lifting, ability to care for oneself, ability to walk, ability to sit, sexual function, ability to stand, social life, sleep quality, and ability to travel • Each section is scored on a 0 to 5 scale with 5 indicating the greatest disability • Total score calculated by taking the mean of the section scores and multiplying by 100	• 10 points[9],
•	*General*	*Generic measure of physical functioning*	
	• 36-Item Short Form Health Survey	Measure overall health status: • 36 items, self-report • 8 domains: physical function, physical role, general health, bodily pain, mental health, social function, vitality/fatigue, and emotional role • Physical Component Summary and Mental Component Summary scores are aggregate scores that can be calculated • Higher scores indicate better health status	• 5 to 10 points[10,11,12],
Emotional functioning			
	• Beck Depression Inventory[13],	• 21 items, self-report • Measures severity of current symptoms of depressive disorders • Scores range from 0 to 63	• ≥5-point decrease[5],

Domain	Outcome Measure	Description	Clinically Meaningful Difference
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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[5,]

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

Review of Evidence

Systematic Reviews

Numerous systematic reviews have been conducted assessing the effectiveness of spinal cord stimulation for a variety of chronic pain conditions, including CRPS [15,16,], spinal pain[17,], failed back surgery syndrome[18,], painful diabetic neuropathy,[19,20,21,22,23,]and mixed chronic pain conditions.[24,] However, these reviews only included 1 to 3 RCTs each of standard spinal cord stimulation; evidence from the relevant individual RCTs is discussed in the next section.

Randomized Controlled Trials

Six RCTs (in 10 publications)[25,26,27,28,29,30,31,32,33,34,](N=528 patients; range, 36 to 218 patients) have evaluated standard spinal cord stimulation for various chronic pain conditions (Table 3). Patient populations had failed back surgery syndrome, diabetic neuropathy, and CRPS. The comparators were primarily conventional medical management, although 1 RCT compared spinal cord stimulation with reoperation for failed back surgery syndrome, and another compared spinal cord stimulation with physical therapy. 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.[28,] Consistent with clinical practice, RCTs included a trial period of spinal cord stimulation, usually a few days to a week. Patients not reporting improvement in pain during the trial period did not continue receiving spinal cord stimulation during the remainder of follow-up. In most RCTs, these patients were included in the intention-to-treat analyses either as failures to respond or using imputation techniques. All RCTs with the responder primary outcomes reported clinically and statistically significant differences in the primary outcomes

at 6 months, favoring spinal cord stimulation (spinal cord stimulation range, 39% to 63% vs. comparator range, 5% to 12%). Outcomes measuring the reduction in analgesic use were consistently numerically larger for spinal cord stimulation, but not statistically significant in all studies. Four of the 5 studies did not report differences in functional, quality of life, or utility outcomes. Device-related complications ranged from 17% to 32%, with the most common being infection and discomfort or pain due to positioning or migration of electrodes or leads. However, 2 studies reported dural puncture headaches and Slangen et al (2014)[31,] reported a dural puncture headache ending in death. Two studies reported longer-term results for both treatment groups. In each, results continued to favor spinal cord stimulation at 2 years, but for 1 with 5 years of follow-up, results were not statistically significant at 5 years.

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

Study	Population	Interventions	N at Baseline and Follow-Up	Results				Complications
				Outcome Measures	*Intervention*	*Control*	*p*	
North et al (2005)[25,]	FBSS	• SCS + CMM • Reoperation + CMM	N=60 n at 6 mo=49	6 mo (SCS vs. reoperation)				17% device-related complications (infections, hardware technical problems)
				• Success (50% pain relief and patient satisfaction)	39%	12%	.04	
				• Stable or decreased opioids	87%	58%	.025	
				• No difference in ADLs impairment due to pain	•			
Kumar et al (2007, 2008)[26,27,]	FBSS with neuropathic pain	• SCS + CMM • CMM	N=100 n at 6 mo=93	6 mo (SCS vs. CMM)				32% device-related complications (electrode migration, infection, loss of paresthesia)
				• 50% reduction in VAS leg pain	48%	9%	<.001	
				• SF-36, favoring SCS all domains except RP	•		≤.02	
				• ODI score	45	56	<.001	
				• Opioid use	56%	70%	.21	
				• NSAID use	34%	50%	.14	
			n at 24 mo=87	24 mo (SCS vs. CMM)				
				• 50% reduction in leg pain on VAS	37%	2%	.003	

Study	Population	Interventions	N at Baseline and Follow-Up	Results			Complications
Kemler et al (2000, 2004, 2008)[28,29,30,]	CRPS	• SCS + PT • PT	N=54 n at 6 mo=54	6 mo (SCS vs. PT)			• 25% device-related complications (dural puncture, infection, unsatisfactory placement of electrode, defective lead) • 42% reoperation rate by 5 y
•				• Reduction in VAS pain score	2.4	0.2	<.001
				• Much improved GPE	39%	6%	.01
				• No difference in functional outcomes or HRQOL	•		
				2 y (SCS vs. PT)			
				• Reduction in VAS pain score	2.1	0.0	<.001
				• Much improved GPE	43%	6%	.001
			n at 5 y=44	5 y (SCS vs. PT)			
				• Reduction in VAS pain score	1.7	1.0	.25
Slangen et al (2014)[31,]Zuidema et al (2022)[35,]	Diabetic neuropathy of LEs	• SCS • CMM	N=36 n at 6 mo=36	6 mo (SCS vs. CMM)			2 SAEs (1 infection, 1 post-dural puncture headache ending in death)
				• Success (50% reduction in pain for 4 d or at least much improved on patient-reported global impression of change)	59%	7%	<.01
				• Reduction in pain medication	32%	0%	
				• No differences in health utility or HRQOL	•		
			n at 24 mo=17[a]	2 y (SCS only)			
				• Success	65%		
				• No improvement in	•		

Study	Population	Interventions	N at Baseline and Follow-Up	Results			Complications
				health utility vs. baseline			
				• ~5-point improvement in SF-36 PCS score vs. baseline	•		
			n at 8 to 10 yrs=19 [a]	8 to 10 years (SCS only)			
				• >50% reduction in VAS pain score, daytime	26%		
				• No improvement in health utility or quality of life vs. baseline	•		
De Vos et al (2014)[32]; Duarte et al (2016)[33],	Diabetic neuropathy of LEs	• SCS • CMM	N=60 n at 6 mo=54	6 mo (SCS vs. CMM)			18% device-related complications (infection, pain due to pulse generator or migration of lead, unsatisfactory placement of electrode)
				• 50% reduction in pain	62.5%	5%	<.001
				• Reduction in analgesic intake (MQS score)	2.9	-0.09	NR
				• Change in health utility	0.39	0.00	<.05
Rigoard P (2019)[34],	FBSS	• SCS + CMM • CMM	N=218 n at 6 mo=116	6 mo (SCS vs. CMM)			18% device-related complications, with 12% requiring surgical re-intervention
				• 50% reduction in pain	14%	5%	.04
				• Change in SF-36 Short Form	7.5	0	<.001

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

36: 36-Item Short-Form Health Survey; VAS: visual analog scale.
[a] SCS only.

Uncontrolled studies

Because RCT data are available for spinal cord stimulation, uncontrolled studies are discussed if they add information not available from the RCTs (eg, 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. [36,] 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 between January 2013 and November 2021 and were permanently implanted with a commercially available spinal cord stimulation (SCS) system were included in analysis (N=1289). The mean (standard deviation) age at enrollment was 58 (14) years and 57% were women. Participants reported duration of chronic pain of 12 (11) years. Study follow-up visits occurred at 6, 12, 24 and 36 months. Ninety-eight participants (8%) required an explant (annualized explant rate of 3.5%); 32 of the explants were due to inadequate pain relief. High lead impedance (5%) and lead migration/movement (5%) were the most common complications. Thirty-two serious adverse events (SAEs) related to device and 51 SAEs related to procedure were reported; device-related implant site infection (11 events) and procedure-related implant site infection (17 events) were the most common SAEs. There were 5 SAEs related to implant site pain, 3 device- or procedure-related neurological deficits, and 2 life-threatening local infections (implant site infection, meningitis). No deaths were reported.

Mekhail et al (2011) retrospectively reviewed 707 patients treated with SCS between 2000 and 2005.[37,] Patients' diagnoses included CRPS (n=345 [49%]), failed back surgery syndrome (n=235 [33%]), peripheral vascular disease (n=20 [3%]), visceral pain in the chest, abdomen, or pelvis (n=37 [5%]), and peripheral neuropathy (n=70 [10%]). Mean follow-up across studies was 3 years (range, 3 months to 7 years). A total of 527 (36%) of the 707 patients eventually underwent permanent implantation of an SCS device. Hardware-related complications included lead migration in 119 (23%) of 527 patients, lead connection failure in 50 (9.5%) patients, and lead break in 33 (6%) patients. Revisions or replacements corrected the hardware problems. The authors noted that rates of hardware failure have decreased due to advances in SCS technology. Documented infection occurred in 32 (6%) of 527 patients with implants; there were 22 cases of deep infection, and 18 patients had abscesses. There was no significant difference in the infection rate by diagnosis. All cases of infection were managed by device removal.

Standard Spinal Cord Stimulation With Burst

Systematic Reviews

Hou et al (2016) published a systematic review of burst spinal cord stimulation for the treatment of chronic back and limb pain.[38,] Reviewers identified 5 studies of burst spinal cord stimulation in patients with intractable chronic pain of more than 3 months in duration who had failed conservative treatment. Three studies, with sample sizes of 12, 15, and 20, respectively, used randomized crossover designs to compare burst stimulation with tonic stimulation; 2 studies also included a placebo stimulation intervention. Also, there were 2 case series with sample sizes of 22 and 48 patients, respectively. Data were collected after 1 to 2 weeks of treatment. Study findings were not pooled. Using the American Academy of Neurology criteria, reviewers originally rated 4 studies as class III and 1 study as class IV. However, given the small sample sizes and short duration of follow-up of the 4 studies, all were downgraded to class IV. Overall, the level of confidence in the evidence on burst spinal cord stimulation for treating chronic pain without paresthesia was rated as "very low."

Randomized Controlled Trials

Six crossover RCTs with a total of 199 patients (range, 12 to 100 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)[39,40,] enrolled patients with neuropathic pain, the trial by Schu et al (2014)[41,] enrolled patients with failed back surgery syndrome, Kriek et al (2017)[42,] enrolled patients with CRPS, Deer et al

(2018)[43,] 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.[44,] All trials compared burst stimulation with spinal cord stimulation. Schu et al (2014), De Ridder et al (2013), Kriek et al (2017), and Eldabe et al (2020) also compared burst with a sham stimulation group. Schu et al (2014) and Eldabe et al (2020) included patients receiving standard spinal cord stimulation while De Ridder et al (2010, 2013) and Deer et al (2018) included patients not previously treated with spinal cord stimulation. It was not clear in Kriek et al (2017) whether patients had previously received spinal cord stimulation. Results were reported for 1 week of stimulation in Schu et al (2014) and De Ridder et al (2013), after 2, 1-hour sessions of spinal cord stimulation or burst in De Ridder et al (2010), after 2 weeks of stimulation in Kriek et al (2017) and Eldabe et al (2020), and after 12 weeks of stimulation in Deer et al (2018). All trials reported reductions in absolute pain scores (numeric rating scale or VAS). Schu et al (2014) and De Ridder et al (2013) did not account for their crossover designs in data analyses, so analyses and p values are incorrect and not reported in Table 4. De Ridder et al (2010) did not provide between-group comparisons. Kriek et al (2017) reported only per-protocol analyses. Four trials reported numerically larger reductions in pain scores with burst than with spinal cord stimulation; Kriek et al (2017) did not report less pain for spinal cord stimulation at any frequency compared with burst. In Kriek et al (2017), 48% of patients preferred the 40-Hz spinal cord stimulation compared with 21%, 14%, 14%, and 3% that preferred 500-Hz spinal cord stimulation, 1200-Hz spinal cord stimulation, and burst and sham, respectively. In Eldabe et al (2020), the mean reduction in pain with 500-Hz spinal cord stimulation was significantly greater than that seen with sham (25%; 95% confidence interval [CI], 8% to 38%; p=.008) or burst (28%; 95% CI, 13% to 41%; p=.002), with no significant differences in pain visual analog score for burst versus sham (p=.59). The interpretation of 5 of the trials was limited by small sample sizes, short follow-up, and incorrect, inadequate, or missing statistical analyses.
The largest trial of burst stimulation is the Success Using Neuromodulation with BURST (SUNBURST) trial reported by Deer et al (2018).[43,] SUNBURST was a 12-week, multicenter, randomized, unblinded, crossover, noninferiority trial evaluating traditional spinal cord stimulation or burst stimulation in 100 patients with chronic pain of the trunk and/or limbs enrolled between January 2014 and May 2015.

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

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

Study	Population	Interventions	N at Baseline and FU	Results				Complications
3×3 crossover design without washout				Outcome Measure	Burst	SCS	Sham	
Schu et al (2014)[41],	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)[39],	Neuropathic limb pain	• Burst stimulation • SCS • No stimulation (sham-control)	N=15 n=15	1 wk (burst vs. SCS vs. sham)[a]				Not reported
				• Mean improvement in VAS scores o Back pain	3.8	2.2	1.4	
				• o Limb pain	3.9	3.9	0.9	
2×2 crossover								
De Ridder et al (2010)[40],	Neuropathic pain	• Burst stimulation • SCS	N=12 n=unclear	Two 1-h sessions (burst vs. SCS)[b]				Not reported
				• Mean improvement in VAS scores o Axial pain	5.3	1.8		
				• o Limb pain	7.3	4.4		
				• Improvement in SF-MPQ	16.7	8.6		

Study	Population	Interventions	N at Baseline and FU	Results				Complications
				sensory scores				
				• Improvement in SF-MPQ affective scores	6.7	4.3		
Deer et al (2018)[43,]	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 (noninferiority) p<.001			
				• Responder (≥30% improvement in VAS score)	60%	51%		
5×5 crossover								
Kriek et al (2017)[42,]	CRPS	• Burst stimulation • SCS 40 Hz • SCS 500 Hz • SCS 1200 Hz • No stimulation (sham-control)	N=33 n=29	2 wk (burst vs. SCS at 40, 500, and 1200 Hz vs. sham)				No SAEs reported; 3 electrodes became dislodged; 2 patients reported itching
				• Mean VAS scores at end of period	48	40[c]	64	
				• Mean global perceived effect (7-point scale where 7 [very satisfied] to 1 [not at all satisfied])	4.7	5.3[c]	3.5	

Study	Population	Interventions	N at Baseline and FU	Results				Complications
3×3 crossover design with washout								
Eldabe et al (2020)[44,]	Chronic back and leg pain	• Burst stimulation • SCS 500 Hz • Sham	N=19 n=16	2 wk treatment phase (burst vs. SCS at 500 Hz vs. sham); each treatment phase included a washout of 9 days				Increased pain was the most commonly reported adverse event at each treatment phase
				• Pain intensity: geometric mean pain VAS	5.4	3.8	5.1	

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.
[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 spinal cord stimulation 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 heterogeneous regarding patient populations and participants were unblinded (no trials used sham surgeries or devices) but they consistently reported reductions in pain, with clinically and statistically significant effect sizes and reductions in medication use for at least 6 months. Even with a sham-controlled surgery or device, blinded outcomes assessment may not be feasible for spinal cord stimulation because active spinal cord stimulation is associated with paresthesias. Given the extensive treatment effects with consistent findings across studies, this evidence suggests that spinal cord stimulation is a reasonable treatment option.

The evidence for standard spinal cord stimulation 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 spinal cord stimulation or burst stimulation in 100 patients with chronic pain of the trunk and/or limbs. The burst was noninferior to spinal cord stimulation 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 spinal cord stimulation and burst at the end of the 24-week crossover portion of the trial, while 7% were satisfied with spinal cord stimulation but not burst and 10% were satisfied with burst but not spinal cord stimulation. However, more patients (70.8%) reported preferring burst stimulation over spinal cord stimulation after the 24-week crossover.

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

Clinical Context and Therapy Purpose

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

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

Populations

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

Interventions

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

Comparators

The following practice is currently being used to treat patients with treatment-refractory chronic pain of the trunk or limbs: standard spinal cord stimulation, 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.[3,] 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).[4,5,]

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.

Review of Evidence

Systematic Reviews

Bicket et al (2016) published a systematic review of controlled trials on high-frequency spinal cord stimulation.[45,] Reviewers searched for RCTs and controlled nonrandomized studies of adults with pain for at least 3 months who were treated with high-frequency spinal cord stimulation (ie, ≥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][46,]) was not rated as having a high-risk of bias in any domain, and the other (Kapural et al [2015][47,]) 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 (ie, study findings were not pooled).

Randomized Controlled Trials

Six RCTs identified addressed high-frequency spinal cord stimulation (Table 5): Perruchoud et al (2013)[46,] compared high-frequency spinal cord stimulation (5000 Hz) with sham-control in a crossover design (N=40), Petersen et al (2021)[48,] compared high-frequency spinal cord stimulation plus medical management with medical management alone, while Kapural et al (2015)[47,] (N=198), Bolash et al (2019) (N=99), [49,]and De Andres et al (2017)[50,] (N=60) compared high-frequency spinal cord stimulation (10000 Hz) with standard spinal cord stimulation. All 6 trials are summarized in Table 5. The trials with N>100 are described individually.

Petersen et al (2021)[48,] randomized 216 participants with painful diabetic neuropathy (baseline lower limb VAS ≥5 cm on a 10 cm scale) refractory to prior pharmacological treatment to high-frequency spinal cord stimulation plus conventional medical management (n=113) versus conventional medical management alone (n=103). All participants were randomized to high-frequency spinal cord stimulation and underwent a trial stimulation period. Participants were eligible for permanent implantation of the stimulation device if at least 50% pain relief was achieved during the trial period. Participants remained in their randomized groups for 6 months, after which time they were eligible to crossover to the other group in the event of inadequate pain relief. The addition of high-frequency spinal cord stimulation to conventional medical management was associated with significantly improved pain scores at 6 month follow-up (Table 5). Results from 12-month follow-up were consistent in finding a significant pain benefit for high-frequency spinal cord stimulation plus medical management versus medical management alone.[51,] Limitations of the study include a lack of blinding for participants and investigators.

Kapural et al (2015, 2016)[47,52,] included 198 patients with chronic leg and back pain who had received conventional medical management but not spinal cord stimulation. Kapural et al (2015) included an active, but unblinded, comparator (standard spinal cord stimulation) and included a trial spinal cord stimulation period up to 2 weeks post-randomization after which only responders continued with stimulation. Outcomes were reported after 3, 12, and 24 months of treatment. The response in the standard spinal cord stimulation group was similar to previous trials of spinal cord stimulation, between 45% and 50% for back pain and 50% to 55% for leg pain at 3, 12, and 24 months. The response was clinically and statistically significantly higher with high-frequency spinal cord stimulation than with spinal cord stimulation for both back (range, »75% to 85%) and leg pain (range, »70% to 85%) at all time points. A limitation of the Kapural et al (2015, 2016) trial was that nonresponders during the stimulation trial period were excluded from statistical analysis. Instead, assuming patients who were not implanted were nonresponders corresponds to response rates at 3 months of about 75% in high-frequency spinal cord stimulation and 37% in spinal cord stimulation for back pain and 74% and 46% for leg pain (calculated, data not shown).

Kapural et al (2022)[53,] enrolled 159 individuals with nonsurgical refractory back pain, defined as patients with chronic back pain refractory to conventional medical management (CMM) who have no history of spine surgery and are not acceptable candidates for spine surgery, who were randomized in a 1:1 ratio to CMM with and without high-frequency (10-kHz) SCS (HFSCS) from September 2018 to January 2020. Conventional medical management was generally consistent with clinical guidelines. Participants randomized to HFSCS received trial stimulation of up to 14 days. Follow-up visits were completed at 1, 3, 6, 9, and 12 months. The median age was between 53 and 58 years and median time from diagnosis was 8 years. Eighty-one percent of CMM + HFSCS participants versus 1% of CMM participants were responders (primary outcome, ≥ 50% pain relief) at 3 months (p<.001) and 80%

versus 3% were responders at 6 months (p<.001). The study was not blinded and nonresponders during the stimulation period were excluded from further analysis.

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

Study	Population	Interventions	N at Baseline and Follow-Up	Results				Complications
				Outcome Measure	*Int*	*Ctrl*	*p*	
Perruchoud et al (2013)[46,]	Chronic low back pain radiating in 1 or both legs; previously treated with SCS	• HFSCS • Sham • 2×2 crossover design with conventional SCS before both arms	N=40 n=33	2 wk (HFSCS vs. sham)				One patient had malaise attributed to a vasovagal attack
				• Responder (at least minimal improvement on patient-reported global impression of change)	42%	30%	.30	
				• VAS score	4.35	4.26	.82	
				• Health utility	0.48	0.46	.78	
Petersen et al (2021)[48,]; Petersen et al (2022)[54,]	Painful diabetic neuropathy	• HFSCS + medical management • Medical management	N=216 n at 6 mo=187	6 mo (HFSCS + medical management vs. medical management)				• SAEs, 12% vs. 0% • Wound complications (dehiscence, impaired healing, or infection): 6% vs. 0%
•				Responder (proportion with ≥50% change in VAS without a meaningful worsening of baseline neurological deficits)	86%	5%	<.0001	
				Remitter (proportion with pain VAS ≤3 cm for 6 consecutive months)	60%	1%	<.001	

Study	Population	Interventions	N at Baseline and Follow-Up	Results			Complications
				Quality of life (EQ-5D-5L Index, mean change from baseline)	0.130 (SD 0.159)	-0.031 (SD 0.127)	<.001
		Originally assigned to HFSCS and crossovers to HFSCS combined	n=104 HFSCS and n=77 crossovers to HFSCS	12 mo (HFSCS + crossovers to HFSCS)			
				Responder (proportion with ≥50% change in VAS)	85%		
				Quality of life (EQ-5D-5L Index, mean change from baseline)	0.14 (95% CI, 0.10 to 0.17)		
Kapural et al (2015, 2016)[47,52,]	Chronic back and leg pain	• HFSCS • SCS	N=198 n at 3 mo=171 n at 24 mo=156	3 mo (HFSCS vs. SCS)			Stimulation discomfort, 0% vs. 47% No stimulated-rated SAEs or neurologic deficits
•				Responder (≥50% back pain reduction with no stimulation-related neurologic deficit): Back pain	85%	44%	<.001
				Leg pain	83%	55%	<.001
			n at 12 mo=171	12 mo (HFSCS vs. SCS)			
				Responders Back pain	80%	50%	NR
				Leg pain	80%	56%	NR
				Decreased opioid use	36%	26%	.41
				Improvement in ODI score	16.5	13.0	NR
				24 mo (HFSCS vs. SCS)			
				Responders o Back pain	77%	49%	<.001
				o Leg pain	73%	49%	<.001
De Andes	FBSS	• HFSCS • SCS	N=60 n=55 analyzed	12 mo (HFSCS vs. SCS)			

Study	Population	Interventions	N at Baseline and Follow-Up	Results			Complications
et al (2017)[50],							
				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)[49],	FBSS	• HFSCS SCS	N=99 n=72 analyzed	6 mo (HFSCS vs SCS)			
				Responder (≥50% reduction VAS for back pain)	92%	82%	Noninferiority <.001
				Remission (VAS for back pain of ≤25 mm)	84%	47%	
Kapural et al (2022)[53],	Nonsurgical refractory back pain	• HFSCS + medical management • Medical management	N=159 n=143 analyzed	3 mo (HFSCS+medical management vs medical management)			
				Responder (≥ 50% pain relief)	81%	1%	<.001
				Mean change in EQ-5D-5L score (SD)	0.21 (0.14)	0.004 (0.02)	<.001
			n=140	6 mo (HFSCS+medical management vs medical management)			
				Responder (≥ 50% pain relief)	80%	3%	<.001
				Mean change in EQ-5D-5L score (SD)	0.21 (0.13)	-0.04 (0.14)	<.001

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

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. [55,] 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<.001) and the mean Oswestry Disability Index score decreased from 53 to 20 (p<.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 spinal cord stimulation consists of a systematic review, RCTs, and a case series. Two RCTs that enrolled participants not previously treated with spinal cord stimulation reported clinically and statistically significant benefits associated with HFSCS. A crossover RCT enrolling patients with pain despite previous treatment with spinal cord stimulation reported no difference between HFSCS and sham stimulation. However, interpretation of this trial is limited due to the significant period effect.

Dorsal Root Ganglion Neurostimulation for Refractory Chronic Trunk or Limb Pain

Clinical Context and Therapy Purpose

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

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

Populations

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

Interventions

The therapy being considered is dorsal root ganglion neurostimulation. Dorsal root ganglion uses the same epidural approach technique as spinal cord stimulation but targets a different anatomical target, the dorsal root ganglion. Dorsal root ganglia consist of sensory cell bodies that transmit input from the peripheral nervous system to the central nervous system and play a role in neuropathic pain perception. Dorsal root ganglia are located in the epidural space between spinal nerves and the spinal cord on the posterior root in a minimal amount of cerebrospinal fluid, amenable to epidural access.

Comparators

The following practice is currently being used to treat patients with treatment-refractory chronic pain of the trunk or limbs: standard spinal cord stimulation, 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.[3,] 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).[4,5,]

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

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

Review of Evidence

Dorsal Root Ganglion Implanted Device

Systematic Reviews

Several systematic reviews of dorsal root ganglion devices have been published: Vuka et al (2019), [56,] Deer et al (2020), [57,] Monan et al (2021), [58,]and D'Souza et al (2022).[59,] The reviews all include one RCT (ACCURATE) and several observational studies. The RCT is described in the following section.

Randomized Controlled Trial

The ACCURATE study (NCT01923285) compared dorsal root ganglion neurostimulation with standard spinal cord stimulation.[60,61,] As reported by Deer et al (2017), eligibility criteria for this multicenter, unblinded, noninferiority trial included chronic (≥6 months) intractable (failed ≥2 drugs from different classes) neuropathic pain of the lower limbs associated with a diagnosis of CRPS or causalgia and no previous neurostimulation. Patients were randomized to dorsal root ganglion stimulation with the Axium device or standard spinal cord stimulation. Patients first underwent a temporary trial of stimulation lasting 3 to 30 days, depending on the protocol at each site. Patients who had a 50% or greater reduction in lower limb pain after the temporary trial were eligible for permanent stimulation. Those who failed temporary stimulation exited the trial but were included in the analysis as treatment failures. Trial characteristics are shown in Table 6.

A total of 152 patients were randomized, and 115 (n=61 dorsal root ganglion, n=54 spinal cord stimulation) had a successful temporary trial and continued to permanent implantation. The primary outcome was a composite measure of treatment success. Success was defined as (1) a 50% or greater reduction in VAS score and (2) no stimulation-related neurologic deficits. The noninferiority margin was set at 10%. Results are shown in Table 7. No patients experienced neurologic deficits in either group. Regarding paresthesias, at 3 months and 12 months, spinal cord stimulation patients were significantly more likely to report paresthesias in nonpainful areas than dorsal root ganglion patients. At 3 months, 84.7% of dorsal root ganglion patients and 65% of spinal cord stimulation patients reported paresthesias only in their painful areas; at 12 months, these percentages were 94.5% and 61.2%, respectively. Limitations in study relevance, design, and conduct are shown in Tables 8 and 9. Mekhail et al (2019) conducted a sub-analysis on the patients receiving dorsal root ganglion neurostimulation in the ACCURATE study, to evaluate the occurrence and risk factors for paresthesia.[62,] Among the 61 patients with dorsal root ganglion implants, the rates of paresthesia at 1 month, 3 months, 6 months, 9 months, and 12 months were 84%, 84%, 66%, 62%, and 62%, respectively. The patients who were paresthesia-free reported similar or better outcomes for pain and quality of life. Risk factors for paresthesia occurrence included higher stimulation amplitudes and frequencies, number of implanted leads, and younger age.

Table 6. RCT Characteristics of DRG Implanted Devices

					Interventions	
Study	**Countries**	**Sites**	**Dates**	**Participants**	**DRG**	**SCS**
Deer et al (2017)[61,]; ACCURATE (NCT01923285)	U.S.	22	2013-2016	• CRPS or causal lower extremities • Chronic pain (6 mo)	AXIUM Neurostimulator System (n=76)	RestoreUltra and RestoreSensor (n=76)

		Interventions
		• Stimulation-naïve • Failed ≥2 pharmacologic treatments

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

Table 7. RCT Results of DRG Implanted Devices

Study	≥50% Reduction in VAS Scores for Pain	Physical Functioning	Emotional Functioning	Quality of Life		Safety
		Mean BPI Interference	*POMS Total Score*	*SF-36 PCS*	*SF-36 MCS*	*SAEs*
Deer et al (2017)[61,]						
At 3 months						
n	139	113	NR	113	113	NR
DRG	81%	4.2	NR	11.8	8.3	
SCS	56%	3.0	NR	9.4	4.8	
TE (95% CI) (p)	NR (noninferiority p<.001; superiority p<.001)	1.1 (0.2 to 2.1) (<.05 favoring DRG)	NR (.04 favoring DRG)	2.5 (-0.7 to 5.7)	3.5 (-0.5 to 7.5)	
At 12 months						
n	132	105	NR	105	105	152
DRG	74%	3.9	»18	11.5	6.2	11%
SCS	53%	2.6	»8	8.0	3.6	15%
TE (95% CI) (p)	NR (noninferiority p<.001; superiority p<.001)	1.3 (0.2 to 2.3)(<.05 favoring DRG)	NR (<.001)	3.5 (-0.1 to 7.1)(.04 favoring DRG)	2.6 (-1.9 to 7.1)	NR (.62)

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

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

Study	Population	Intervention	Comparator	Outcomes	Follow-Up
Deer et al (2017)[61,]					

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

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

Study	Allocation	Blinding	Selective Reporting	Follow-Up	Power	Statistical
Deer et al (2017)[61,]		1, 2. Patients and study staff not blinded. Outcomes mostly patient reported which could lead to bias. However, an active control (SCS) was used.				4. Treatment effects not reported for some outcomes but p values reported

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

Observational Studies

Because RCT data are available for dorsal root ganglion neurostimulation, observational studies are discussed if they add information not available from the RCTs (e.g., longer follow-up including adverse events, data on an important subgroup, etc). Deer et al (2019) compared the safety and complaint records from the manufacturers of dorsal root ganglion neurostimulation (n=500+) and spinal cord stimulation (n=2000+) devices, from April 2016 through March 2018.[63,] 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.[64,] 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).[65,] This study included patients with failed back surgery syndrome who had chronic intractable neuropathic pain of the

trunk and/or lower limbs. Five patients participated in phase 1 of the study (device not anchored), and 6 additional patients participated in phase 2 (device anchored). During phase 1, the device migrated more than was recommended and thus it was anchored in the remaining patients. Baseline VAS scores were 5 or higher in all patients. Seven (63%) of the 11 patients reported good to excellent overall pain relief (VAS score reduction, ≥50%), 2 patients reported fair overall intensity pain relief (25% to 50% reduction), and 2 patients reported poor or no overall pain relief (0% to 25%). No adverse events were reported.

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

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

Spinal Cord Stimulation for Critical Limb Ischemia

Clinical Context and Therapy Purpose

The purpose of spinal cord stimulation in individuals who have critical limb ischemia is to provide a treatment option that is an alternative to or an improvement on existing therapies.
The following PICO was used to select literature to inform this review.

Populations

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

Interventions

The therapy being considered is spinal cord stimulation. Spinal cord stimulation 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. Spinal cord stimulation 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 spinal cord stimulation 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. Spinal cord stimulation 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.[3,] 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).[4,5,]

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

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

Review of Evidence

Systematic Reviews

An updated Cochrane review by Ubbink and Vermeulen (2013) assessed the use of spinal cord stimulation in peripheral vascular diseases.[66,] Reviewers included RCTs and non-RCTs evaluating the efficacy of spinal cord stimulation in adults with non-reconstructable, chronic critical leg ischemia. Six trials were identified; all were conducted in Europe and 5 were single-country studies. Spinal cord stimulation was compared with other nonsurgical interventions. One study was not randomized, and none were blinded. In a pooled analysis of data from all 6 studies, there was a significantly higher rate of limb survival in the spinal cord stimulation group than in the control group at 12 months (relative risk [RR], 0.75; 95% CI, 0.57 to 0.95;absolute risk difference, -0.11; 95% CI, -0.20 to -0.02). The 11% difference in the rate of limb salvage means that 9 patients would need to be treated to prevent 1 additional amputation (95% CI, 5 to 50 patients). However, when the nonrandomized study was excluded, the difference in the rate of amputation no longer differed significantly between groups (RR, 0.78; 95% CI, 0.58 to 1.04; absolute risk difference, -0.09; 95% CI, -0.19 to 0.01). The spinal cord stimulation patients required significantly fewer analgesics, and more patients reached Fontaine stage II (intermittent claudication) than in the control group. There was no difference in ulcer healing (but only 2 studies were included in this analysis). In the 6 trials, 31 (15%) of 210 patients had a change in stimulation requiring intervention, 8 (4%) experienced the end of battery life, and 6 (3%) infections required device removal.

Previously, Klomp et al (2009) published a meta-analysis of RCTs that used spinal cord stimulation to treat patients with critical limb ischemia.[67,] The same 5 RCTs identified in the Cochrane review were included. Reviewers did not find a statistically significant difference in the rate of amputation in the treatment or control groups. The RR of amputation was 0.79 (95% CI, 0.59 to 1.06), with a risk difference of -0.07 (95% CI, -0.17 to 0.03). Reviewers also conducted additional analyses of data from their 1999 RCT to identify factors associated with better or worse prognoses.[68,] They found that patients with ischemic skin lesions had a higher risk of amputation than patients with other risk factors. There were no significant interactions between this and any other prognostic factor. The analyses did not identify subgroups of patients who might benefit from spinal cord stimulation.
A systematic review of non-revascularization-based treatments by Abu Dabrh et al (2015) for patients with critical limb ischemia included spinal cord stimulation as 1 of the treatments. The review identified 5 RCTs for inclusion.[69,] In the pooled analysis, reviewers found that spinal cord stimulation was associated with reduced risk of amputation (odds ratio [OR], 0.53; 95% CI, 0.36 to 0.79); risk difference was not reported.

Section Summary: Critical Limb Ischemia

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

Spinal Cord Stimulation for Selected Other Medical Conditions

Clinical Context and Therapy Purpose

The purpose of spinal cord stimulation 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 review.

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 spinal cord stimulation. Spinal cord stimulation 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. Spinal cord stimulation 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 spinal cord stimulation 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.[3,] 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).[4,5,]

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

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

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

Review of Evidence

Refractory Angina Pectoris

Systematic Reviews

Pan et al (2017) identified 12 RCTs that evaluated spinal cord stimulation versus control in patients with refractory angina pectoris.[70,] 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).[71,] It included 9 RCTs evaluating spinal cord stimulation for refractory angina: 7 compared spinal cord stimulation with low or no stimulation and 2 compared spinal cord stimulation with alternative medical or surgical therapy for angina. Reviewers found that most RCTs were small and variable in quality based on modified Jadad criteria. Reviewers reported: "2 of the RCTs were of high quality (Jadad score 4); 2 were of low quality (Jadad score 1), and the remaining ones were of intermediate quality (Jadad score 2 to 3)." Most trials comparing spinal cord stimulation with low or no stimulation found improvements in outcomes with spinal cord stimulation; however, given limitations in the evidence base, reviewers concluded that larger multicenter RCTs would be needed to assess the efficacy of spinal cord stimulation for angina.

Randomized Controlled Trials

Two of the largest RCTs included in the systematic reviews were Zipes et al (2012)[72,] and Lanza et al (2011).[73,]

Zipes et al (2012) published an industry-sponsored, single-blind, multicenter trial with sites in the United States and Canada.[72,] This trial was terminated early because interim analysis by the data and safety monitoring board found the treatment futile. A total of 118 patients with severe angina, despite maximal medical treatment, were enrolled. Of the 118 patients, 71 (60%) underwent spinal cord stimulation implantation with the Intrel III neurostimulator (Medtronic). The remaining 47 patients did not meet eligibility criteria post-enrollment or had other issues (e.g., withdrew consent).

The investigators had originally been planning to randomize up to 310 patients but enrollment was slow. Implantation was successful in 68 patients; this group was randomized to high-stimulation (n=32) or a low-stimulation control (n=36). The low-stimulation control was designed so that patients would feel paresthesia but the effect of stimulation would be subtherapeutic. The primary outcome was a composite of major adverse cardiac events, which included death from any cause, acute myocardial infarction, or revascularization through 6 months. Fifty-eight (85%) of 68 patients contributed data to the 6-month analysis; analysis was by intention-to-treat. The proportion of patients experiencing major adverse cardiac events at 6 months did not differ significantly between groups (12.6% in the high-stimulation group vs. 14.6% in the low-stimulation group; p=.81). The trial sample size was small, and it might have been underpowered for clinically meaningful differences.

A controlled trial from Italy by Lanza et al (2011) randomized 25 patients to 1 of 3 treatment groups: spinal cord stimulation with standard stimulation (n=10), spinal cord stimulation with low-level stimulation (75% to 80% of the sensory threshold) (n=7), or very low-intensity spinal cord stimulation (n=8).[73,] Thus, patients in groups 2 and 3 were unable to feel sensation during stimulation. After a protocol adjustment at 1 month, patients in the very low-intensity group were re-randomized to 1 of the other groups of which there were 13 patients in the standard stimulation group and 12 patients in the low-level stimulation group. At the 3-month follow-up (2 months after re-randomization), there were statistically significant between-group differences in 1 of 12 outcome variables. There was a median of 22 angina episodes in the standard stimulation group and 10 in the low-level stimulation

group (p=.002). Nonsignificant variables included the use of nitroglycerin, quality of life, VAS score, Canadian Cardiovascular Society angina class, exercise-induced angina, and scores on 5 subscales of the Seattle Angina Questionnaire.

Uncontrolled studies

Because RCT data are available for spinal cord stimulation, uncontrolled studies are discussed if they add information not available from the RCTs (e.g., longer follow-up including adverse events, data on an important subgroup, etc). Lanza et al (2012) reviewed observational studies on spinal cord stimulation in patients with refractory angina pectoris.[74,] 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 (ie, electrode dislodgement or fracture requiring repositioning) or internal programmable generator failure during substitution. Lead issues were reported by 10 studies (N=450 patients). In these studies, 55 cases of lead or internal programmable generator failure were reported. No fatalities related to spinal cord stimulation treatment were reported.

Section Summary: Refractory Angina Pectoris

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

Heart Failure

Randomized Controlled Trials

Findings of a small pilot crossover RCT evaluating spinal cord stimulation for heart failure were published by Torre-Amione et al (2014).[75,] 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 spinal cord stimulation 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 1 of the events in the composite endpoint. The events occurred in 2 patients while the device was turned on and in 2 while it was turned off. One patient died about 2 months after implantation with the device turned off. The spinal cord stimulation devices did not interfere with the functioning of implantable cardioverter defibrillators.

Zipes et al (2016) reported on the results of Determining the Feasibility of Spinal Cord Neuromodulation for the Treatment of Chronic Heart Failure (DEFEAT-HF) study, a prospective, multicenter, single-blind RCT 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.[76,] Sixty-six patients were implanted with a spinal cord stimulation and randomized 3:2 to spinal cord stimulation on (n=42) or spinal cord stimulation 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=.30). Other endpoints related to heart failure hospitalization and heart failure-related quality of life scores and symptoms did not differ significantly between groups. After completion of the 6-month randomization period, all subjects received active spinal cord stimulation. From baseline to 12-month follow-up, there were no significant treatment effects in the overall patient population for echocardiographic parameters (p=.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 spinal cord stimulation for heart failure.

Section Summary: Heart Failure

Two RCTs have evaluated spinal cord stimulation 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 spinal cord stimulation for the treatment of cancer-related pain in adults.[77,] Reviewers did not identify any RCTs evaluating the efficacy of spinal cord stimulation in this population. Four case series using a before-after design (N=92 patients) were identified. Peng et al (2015) updated this review, finding no new studies meeting inclusion criteria identified.[78,] They concluded: "Current evidence is insufficient to establish the role of spinal cord stimulation in treating refractory cancer-related pain."

Section Summary: Cancer-Related Pain

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

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, the evidence includes systematic reviews and randomized controlled trials (RCTs). Relevant outcomes are symptoms, functional outcomes, quality of life, 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 spinal cord stimulation. Systematic reviews have supported the use of spinal cord stimulation 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 spinal cord stimulation, the evidence includes a systematic review and 4 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 spinal cord stimulation reported clinically and statistically significant benefits associated with high-frequency spinal cord stimulation. Another RCT in patients who had chronic pain despite previous treatment with standard spinal cord stimulation 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 spinal cord stimulation 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 neurostimulation, the evidence includes a systematic review, an RCT, and case series. Relevant outcomes are symptoms, functional outcomes, quality of life, medication use, and treatment-related morbidity. The unblinded RCT found that patients receiving dorsal root ganglion neurostimulation had significantly higher rates of treatment success (physical functioning score and quality of life measures), at 3 and 12 months compared with those receiving standard spinal cord stimulation devices. Dorsal root ganglion neurostimulation was found to be noninferior to spinal cord stimulation in the percentage achieving $\geq$50% pain reduction, emotional functioning score, and 36-Item Short-Form Health Survey scores. Both groups experienced paresthesias but patients in the

dorsal root ganglion group reported less postural variation in paresthesia and reduced extraneous stimulation in nonpainful areas. Rates of serious adverse events were similar between the 2 study arms. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Critical Limb Ischemia

For individuals who have critical limb ischemia who receive spinal cord stimulation, 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, spinal cord stimulation was associated with a lower risk of amputation versus control, but results were not consistently statistically significant due to differences in methodologies. 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 spinal cord stimulation, 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 spinal cord stimulation 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 spinal cord stimulation, 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 spinal cord stimulation, the evidence includes case series. Relevant outcomes are symptoms, functional outcomes, medication use, and treatment-related morbidity. No RCTs evaluating spinal cord stimulation in this population were identified. The evidence is insufficient to determine that the technology results in an improvement in the net health outcomes.

Supplemental Information

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

Practice Guidelines and Position Statements

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

American Association of Clinical Endocrinology

In 2022, the American Association of Clinical Endocrinology published evidence-based recommendations for the care of individuals with diabetes mellitus.[79,]. 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 for the management of chronic spinal pain.[80,] The guidelines included a statement that there is fair evidence for the following recommendation for spinal cord stimulation: "spinal cord stimulation is indicated in chronic low back pain with lower extremity pain secondary to failed back surgery syndrome, after exhausting multiple conservative and interventional modalities".

American Society of Pain and Neuroscience

The American Society of Pain and Neuroscience issued a comprehensive guideline in 2021 on the management of cancer-related pain.[81,] The guideline found that spinal cord stimulation 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.[82,] 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 (ie, 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. [83,] The guidelines make the following recommendations for spinal cord stimulation:

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

Recommendation	Grade	Level of evidence	Level of certainty of net benefit
Following lumbar surgery	A	I-A	Strong
Treatment of non-surgical low back pain	B	I-C	Moderate
Treatment of lumbar spinal stenosis	C	I-C	Moderate

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.[84,] The Association issued recommendations on spinal cord stimulation, considered weak due to the amount and consistency of the evidence. The recommendations supported the use of spinal cord stimulation for failed back surgery syndrome and CRPS (Table 11). In regards to high-frequency stimulation and dorsal root ganglion 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, the 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 dorsal root ganglion stimulation for the treatment of chronic pain syndromes.[85,] 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 United States Preventive Services Task Force criteria. Table 12 summarizes the consensus recommendations on the use of dorsal root ganglion stimulation. Additional recommendations on the dorsal root ganglion stimulation procedure are provided in the publication.

Table 12. NACC Consensus Recommendations for the Use of DRG 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

In 2008, NICE issued guidance on spinal cord stimulation for chronic pain of neuropathic or ischemic origin, which was reaffirmed in 2014.[86,] The NICE recommended spinal cord stimulation as a treatment option for adults with chronic pain of neuropathic origin (measuring at least 50 mm on a 0 to 100 mm visual analog scale) that continues for at least 6 months despite appropriate conventional

medical management, and who have had a successful trial of stimulation as part of an assessment by a specialist team.
In the same guidance, the NICE stated that spinal cord stimulation was not recommended for chronic pain of ischemic origin except in the context of research.

U.S. Preventive Services Task Force Recommendations
Not applicable.

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."[87,]

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this review are listed in Table 13.

Table 13. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
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
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
NCT03318172	High-Density Spinal Cord Stimulation for the Treatment of Chronic Intractable Pain Patients: A Prospective Multicenter Randomized Controlled, Double-blind, Crossover Exploratory Study With 6-m Open Follow-up	100	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	28	Sep 2021

NCT No.	Trial Name	Planned Enrollment	Completion Date
	Failed Back Surgery Syndrome (FBSS) Patients After a 32-contact Surgical Lead Implantation		

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

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Documentation for Clinical Review

Please provide the following documentation:

- History and physical and/or consultation notes including:
  - o Reason for spinal cord stimulation
  - o Description/type of pain
  - o Previous treatment(s) and response(s)
  - o Multidisciplinary evaluation
  - o Results of temporary implanted electrode trial if done
  - o Prior procedure report(s)

Post Service (in addition to the above, please include the following):

- Procedure report(s)

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	63650	Percutaneous implantation of neurostimulator electrode array, epidural
	63655	Laminectomy for implantation of neurostimulator electrodes, plate/paddle, epidural
	63661	Removal of spinal neurostimulator electrode percutaneous array(s), including fluoroscopy, when performed
	63662	Removal of spinal neurostimulator electrode plate/paddle(s) placed via laminotomy or laminectomy, including fluoroscopy, when performed
	63663	Revision including replacement, when performed, of spinal neurostimulator electrode percutaneous array(s), including fluoroscopy, when performed
	63664	Revision including replacement, when performed, of spinal neurostimulator electrode plate/paddle(s) placed via laminotomy or laminectomy, including fluoroscopy, when performed
	63685	Insertion or replacement of spinal neurostimulator pulse generator or receiver, direct or inductive coupling
	63688	Revision or removal of implanted spinal neurostimulator pulse generator or receiver
	95970	Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, pulse duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple or

Type	Code	Description
		complex brain, spinal cord, or peripheral (i.e., cranial nerve, peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, without reprogramming
	95971	Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, pulse duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple spinal cord, or peripheral (i.e., peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming
	95972	Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, pulse duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); complex spinal cord, or peripheral (i.e., peripheral nerve, sacral nerve, neuromuscular) (except cranial nerve) neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming
HCPCS	C1767	Generator, neurostimulator (implantable), nonrechargeable
	C1778	Lead, neurostimulator (implantable)
	C1787	Patient programmer, neurostimulator
	C1820	Generator, neurostimulator (implantable), with rechargeable battery and charging system
	C1822	Generator, neurostimulator (implantable), high frequency, with rechargeable battery and charging system
	C1883	Adaptor/extension, pacing lead or neurostimulator lead (implantable)
	C1897	Lead, neurostimulator test kit (implantable)
	L8679	Implantable neurostimulator, pulse generator, any type
	L8680	Implantable neurostimulator electrode, each
	L8685	Implantable neurostimulator pulse generator, single array, rechargeable, includes extension
	L8686	Implantable neurostimulator pulse generator, single array, nonrechargeable, includes extension
	L8687	Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension
	L8688	Implantable neurostimulator pulse generator, dual array, nonrechargeable, includes extension

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
10/01/2010	BCBSA Medical Policy adoption
10/29/2010	Coding Update
12/15/2014	Policy revision with position change effective 2/15/2015
02/15/2015	Policy revision with position change
04/30/2015	Policy revision without position change
02/01/2016	Coding update
06/01/2016	Policy revision without position change

Effective Date	Action
06/01/2017	Policy revision with position change
09/01/2017	Policy title change from Spinal Cord Stimulation Policy revision without position change
06/01/2018	Policy revision without position change
06/01/2019	Policy revision without position change
07/01/2023	Policy reactivated. Previously archived from 06/01/2020 to 06/30/2023.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must

be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT	
BEFORE	**AFTER** **Blue font: Verbiage Changes/Additions**
Reactivated Policy **Policy Statement:** N/A	**Spinal Cord and Dorsal Root Ganglion Stimulation 7.01.25** **Policy Statement:** I. Spinal cord stimulation with standard or high-frequency stimulation 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 performed according to policy guidelines. II. Dorsal root ganglion neurostimulation is 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 performed according to policy guidelines. III. Spinal cord stimulation is considered **investigational** in all other situations including, but not limited to, treatment of critical limb ischemia to forestall amputation and treatment of refractory angina pectoris, heart failure, and cancer-related pain.